# IS CONVENTIONAL SUGAR-FREE CHEWING GUM EFFECTIVE IN THE MANAGEMENT OF ORTHODONTIC PAIN ASSOCIATED WITH FIXED APPLIANCES?

## A RANDOMISED CLINICAL TRIAL COMPARING THE PAIN-REDUCING EFFECTS OF SUGAR-FREE CHEWING GUM VERSUS A PLACEBO MEDICAMENT


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A research thesis submitted in partial fulfilment of the requirements for the degree Master of Science in Dentistry in the discipline of Orthodontics to the Faculty of Dentistry, University of the Western Cape

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**KEYWORDS**

Conventional sugar-free chewing gum

Placebo medicament

Placebo effect

Gender

Orthodontic pain

Consort guidelines

Visual Analogue Scale

Non- steroidal anti- inflammatory drugs

Conventional brackets

Self -ligating brackets

# ABSTRACT

**IS CONVENTIONAL SUGAR-FREE CHEWING GUM EFFECTIVE IN THE MANAGEMENT OF ORTHODONTIC PAIN ASSOCIATED WITH FIXED APPLIANCES? A RANDOMISED CLINICAL TRIAL COMPARING THE PAIN-REDUCING EFFECTS OF SUGAR-FREE CHEWING GUM VERSUS A PLACEBO MEDICAMENT**

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**Background and aim:** Managing orthodontic pain traditionally involves the prescription of non-steroidal anti-inflammatory drugs combined with other analgesic medication. Sugar-free chewing gum has been advocated in the control of orthodontic pain due to its mechanical and physiological effects on periodontal tissue; however, the literature is scant. The 'placebo effect' that conventional sugar-free chewing gum may have in the relief of orthodontic pain has not been documented. The aim of this study was to compare the effectiveness of conventional sugar-free chewing gum in reducing orthodontic pain associated with fixed appliances with a placebo (sugar-free sweets) medicament.

**Objectives:** The objectives of the study were to determine if there were differences in pain reporting between the sugar-free chewing gum and the placebo, to ascertain whether gender influenced pain scores and to observe any differences in pain reporting between different orthodontic techniques.

**Method:** In this double-blinded randomised clinical trial, 60 participants comprising 36 females and 24 males with a mean age of 14.82 years (SD 4.02) were randomly assigned to two intervention groups, the conventional sugar-free chewing gum group and the placebo group. The study was conducted across three practice groups: two specialist orthodontic practices and one general dental practice. Each site had ten participants who received the experimental medicament and ten participants who received the placebo medicament (n = 20 per practice). Participants were asked to chew gum or to suck sweets at 4 hours, 8 hours, 24 hours,

and 48 hours following the placement of a fixed appliance. Participants recorded their pain scores at these time intervals using a 10-point visual analogue scale. Repeated measures ANOVA was used to compare the difference in mean pain scores between the two intervention groups, between gender (male and female) and between orthodontic techniques used (MBT™ and Damon$^{TM}$). Post-hoc testing with pairwise comparison further assessed the accuracy of where any differences occurred.

**Results:** All 60 participants completed the questionnaire. The mean pain score decreased with time in both the chewing gum group and the placebo group. Repeated measures ANOVA and pairwise comparison showed significantly lower mean pain scores in the chewing gum group at 48 hours ($p<0.001$) than in the placebo group. In addition, the male participants showed significantly lower mean pain scores at 48 hours ($p<0.001$) than the female participants. Mean pain scores among the different orthodontic techniques / bracket systems groups decreased similarly with time. There was no statistical difference between the specific systems used during the study.

**Conclusion:** Both conventional sugar-free chewing gum and the placebo medicament were effective in reducing orthodontic pain over time. However, at 48 hours, chewing gum significantly reduced pain compared with the placebo. This is most likely due to the combined physiological and 'placebo effect' of conventional chewing gum. Male participants showed significantly lower mean pain scores after 48 hours. There was no difference between the different orthodontic systems in reducing orthodontic pain.

July 2020

# DECLARATION

I, Yolin Govender, declare that the thesis *Is Conventional Sugar-Free Chewing Gum Effective in the Management of Orthodontic Pain Associated with Fixed Appliances? A Randomised Clinical Trial Comparing The Pain-Reducing Effects Of Sugar-Free Chewing Gum Versus A Placebo Medicament* is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

Full name: Yolin Govender Date: 2020/07/06

Signed.....

# ACKNOWLEDGEMENTS

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To Lydia Searle: Thank you for the editing services and making sure the document followed University of the Western Cape guidelines.

# DEDICATION

This work is dedicated to my beautiful son,

Aaric Nikhil Govender

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# DEFINITIONS

**Arch wires:** In orthodontic therapy, an archwire is a long, thin and flexible metal wire inserted into orthodontic brackets and bands and ligated along the dental arch through slots in brackets to control tooth movement

**Damon brackets:** A self-ligating orthodontic bracket system that is fitted in the same way as traditional brackets; however, the system uses a slide and lock mechanism that attaches wires to brackets with more freedom of movement and, therefore, less friction in the slot.

**Edgewise brackets:** A bracket system that uses light,continuous forces, lacebacks and bendbacks. It was designed to work ideally with sliding mechanics. The archwire can be ligated to the bracket with an elastic or metal ligature.

**Fixed orthodontic appliances:** A mechanical device cemented to teeth or attached by other adhesive materials for changing the relative positions of teeth. The device cannot be removed by the patient during treatment.

**Medicament:** A substance used for medical treatment. In this study, it refers to the experimental medicament of conventional sugar-free chewing gum and to the placebo medicament of sugar-free sweets.

**Sugar-free chewing gum:** A conventional (unmedicated), commercial chewing gum that does not contain sugar and is usually sweetened with a sugar-like substitute.

**Sugar-free sweets:** Sweets that contain no sugar and are usually sweetened with a sugar-like substitute.

**Placebo:** An inert substance or treatment that is designed to have no therapeutic value.

**Placebo effect:** An effect (usually beneficial) produced by a placebo medicament or treatment that cannot be linked to the properties of the placebo itself and must, therefore, be due to the patient's belief in that treatment. Aspects of positive and negative placebo effects are discussed in more detail in the thesis.

**Variable:** An element, feature or factor that is liable to vary or change. For the purposes of this study, the variables are age, gender, orthodontic system (MBT™ and Damon™), medicaments (sugar-free chewing gum, sugar-free sweets), pain scores and time. Further explanations are presented in Chapter 3.

**Visual analogue scale (VAS):** A measurement tool that attempts to measure a characteristic, perception or attitude that is believed to range across a continuum of values and that cannot easily be directly measured. In response to a VAS item, respondents specify and document their level of agreement to a statement by indicating a position along a continuous line between two end-points. In this study, VAS was used to determine pain scores.

**Non-steroidal anti-inflammatory drugs (NSAIDs):** Agents of a drug group that reduces pain, decreases fever, prevents blood clots and in higher doses, decreases inflammation. The term non-steroidal distinguishes these drugs from typical steroids, which while having similar eicosanoid-depressing, anti-inflammatory actions have a broad range of other effects. Side effects of NSAIDs depend on the specific drug but largely include an increased risk of gastrointestinal ulcers, bleeding, and kidney disease.

# LIST OF ABBREVIATIONS

| | |
|---|---|
| ACC | Anterior cingulate cortex |
| ANOVA | Analysis of variance |
| ASIC3 | Acid-sensing ion channel |
| BMREC | Biomedical Research Ethics Committee |
| CGRP | Calcitonin gene-related peptide |
| CONSORT | Consolidated Standards of Reporting Trials |
| IASP | International Association for the Study of Pain |
| IL | Interleukin |
| IQR | Interquartile range |
| MBT | McLaughlin Bennet Trevisi (bracket system) |
| NiTi | Nickel titanium (arch wire) |
| NSAIDs | Non-steroidal anti-inflammatory drugs |
| PET | Positron emission tomography |
| PPT | Pressure pain threshold |
| RCT | Randomised clinical trial |
| SD | Standard deviation |
| SLB | Self-ligating bracket |
| SP | Substance P |
| TNF | Tissue necrosis factor |
| TENS | Transcutaneous electrical nerve stimulation |
| VAS | Visual analogue scale |

# CHAPTER 1: CONTEXT

## 1.1 Background and rationale

Orthodontics is a sub-discipline of dentistry, which aims to optimise function, occlusion, and aesthetics of the maxillo-facial complex through the treatment of malocclusions associated with underlying skeletal and/or dental causes. Fixed orthodontic treatment has been accepted as a predictable (evidence-based) form of treatment for most malocclusions.

Worldwide, the prevalence of malocclusions is high, with Africans showing the highest prevalence of Class 1 malocclusions in the mixed and permanent dentition (Alhammadi, Halboub, Fayed, Labib & El-Saaidi, 2018). The need for orthodontic treatment is unquestionable, yet many factors, including pain, make it a service that is often avoided.

Pain associated with orthodontic treatment has always posed a challenge to the treating orthodontist and dentist. Orthodontic procedures such as separator placement, arch wire insertion and activations, application of orthopaedic forces and even debonding procedures produce pain in patients. Most patients experience mild to moderate pain for the first 24–48 hours following the placement of a fixed orthodontic appliance (Krishnan, 2007). Factors influencing orthodontic pain may include the choice of pain management, the psychological status of the individual undergoing treatment, the gender of the patient and the orthodontic technique / bracket system used.



The advice given by orthodontists for pain management may vary, but it predominantly includes the use of an analgesic medication, a non-steroidal anti-inflammatory drug (NSAID) or a combination of the two (Shedam, 2015). These medications may interfere with physiological bone activity (induction), which is essential in initial tooth movement (Bartzela, Türp, Motschall & Maltha, 2009; Karthi *et al*., 2012). In addition, the use of NSAIDs can have undesirable side effects that may range from mild to severe, and the addictive properties of certain combinations of analgesic medications cannot be excluded (Harirforoosh, Asghar & Jamali, 2013).

The use of sugar-free chewing gum for the relief of orthodontic pain due to its physiological effect on receptors in the periodontium is briefly documented in the

literature. It is hypothesised that chewing gum suppresses nociceptive responses via serotonergic (5-HT) descending inhibitory pathways and thus reduces the initial pain response (Kamiya *et al.*, 2010). Sugar-free chewing gum has the added clinical benefit of improving a patient's oral health condition by increasing salivary flow and thus naturally cleaning teeth, which is essential during orthodontic treatment.

The psychosomatic benefits of chewing gum as a distractor in general pain studies have been demonstrated to some degree (Kamiya *et al.*, 2010; Weijenberg & Lobbezoo, 2015). Unfortunately, there are no published reports that detail both the physiological and the 'placebo-inducing' effects of conventional sugar-free chewing gum in reducing orthodontic pain. The findings of this thesis add value to a new concept of conservative pain management in patients undergoing orthodontic treatment. In addition, other factors influencing orthodontic pain (gender and orthodontic techniques / bracket systems used) were explored to incorporate a holistic approach to these patients.

## 1.2 Problem statement

The management of orthodontic-related pain has largely centred on the use of analgesics and NSAIDs. Studies assessing the efficacy of sugar-free chewing gum in reducing pain scores have only recently been documented, with no published reports in South Africa. There are no studies assessing the role of placebos, 'placebo effects' and combined physiological and placebo effects in orthodontic pain management. The undesirable effects of NSAIDs are well documented, both locally in the oral cavity and systemically with other body functions. A more suitable, biologically friendly aid for pain management that is easily accessible is needed for young orthodontic patients in South Africa.

## 1.3 Research questions

A research question is "an answerable inquiry into a specific issue and is the first active step taken in research" (Kowalczyk, 2013). It must be seen as the foundation upon which one sets up the thesis from the protocol through to the final report. For the purposes of this thesis, the research questions were as follows:

- Can conventional sugar-free chewing gum effectively reduce orthodontic pain associated with fixed appliances?
- Are the pain-reducing effects of conventional sugar-fee chewing gum, physiological, placebo related or a combination of both?

## 1.4 Aim of the study

The study aimed to determine the effects of conventional sugar-free chewing gum in the management of orthodontic pain associated with fixed appliances compared with a placebo medicament (sugar-free sweets).

## 1.5 Objectives of the study

The objectives of the study were as follows:

- To determine if there were differences in the effects and the pain scores over time between the two interventions.
- To explore the role of gender on pain scoring over time.
- To determine if different orthodontic techniques / bracket systems used influenced pain scores over time.



## 1.6 Purpose and significance of the study

Positive 'placebo effects' have been discussed in general pain studies (Weijenberg & Lobbezoo, 2015). However, the literature shows scanty, convoluted information about this 'effect' in orthodontics. It has been hypothesised that chewing gum reduces the initial pain response through a physiological process. It may, however, induce a positive 'placebo effect', making it a valuable medicament in reducing orthodontic pain.

The thesis explores the pain-reducing effects of chewing gum by comparing chewing gum with a placebo medicament and discusses these effects in view of other available orthodontic pain studies. Comparisons between conventional chewing gum and placebo

medicaments have not been documented in South Africa or worldwide to date. Both medicaments (chewing gum and the placebo) potentially reduce pain through endogenous, psychosomatic responses. Analytical comparisons of varying pain responses observed in this study may help understand the effects that conservative and endogenous techniques have on the overall management of orthodontic pain and may lend suggestions when developing a non-invasive, therapeutic protocol for such management.

The combination of positive physiological effects on periodontal tissue to reduce pain together with minimal side effects, good hygiene promotion, low cost and 'placebo inducing effects' may make conventional sugar-free chewing gum a valuable medicament to consider in orthodontic pain management.

## 1.7 Thesis layout

**Chapter 1** describes the background and purpose of the study in addition to its aim, objectives, and its significance.

**Chapter 2** reviews the literature regarding orthodontic pain and current information on sugar-free chewing gum and its use in orthodontics.

**Chapter 3** describes the methodological sequence of how the research was conducted.

**Chapter 4** reports on the findings of the research trial.

**Chapter 5** discusses the current findings and limitations by comparing the results of this study with the available scientific literature.

**Chapter 6** concludes the findings of this thesis and makes recommendations for further exploration.

# CHAPTER 2: LITERATURE REVIEW

## 2.1 Introduction

This chapter introduces the scientific literature regarding orthodontic pain. The search strategy used in this thesis involved computer-based searches of the databases Mendeley, MEDLINE, PubMed Central and the Cochrane Library in addition to a review of well-respected scientific textbooks for physiology- and neurochemistry-related topics. The search was repeated throughout the study and aimed at retrieving information to understand orthodontic pain and the current management.

Orthodontic pain is not well documented, and there are no current publications regarding the combined physiological and 'placebo effect' of conventional sugar-free chewing gum in reducing this pain. As such, there were no limitations regarding the year of publication in the thesis exploratory exercise. Key terms used in the search included pain, factors influencing pain, orthodontic pain, managing orthodontic pain, use of chewing gum in orthodontic treatment, the 'placebo effect', endogenous relief of pain, and the effects of different techniques and bracket systems on orthodontic pain.

The reference lists of sources identified in the process were also scanned to reveal further information relating to the field of orthodontic pain. Likewise, recommendations by Mendeley subscription formed part of the exploratory and review process.

To review the efficacy of conventional sugar-free chewing gum on orthodontic pain management, it was initially important to understand the mechanisms involved in the general pain process and to have a thorough appreciation of orthodontic pain and its related physiology. Therefore, the factors influencing orthodontic pain, namely gender, age, orthodontic techniques used and endogenous mechanisms for pain relief (including the 'placebo effect') were also reviewed. Additionally, a detailed inquiry into the various management strategies for this specific type of pain was critical if the thesis were to recommend conventional sugar-free chewing gum as the medicament of choice.

## 2.2 Definition of pain

Pain, as defined by the International Association for the Study of Pain (International Association for the Study of Pain [IASP], 1994), is: "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or is described in terms of such damage. The reporting of pain in the absence of tissue damage or any likely pathophysiological causes usually occurs for psychological reasons. There is usually no way to distinguish the latter experience of pain from pain due to tissue damage. Thus, if an experience is regarded as pain, and if it is reported in the same way as pain caused by tissue damage, it should be accepted as pain" (IASP, 1994).

## 2.3 Neural pathway of facial pain

There are numerous free nerve endings in the craniofacial region that act as nociceptors, which are sensory organs that respond to the noxious (painful) stimulation of peripheral tissues. The activation of these sensory organs results in the excitation of the associated afferent nerve fibres and provide sensory-discriminative information to the brain about the location, intensity, quality, and duration of the noxious stimulus. A number of neurochemicals (e.g. substance P [SP] and 5-HT) are involved in the activation of these peripheral endings by noxious stimulation (Dubner, 1990).

The afferent nerve fibres receiving pain signals in the facial region project to the trigeminal cranial nerve complex in the brainstem (see Figure 2.1) where the sub nucleus caudalis is seen as the main brainstem relay site of trigeminal nociceptive (pain-related) information (Long *et al.*, 2016).

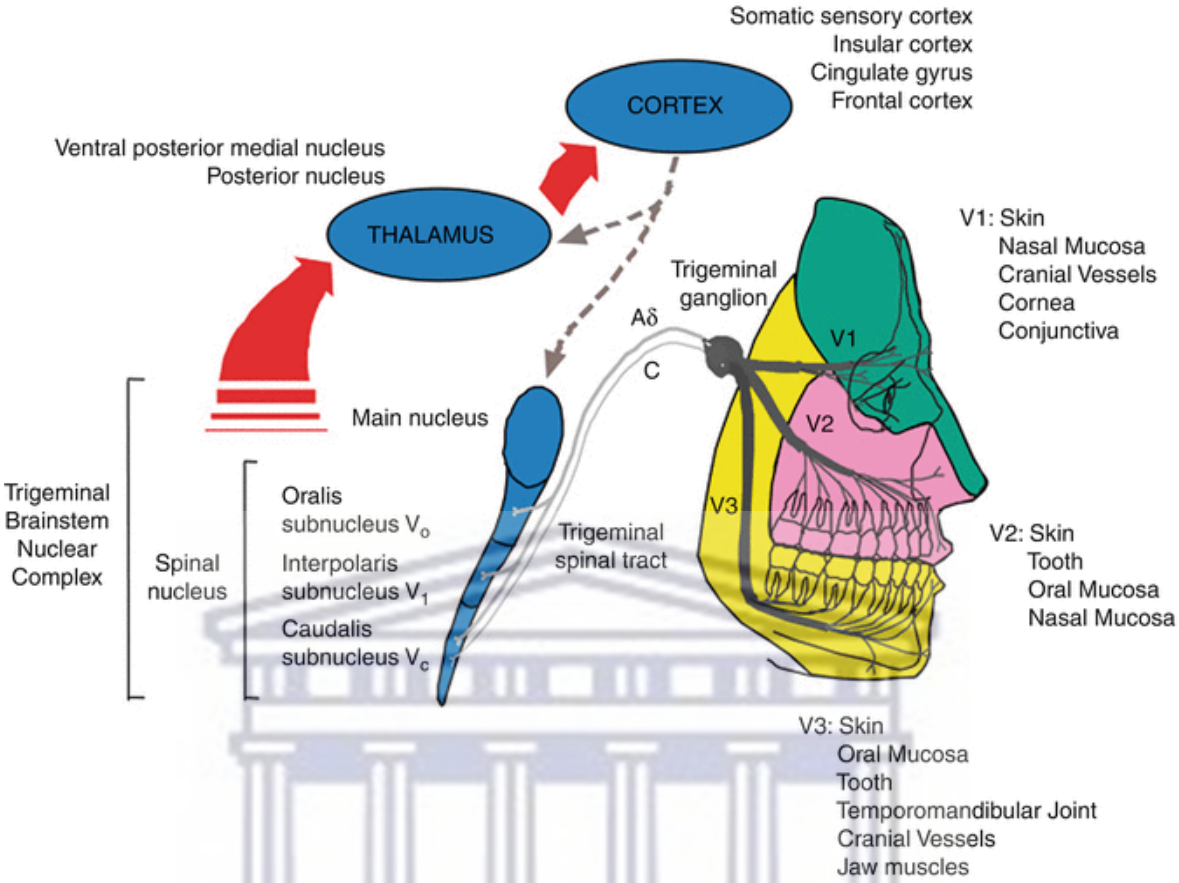


**Figure 2.1: Illustration showing neural processing of facial pain via the trigeminal pathway**

Source: Hu & Woda, 2013



Neurones from all levels of the trigeminal brainstem complex project to various regions of the brain, including the thalamus, reticular formation, and the cerebral cortex. As such, the sensation of pain can be modified according to perception, sensory discrimination and motivational influence (Scadding, 2011).

## 2.4 Introduction to orthodontic pain

Orthodontic pain refers to a dull sensation with hypersensitivity in affected teeth; it is understood and explained as tooth discomfort induced by orthodontic tooth movement. Forces exerted by orthodontic appliances on teeth initially activate sensory receptors in periodontal tissues, generating a cascade of nociceptive pain processes with transduction in both the peripheral and central nervous system (Krishnan, 2007).

Orthodontic pain can be experienced during almost all treatment procedures, including the placement of separators, banding, initial wire engagement, the wearing of elastics, rapid maxillary expansion and even debonding procedures. It has been well documented that orthodontic pain begins 4–12 hours after applying orthodontic force, peaks at 24 hours and gradually diminishes 3–7 days thereafter, returning to baseline levels after one month (Long *et al.*, 2016).

Although orthodontic pain subsides in most patients within a week following orthodontic treatments, in the study of Bergius, Kiliaridis and Berggren (2000), more than 40% of the adolescent patients reported orthodontic pain after one week, indicating a potentially longer duration of orthodontic pain.

The central processing of pain was discussed in Section 2.3: Neural pathway of facial pain. Information on the peripheral response to orthodontic forces is presented in the following section.

## 2.5 Biology/mechanism of orthodontic pain

Once force is applied to a tooth, the root is displaced towards the alveolar bone with the periodontium between (see Figure 2.2). With the resulting vascular compression and local ischaemia, periodontal cells, mainly fibroblasts, undergo anaerobic respiration, causing local acidosis. The proton ion ($H^+$) generated by this acidosis binds to acid-sensing ion channel 3 (ASIC3) receptors on sensory nerve endings and pain is generated. As ischaemia progresses, neutrophils and monocytes (leukocytes) are recruited by chemotaxins released by mast cells and fibroblasts. Leucocytes release abundant inflammatory mediators such as bradykinin and prostaglandin in addition to the cytokine's interleukin 1 (IL-1) and tissue necrosis factor (TNF) (Long *et al.*, 2016).

Bradykinin and prostaglandin adhere to sensory endings and generate painful sensations. The cytokines released significantly amplify local inflammation and stimulate monocyte-derived macrophages to become involved in alveolar bone remodelling. At the same time, sensory endings release various neurogenic mediators such as calcitonin gene-related

peptide (CGRP) and SP that dilate local blood vessels and enhance local inflammation, thereby amplifying local pain and alveolar remodelling (Long *et al.*, 2016).

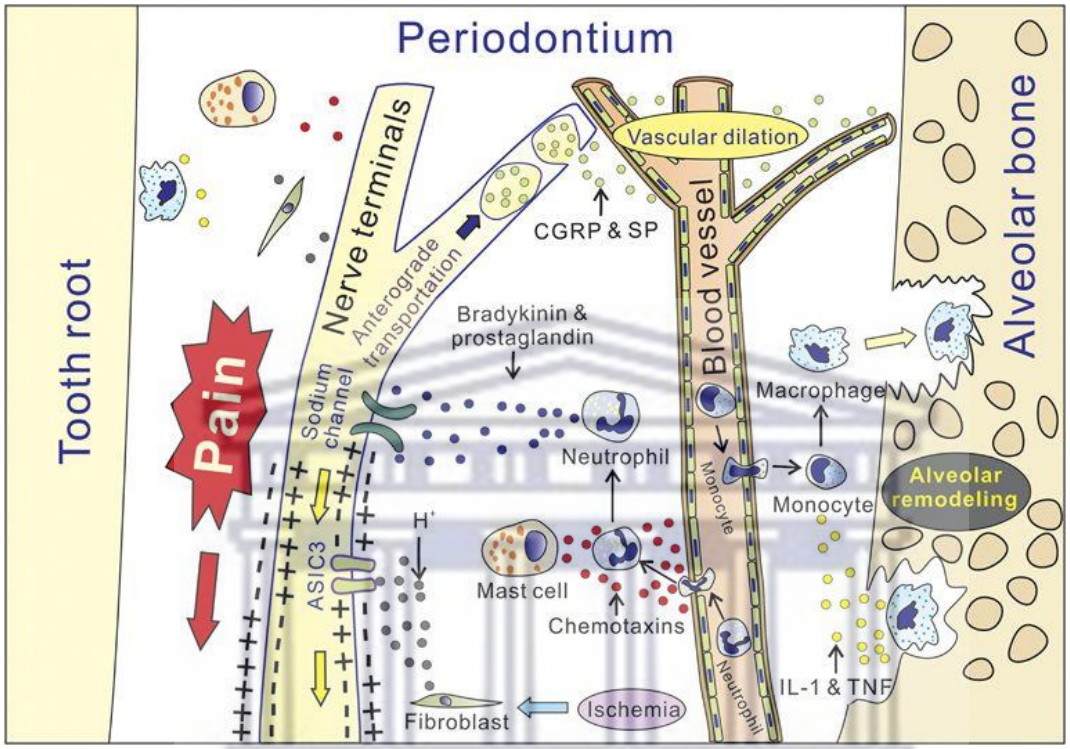


**Figure 2.2: Illustration showing local response to orthodontic force applied to a tooth**

Source: Long *et al.*, 2016

## 2.6 Factors that influence pain perception in the orthodontic patient

The complexity of pain makes pain difficult to score and often, results are yielded based on the perception of pain rather than a physical, reproducible measurement. Investigations using brain imaging and mapping during painful stimulation aim to quantify or categorise this sensory information, but this method is still a field in progress. These experiments also focus on how pain can be modulated and desensitised in various parts of the brain. Numerous factors such as the psychological state of the person may in fact alter and influence the perceived intensity of pain (Bantick *et al.*, 2002).

There are common baseline variables that possibly influence the way pain is perceived, irrespective of the psychological state of the person undergoing orthodontic treatment.

These variables include gender, age and orthodontic techniques used in fixed orthodontic treatment. As such, the literature was scanned appropriately and is discussed below.

### *2.6.1 Gender*

Studies investigating gender and pain perception have shown robust interest and growth in the last decade. A systematic review of the literature published by the American Pain Society in 2009 notes some interesting evidence that indicates that women are at substantially greater risk for many clinical pain-related conditions. In addition, there is the suggestion that post-operative and procedure related pain may be more severe among women than among men, including greater pain sensitivity in females than in males for most pain modalities. Findings regarding gender differences in laboratory measures of endogenous pain modulation are mixed, as are findings from studies using functional brain imaging to ascertain sex differences in pain-related cerebral activation. There is, in addition, inconsistent data regarding sex differences in responses to pharmacologic and non-pharmacologic pain treatments (Fillingim, King, Ribeiro-Dasilva, Rahim-Williams & Riley III, 2009).

A review published in the *Journal of Orofacial Pain* in 2000 (Dao & LeResche, 2000) reveals that females receive substantially more treatment for pain-related conditions than males and indicates that females often report more 'severe pain', more 'frequent pain', and pain of longer duration than males (Dao & LeResche, 2000). Furthermore, laboratory studies investigating gender differences in pain perception through experimentally induced pain appear to show definite sex disparity; females generally show lower pain thresholds and tolerance than males. There is, however, little consensus on whether these differences reflect the way males and females respond to pain, the differing social rules for the expression of pain, or the biologic differences in the way noxious stimuli are processed (Dao & LeResche, 2000).

Orthodontic pain is often described as a 'pressure-related pain', and the literature was, therefore, scanned for any disclosure on gender differences in pressure pain. A study in 2003 looked at quantifying the magnitude of putative gender differences in experimental pressure pain threshold (PPT) with the use of a pressure algometer (Chesterton, Barlas,

Foster, Baxter & Wright, 2003). The investigation found that healthy females exhibited a significantly lower mean PPT calculated from repeated measurements of 14 PPTs over a one-hour period (Chesterton *et al.*, 2003).

A systematic review conducted over a ten-year period (between 1998 and 2008) analysed 172 published articles regarding gender differences on pain perception ((Racine *et al.*, 2012). These studies largely involved laboratory-induced pressure, thermal, ischaemic, muscle, chemical, electrical, and visceral pain in healthy subjects. The findings of the review suggest that females and males have comparable thresholds for cold and ischaemic-type pain, while PPTs are generally lower in females (Racine *et al.*, 2012).

### *2.6.2 Age*

There is some debate in the literature about whether age affects the perception of pain. The occurrence of physiological alteration in the processing of pain forms the basis of this argument in which ageing may be associated with changes in pain perception, including chronic pain occurrence and pain-threshold modification (Eltumi & Tashani, 2017).

Ageing can be described as: "A dynamic process in which there are changes and compensations in the structure and function of different physiological and psychological components, including the anatomical structures that are involved in the sensation of pain" (Hedden & Gabrieli, 2004).

With increased life expectancy and demographic changes, a thorough inspection of pain perception and its relationship with age is deemed necessary. Although biopsychosocial studies on age-related changes in pain perception have been conducted for more than 70 years, meta-analyses are still uncommon. A recent meta-analysis aimed to quantify evidence on age-related changes in pain perception was categorised by pain thresholds and pain tolerance thresholds in young and older healthy adults (Lautenbacher, Peters, Heesen, Scheel & Kunz, 2017). The review involving searches on PubMed, Google Scholar and PsycINFO incorporated 31 studies on pain threshold and 9 studies assessing pain tolerance threshold. The review found that pain threshold increases with age. In

contrast, pain tolerance thresholds did not show substantial age-related changes. The study concluded that ageing reduces pain sensitivity for lower pain intensities (Lautenbacher *et al.*, 2017).

A recent investigation that examined the influence of gender and age on orthodontic pain among adolescents included 115 subjects with a mean age of 14.9 years (SD1.90) (Sandhu & Leckie, 2016). The sample population comprised 56 boys and 59 girls. Orthodontic separators were inserted in the mesial and distal contacts of the maxillary and mandibular first molars. A 100-mm VAS was used for pain assessment at specified time intervals. The study revealed that 12–15-year-old boys reported the lowest mean average pain intensity and the least subjective variation. In contrast, 15–18-year-old girls experienced the highest mean pain intensity and the most daily fluctuations in pain intensity. The 12–15-year-old girls were the most varied in their overall pain experience (Sandhu & Leckie, 2016).

### *2.6.3 Choice of orthodontic technique / bracket system*

Fleming, Dibiase, Sarri and Lee (2009) assert that pain and discomfort are common after the insertion of an initial arch wire during orthodontic treatment, as reported at some stage during treatment by 91% of their patients. The level of pain reported after arch wire placement is believed to be greater and more prolonged than that following extraction of teeth (Fleming *et al.*, 2009).

Although pain may arise during various orthodontic procedures, it is noted that fixed appliances produce more pain than removable or functional appliances where there is little correlation between applied force magnitude and pain experienced (Krishnan, 2007).

Numerous brackets and techniques are used in orthodontic treatment, and some practitioners align themselves with a specific system or philosophy in their practice. The articles reviewed for this subsection of the thesis concentrated on methods utilising traditional ligation (MBT™, Edgewise brackets) and self-ligation (Damon™ brackets) as a means of understanding the treatment systems used during this randomised clinical trial (RCT).

The MBT™ bracket prescription introduced in 1997 established itself as one of the most popular bracket prescriptions on the market. The main differences from other bracket prescriptions are the increased palatal and lingual torques of the upper and lower incisors respectively and a decreased torque of the upper canines when compared with other popular bracket systems (Moesi, Dyer & Benson, 2013).

Self-ligating brackets (SLBs) claim to have advantages over conventional appliance systems due to their supposed ability to reduce frictional resistance, overall treatment time and subjective pain and discomfort (Miles, 2009). The use of SLBs has increased exponentially; retrospective studies showed 42% of American practitioners in 2008 reported using at least one SLB system in their practice compared with under 9% in 2002 (Fleming & Johal, 2010).

A prospective trial using a split-mouth technique for ligation techniques (half the mouth had conventional MBT™ twin brackets and elastic ligatures and the other half had self-ligating Damon™ 2 brackets) compared variables at different time intervals. The study showed that compared with the conventional brackets, participants initially reported less pain with the Damon™ 2 brackets but significantly more pain when engaged with a thicker wire (0.016 nickel titanium [NiTi]) ten weeks later (Miles, Weyant & Rustveld, 2006).

A RCT compared pain scores of patients treated with SmartClip™ SLBs versus Victory MBT™ conventional brackets (Fleming *et al.*, 2009). The scores reported in this study using visual analogue scales (VASes) were at the specified time intervals of 4 hours, 24 hours (maximum pain), 72 hours, 7 days and at arch wire changes (with rectangular wires) later in the treatment. Initially, the conclusion was that subjective pain experienced was independent of bracket type. However, insertion and removal of rectangular arch wires at later appointments resulted in an enhanced pain experience with the SmartClip™ passive self-ligating appliance that was statistically significant (Fleming *et al.*, 2009).

A systematic review by the same authors looked at studies comparing SLBs with conventional MBT brackets (Fleming & Johal, 2010).

Articles that reviewed pain differences between the bracket systems were discussed based on study design, methodology and outcomes. Pain scores at four time intervals were

extracted from each study to facilitate this. Pain intensity over the first seven days was reported in three studies involving 160 patients, with 83 patients in the SLB group and 77 patients in the conventional bracket group. Patients in the SLB group reported a lower mean difference in pain intensity than the conventional bracket group, where the greatest difference was reported after three days following appliance placement. The differences were not statistically significant. Furthermore, both studies reported greater pain experience during chairside manipulation of self-ligating appliances at later appointments (Fleming *et al.*, 2009), (Fleming & Johal, 2010).

A similar study comparing SmartClip™ SLBs with Victory™ Edgewise brackets that was published in the journal, *The Angle Orthodontist* (2016) consisted of 113 participants reporting on pain experienced following the placement of fixed appliances using these bracket systems (Rahman *et al.*, 2016). Subsequent reporting occurred after each wire change. Verbal rating scales were used instead of VAS. The study found that perceived pain was statistically higher with the SmartClip™ self-ligating system than with the conventional Victory™ system, but this difference was not deemed clinically significant. Discomfort was rated the highest after placement of the initial 0.014 NiTi arch wire compared with all subsequent wire changes. Intensity was always greatest on Day 1 after each arch wire change during the course of treatment. Age and gender did not affect the level of discomfort experienced by subjects undergoing fixed appliance treatment (Rahman *et al.*, 2016).

There are speculations whether the size and material of the initial arch wire play significant roles in orthodontic pain. Although the information in the literature is limited, there are studies that report on the general effects associated with various initial arch wires. (Fernandes, Ogaard & Skoglund, 1998), (Jian *et al.*, 2013).

A systematic review that incorporated a search of randomised trials investigated the general effects associated with different arch wires; the variables root resorption, rate of alignment and pain were analysed (Jian *et al.*, 2013). The study comprised a review of nine trials and compared the three variables listed above. The first comparison examined the differences between multistrand stainless steel initial arch wires and super elastic NiTi initial arch wires. There was insufficient evidence of a difference in the rate of alignment and pain between the stainless steel and the NiTi initial arch wires (Jian *et al.*, 2013). The

second comparison considered the differences between conventional (stabilised) NiTi initial arch wires and super elastic NiTi initial arch wires. There was insufficient evidence to indicate any differences between the conventional and the super elastic NiTi initial arch wires. The conclusion of the systematic review was that no reliable evidence exists that indicates a specific initial arch wire material being better than another in regard to speed of alignment, root resorption or pain (Jian *et al.*, 2013).

A study by Fernandes, Ogaard and Skoglund (1998) published in the *Journal of Orofacial Orthopaedics* compared the pain experienced when using a type of super elastic NiTi initial wire with the pain experienced when using a conventional NiTi wire. Assessments of pain were made using VASes. The results showed pain experienced after placement of a super elastic NiTi arch wire was less than after placement of a conventional NiTi arch wire in the first ten hours, although a significant difference was only found at four hours. There were no significant differences reported between gender and pain within different arch wire groups (Fernandes, Ogaard & Skoglund, 1998).

### *2.6.4 'Placebo effects' on pain perception*

The literature supports that perception of pain is reduced when attention is directed away from a noxious stimulation since the psychological state of a person can modulate their pain experience (Bantick *et al.*, 2002).

The anterior cingulate cortex (ACC) in the brain is responsible for a multitude of complex processes and is known for its high concentration of opiate receptors. According to studies using positron emission tomography (PET), these receptors are activated during noxious stimulation, which suggests that cognitive function may in fact modulate the intensity of the pain that is experienced (Turken & Swick, 1999).

A placebo simply refers to an inert substance, but the 'placebo effect' is a "psychobiological phenomenon that can be influenced by different mechanisms, including expectation of clinical improvement" (Benedetti, Mayberg, Wager, Stohler & Zubieta, 2005).

The study of the 'placebo effect' is directly related to how the context of beliefs and values shape brain processes related to perception and emotion and ultimately, mental and physical health (Benedetti, Mayberg, Wager, Stohler & Zubieta, 2005).

The 'effect' may be a 'positive placebo effect', simply called a 'placebo effect'; the patient is given an inert material and their condition/illness improves. In contrast, a 'negative placebo effect', otherwise known as a 'nocebo effect', relates to a patient receiving an inert material whose condition worsens due to anxiogenic mechanisms (Enck, Benedetti & Schedlowski, 2008).

Placebo effects in randomised trials have been a topic of debate due to responses in the placebo arm not always being genuine psychosocial responses to the simulation of treatment but rather reflecting the natural course of a disease, changes in symptoms, regression to the mean, response bias with respect to the patient reporting subjective symptoms and other concurrent treatments. It is, therefore, important to consider placebos and 'placebo effects' as psychobiological phenomena, moving the focus from the 'inert' content of a placebo or sham procedure to what the placebo intervention consisting of a simulated treatment and the surrounding clinical context is actually doing to the patient (Finniss, Kaptchuk, Miller & Benedetti, 2010).

Various studies have focused on the role that 'placebo effects' play in specific gender categories. A meta-analysis focused on pain ratings post third-molar extractions (Averbuch & Katzper, 2001). The results of this study showed post-operative baseline pain was greater in females, and this was statistically significant. Both pain intensity and pain relief scores demonstrated the well-established 'placebo effect' in 10% of the pooled subjects. Over time, the mean pain intensity and pain relief scores for female and male treatment groups were not noticeably different after medication. The study concluded that there was no gender difference in response to a placebo (Averbuch & Katzper, 2001).

The study of Aslaksen, Bystad, Vambheim and Flaten (2011) published in the *Journal of Psychosomatic Medicine* investigated whether placebo medication reduced anticipatory stress, and if this reduction could explain the placebo analgesic response. The study found that there were reports of gender differences in placebo analgesia. The sample comprised 33 participants, 17 of whom were female. The participants were exposed either to pain

with no intervention (natural history) or to painful thermal pulses followed by a placebo. The study found that the men responded with lower stress after placebo medication, and this placebo response to pain was observed in the men only (Aslaksen *et al.*, 2011).

Similar postulations have been made by other researchers, suggesting that males are more suggestive towards placebo manipulation than females. Recommendations for further studies have been put forward. Numerous compounding factors such as gender of the person conducting the investigation and how this person is perceived from a trust point of view in addition to physiological interruptions such as the menstrual cycle, which may affect mood and hormonal influences, have been implicated in why the disparity between gender and 'placebo effects' may exist (Enck, Benedetti & Schedlowski, 2008).

## 2.7 Assessment of orthodontic pain

A study that assessed pain in 109 patients undergoing orthodontic treatment concluded that pain was initially perceived at 2 hours, peaked at 24 hours and subsided by the third day (Ertan Erdinç & Dinçer, 2004)

This is similar to other pain studies and subsequently prompted researchers investigating various pain interventions to assess pain scores initially at 24 hours (Farzanegan, Zebarjad, Alizadeh & Ahrari, 2012).

There are different modalities of assessing orthodontic pain, with the most common tool being a type of VAS. Visual analogue scales are psychometric measuring instruments designed to document the characteristics of disease-related symptoms and severity in individual patients and use this information to achieve a rapid (statistically measurable and reproducible) classification of symptoms, severity, and disease control. Visual analogue scales can also be used in routine patient history taking and to monitor the course of chronic disease (Klismek *et al.*, 2018). Visual analogue scales are a modification of the original Likert scale. The original Likert scale is a series of statements (items) offered for genuine or hypothetical situations under study. Participants are asked to show their level of agreement (from strongly disagree to strongly agree) with given statements

(items) on a metric scale. The statements, in combination, reveal the specific dimension of the attitude towards the issue (Joshi, Kale, Chandel & Pal, 2015).

Visual analogue scales are commonly used in the subjective reporting of pain. A systematic review published in the *Journal of Pain and Symptom Management* reviewed 239 articles using different scales, including visual analogue, numerical rating and verbal rating (Hjermstad *et al.*, 2011). The study found that numerical rating had the most compliance in reporting although VASes are more commonly used. A proposal to include features of both visual and numerical scores in a scale was made for better understanding and reporting (Hjermstad *et al.*, 2011).

Pain may also be assessed using brain imaging techniques. However, the multimodal response to pain and how it is perceived does not necessarily make imaging a more accurate measurement of pain (Bantick *et al.*, 2002). Studies focusing on orthodontic pain have made use of VAS and numerical ratings to quantify the level of discomfort experienced (Long *et al.*, 2016; Waheed-Ul-Hamid, Haq, Mahmood, Azeem & Irfan, 2016; Ireland *et al.*, 2017).

## 2.8 Management of orthodontic pain

Pain experienced during orthodontic treatment is commonly mistaken by professionals as insignificant, yet many orthodontic patients may contact their treating orthodontist for advice regarding pain management. Most orthodontists do not follow a strict protocol for pain management and often recommend a pharmacological agent should the patient report pain. This often leaves pain management decisions to be made by the patient, who is usually an adolescent (Shedam, 2015). Orthodontic pain arises from a periodontal inflammatory response in which ischaemia and oedema in the compressed periodontal ligament space are noted (Furstman & Bernick, 1972; Long *et al.*, 2016). For many years, the prescription of analgesics and NSAIDs have formed the gold standard when dealing with the pain experienced during fixed orthodontic treatment (Krishnan, 2007).

A systematic review by Xiaoting, Yin and Yangxi (2010) examined a series of randomised controlled trials for pain reduction during orthodontic treatment. The search

concluded that anti-inflammatory and traditional pharmaceutical analgesics are still the main treatment modality to reduce orthodontic pain despite their side effects. Certain long-acting NSAIDs and selective cyclooxygenase enzyme (COX-2) inhibitors are recommended for their 'comparatively few' side effects (Xiaoting, Yin & Yangxi, 2010).

The side effects of NSAIDs range from local effects (reduced tooth movement) to systemic effects, including gastrointestinal upset, anti-clotting effects, disturbance in renal function, hypertension, and rashes. This prompted the introduction of non-pharmacological methods such as low-level laser therapy, chewing gum and bite wafers (Doshi-Mehta & Bhad-Patil, 2012; Harirforoosh, Asghar & Jamali, 2013; Dalaie, Hamedi, Kharazifard, Mahdian & Bayat, 2015)

In addition to analgesics and NSAIDs, there have been other suggestions regarding the management of orthodontic pain. A review by Krishnan (2007) investigated the causes and management of pain during orthodontic treatment. The study confirmed that apart from the traditional analgesics, other approaches have been tested to reduce pain. Anaesthetic gels were found to be useful when performing orthodontic procedures such as band cementation, arch wire ligation and band/bracket removal (Krishnan, 2007). Anecdotal reports on other techniques include vibratory stimulation, transcutaneous electrical nerve stimulation (TENS) and low-level laser application. However, the use of vibratory stimulation demonstrated that most participants were unable to tolerate vibrations once discomfort had set in. This led to the recommendation that if vibratory stimulation were employed, it should be used prior to the onset of pain. The use of TENS in reducing periodontal pain after separator placement was effective within six seconds of electrode placement (Krishnan, 2007). As reported by most orthodontic patients, low-level laser therapy was not effective in immediate pain relief. The overall findings indicate that analgesics are still the main treatment modality to reduce orthodontic pain. The recommendations were that further blinded randomised trials were needed to understand the full spectrum of orthodontic pain better when developing protocols for management (Krishnan, 2007).

The use of sugar-free chewing gum in the relief of orthodontic pain has been documented in the literature as a physiologically friendly aid (Fleming *et al.*, 2016). It is hypothesised that chewing gum reduces ischaemia in the periodontal ligament space by mechanical

stretching and relaxing of the periodontal ligament, which suppresses nociceptive responses via serotonergic (5-HT) descending inhibitory pathways. The initial pain response is reduced (Kamiya *et al.*, 2010).

An added benefit of sugar-free chewing gum is its ability to increase salivary flow. This aids in maintaining good oral hygiene, which is essential during orthodontic treatment (Imfeld, 1999; Mickenautsch, Leal, Yengopal, Bezerra & Cruvinel, 2007). Sugar-free chewing gum has been shown to reduce the overall amount of analgesics used by patients receiving orthodontic treatment with fixed appliances (Ireland *et al.*, 2016).

A study conducted in Pakistan compared ibuprofen and chewing gum for orthodontic pain control (Waheed-Ul-Hamid *et al.*, 2016). The study comprised 250 patients divided into two intervention groups. Each group consisted of 125 participants each. The participants received prescribed pain control at the initial arch wire insertion and at 8-hour intervals until the seventh day. Participants in the ibuprofen group were prescribed 400 mg ibuprofen immediately after the first visit and thereafter 8-hourly for one week. Participants in the chewing-gum group were prescribed sugar-free chewing gum (Orbit from the Wrigley Company) to chew for five minutes immediately after the first visit and thereafter at the same 8-hourly intervals as the ibuprofen group for one week. All patients were asked to complete a VAS questionnaire at 24 hours and after each arch wire change. The results of the study indicated that the patients who received chewing gum showed a greater decrease in pain scores than the patients receiving ibuprofen, concluding that sugar-free chewing gum is a good substitute for NSAIDS in managing orthodontic pain (Waheed-Ul-Hamid *et al.*, 2016).

A similar large-scale study comprising 826 participants compared ibuprofen and sugar-free chewing gum across nine trial sites in South West England in 2016 (Ireland *et al.*, 2016). In total, 1 000 patients were recruited and randomly assigned in a ratio of 1:1 to the chewing gum or ibuprofen (control) group. The male-to-female ratios were similar for both groups. The study inclusion criteria included patients undergoing upper and lower fixed appliance therapy, patients between the ages of 11 years and 17 years, and patients who were able to use ibuprofen and chewing gum. The response rate for the study was chewing gum (419) and ibuprofen (407). The primary outcome measure was pain experienced, using a mean of three recordings on a scale of 0–10. The secondary outcome

measures were pain experienced in the subsequent three days, pain experienced after the first arch wire change, the use of ibuprofen in the chewing gum group and appliance breakages. Pain scores were recorded using a questionnaire. Randomisation was by means of a central telephone service and comprised computer-generated pseudo-random numbers that were used to generate a sequential allocation list. Neither clinicians nor participants were blinded to the intervention. Participants in the control group were only permitted to use ibuprofen if they needed analgesic support while participants in the experimental group were allowed to use ibuprofen if they did not receive sufficient analgesia from chewing gum (Ireland *et al.*, 2016).

The primary outcomes were similar for both groups (Ireland *et al.*, 2016). The mean pain scores were 4.31 in the chewing gum group and 4.17 in the ibuprofen group. Relative pain scores for both groups changed over time, with the chewing gum group experiencing slightly more pain on the day of appliance fitting and less pain on the subsequent three days. The differences were not clinically significant (Ireland *et al.*, 2016). The reported use of ibuprofen was less in the chewing gum group than in the control ibuprofen group. The mean usage of ibuprofen was 2.1 in the chewing gum group and 3.0 in the ibuprofen group, which was statistically significant ($p<0.001$) (Ireland *et al.*, 2016).

A follow up study published in 2017 investigated pain perception and anxiety levels associated with orthodontic pain (Ireland *et al.*, 2017). It was concluded that a weak positive correlation exists between pain scores and anxiety levels in participants taking ibuprofen, which was demonstrated by a greater need for ibuprofen than recommended. In contrast, there was no correlation between anxiety levels and pain scores in participants using chewing gum (Ireland *et al.*, 2017). These results are similar to other research findings, which demonstrates that chewing gum reduces stress-related responses and, therefore, may indirectly affect pain perception and the need for analgesia (Konno *et al.*, 2016).

A randomised trial assessing the effects of chewing gum on orthodontic pain was conducted in India (Shedam, 2015). Sixty randomly selected subjects undergoing orthodontic treatment in the Department of Orthodontics and Dentofacial Orthopaedics were divided into two groups (30 patients each). Subjects were between the ages of 13 years and 30 years. Participants in the first group (intervention group) were given

sugar-free chewing gum to chew twice daily for one week. The participants in the control group received no intervention and were asked not to chew gum for a period of one week. Participants were required to complete a daily compliance schedule that consisted of VAS ratings at 24 hours and after one week. The results indicated that the average pain score after 24 hours was significantly higher in the control group than the chewing gum group ($p<0.001$). In addition, the average pain score after seven days was significantly higher in the control group than the chewing gum group ($p<0.001$). The conclusion was that sugar-free chewing gum significantly reduces the amount of pain from fixed orthodontic appliances after initial placement and further activation (Shedam, 2015).

A double-blinded RCT was conducted in Iran (Eslamian, Dehghani & Amraie, 2016). The study involved 115 participants between the ages of 14 years and 29 years who had had pain in previous orthodontic sessions. The participants were randomly divided into three experimental groups: ketoprofen chewing gum, ketoprofen gel and conventional chewing gum. All participants were instructed to use the gum/gel three times daily for three days after activation of their fixed orthodontic appliance. Participants recorded their level of pain at 2 hours, 6 hours, and 24 hours on the first day and thereafter on Day 2, Day 3 and Day 7 using a 5-score VAS. Two-way and repeated measures ANOVA were used to compare differences in the pain scores among the three groups. The study found that the mean pain score decreased over time in both males and females in all groups ($p<0.001$). The mean pain score was also slightly (but not significantly) lower in the ketoprofen chewing gum group than in the gel and conventional gum groups ($p>0.05$). The highest pain score was observed at 6 hours and was seen to decrease thereafter (Eslamian, Dehghani & Amraie, 2016).

Concerns posed by clinicians regarding the use of chewing gum during fixed orthodontic treatment often centre around breakages associated with this type of practice. A study conducted in 2012 at the Charles Clifford Dental Hospital in the United Kingdom investigated the effects that chewing gum had on the impact, pain and breakages associated with fixed orthodontic appliances (Benson, Razi & Al-Bloushi, 2012). The conclusion of this RCT showed that chewing gum significantly decreases the impact and pain from fixed appliances. In addition, no evidence was found to show that chewing gum increased the incidence of appliance breakages (Benson, Razi & Al-Bloushi, 2012).

The literature search regarding the benefits of sugar-free chewing gum in the management of orthodontic pain highlighted that it is a field of research that needs further review. The standard practice remains prescribing analgesic drugs and NSAIDs should the patient complain about discomfort. There is limited information about the 'placebo effects' of conventional chewing gum and its use in orthodontic pain management. The information disclosed in this thesis adds value to the research pool and may help in developing a sound protocol for orthodontic pain management using a non-medicated and easily accessible method.

# CHAPTER 3: METHODOLOGY

## 3.1 Introduction

The review of the literature in the previous chapter demonstrated that orthodontic pain is not fully understood and may lead to patients declining treatment based on their perception of the pain process involved. Conventional sugar-free gum has emerged as a possible benefit due to its mechanical analgesic effects, but the data is limited. In addition, the benefits of 'placebo-related effects' in orthodontic pain management have not been documented.

This chapter describes the constructive framework designed to navigate the way in which the research was undertaken in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. These statements improve the quality of reporting RCTs by following appropriate randomisation. Proper randomisation depends on two steps: generation of an unpredictable allocation sequence; and concealment of this sequence from the investigators enrolling participants (Moher *et al.*, 2010).

Chapter 3 begins with descriptions of the hypothesis tested, the variables that formed part of the study, the research setting and the characteristics of the study sample. Thereafter, the chapter describes the methods used to conduct the experiment, including how randomisation and blinding was assured and finally, the way that data collection was achieved and captured. The chapter concludes with the ethical considerations that were maintained throughout the study.



## 3.2 Quantitative experimental design

> Hypothesis testing is the way we use evidence to examine the validity of ideas. If these ideas, or theories, have logical consequences, then we can test these hypotheses by collecting data that would show them to be false, if indeed we had been mistaken in our beliefs. (Haines-Young & Fish, 2009)

The experimental hypothesis investigated in the thesis is stated as follows:

Experimental Hypothesis

H1 – There will be a significant difference between the analgesic effects of conventional sugar-free chewing gum and a placebo medicament (sugar-free sweets) in pain resolution following the placement of fixed orthodontic appliances.

Null Hypothesis

H0 – There will be no significant difference between the analgesic effects of conventional sugar-free chewing gum and a placebo medicament (sugar-free sweets) in pain resolution following the placement of fixed orthodontic appliances.

Variables

An independent variable is changed or controlled in a scientific exercise to test the effects on a dependent variable. A dependent variable is the variable being tested and measured in a scientific exercise. As the experimenter changes the independent variable, the effect on the dependent variable is observed and recorded (Helmenstine, 2017).

The variables that were manipulated in this study are as follows:

*Independent variables*

1) Experimental medicament – conventional sugar-free chewing gum
2) Placebo medicament – sugar-free sweets
3) Gender
4) Bracket systems and orthodontic technique used in the application of the fixed orthodontic appliance

*Dependent variable*

1) Pain

*Controlled variables*

1) Standardised number and duration of intervention sessions
2) Standardised assessment tool (VAS) for patients within each group
3) Standardised time intervals for the assessment of pain

Where:

T0 = 4 hours post the placement of the fixed appliance; no intervention with any medicament (start of the experiment)

T1 = 8 hours post the placement of the fixed appliance

T2 = 24 hours post the placement of the fixed appliance

T3 = 48 hours post the placement of the fixed appliance (end of the experiment)

## 3.3 Research setting

The study was conducted across three private practices in Tableview, South Africa. Two practices were specialist orthodontic practices, one of which used the MBT™ prescription appliance to treat participants while the second practice used the Damon™ technique with its unique SLBs. The third practice in the study was a general dental practice that offered orthodontic treatment; the system employed at this practice was based on MBT™ prescription techniques using conventional Edgewise-type brackets.

## 3.4 Participants

### *3.4.1 Study population*

Inclusion criteria for the study population were patients aged between 12 years and 30 years receiving fixed orthodontic appliance treatment for the first time, irrespective of gender. A finite number for the population could not be determined because records pertaining to every patient receiving orthodontic treatment in South Africa, even within the said inclusion criteria, were not available. Exclusion criteria were patients who were hypersensitive to ingredients in conventional sugar-free chewing gum or sugar-free sweets; medically compromised patients, including patients with temporomandibular joint disorders; patients who underwent any surgery in the previous three weeks (inclusive of dental extractions); patients reporting the use of pain medication at the time of the initial bracket placement; and orthodontic retreatment cases.

### *3.4.2 Sample size*

The sample comprised 60 (n = 60) orthodontic patients from two specialist orthodontic private practices and one general dental private practice with a special interest in orthodontics in the Tableview area of Cape Town, South Africa. The sample size was calculated conveniently due to time limitations and willingness of the participants to complete the study.

### *3.4.3 Study design*

The study design that was chosen to confirm or negate the study hypothesis and to fulfil the study objectives was an RCT using parallel and descriptive techniques to evaluate the effectiveness of the experimental medicament (conventional sugar-free chewing gum) in comparison with a placebo (sugar-free sweets) in the management of orthodontic pain. The method employed in randomly assigning participants to the intervention groups conformed to the recommended CONSORT guidelines.

As mentioned in the literature review, randomisation following CONSORT guidelines minimises the influence of selection bias on the conclusions of the study and is the most effective method of removing the influence of both known and unknown confounders. Clinical studies in which randomisation is used are more effective in finding significant outcomes in suggested treatments (Moher *et al.*, 2010).

The allocation ratio for the experimental intervention to placebo intervention in this trial was 1:1 in each subgroup.

## 3.5 Interventions

The study sample (n = 60) was divided into two intervention groups; one group received conventional sugar-free chewing gum (n = 30) as the experimental medicament and the other group received sugar-free sweets (n = 30) as the placebo medicament. In total, 60 questionnaires and medicament envelopes were distributed across three practices/subgroups, where each subgroup had an equal experimental group and placebo

group; 20 questionnaires and medicament envelopes were received by each subgroup (ten sugar-free chewing gum and ten sugar-free sweets alike).

Distribution of the medicaments into Group A1 and Group A2 for Practice/Subgroup 1; Group B1and Group B2 for Practice/Subgroup 2; and Group C1 and Group C2 for Practice/Subgroup 3 is shown in Figure 3.1.

Groups A1, B1 and C1 received conventional sugar-free chewing gum to chew at specified intervals following the placement of fixed orthodontic appliances (experimental group).

Group A2, B2 and C2 received sugar-free sweets to suck at specified intervals following the placement of fixed orthodontic appliances (placebo group).

See Annexure C: Patient Instructions for Medicament Use.

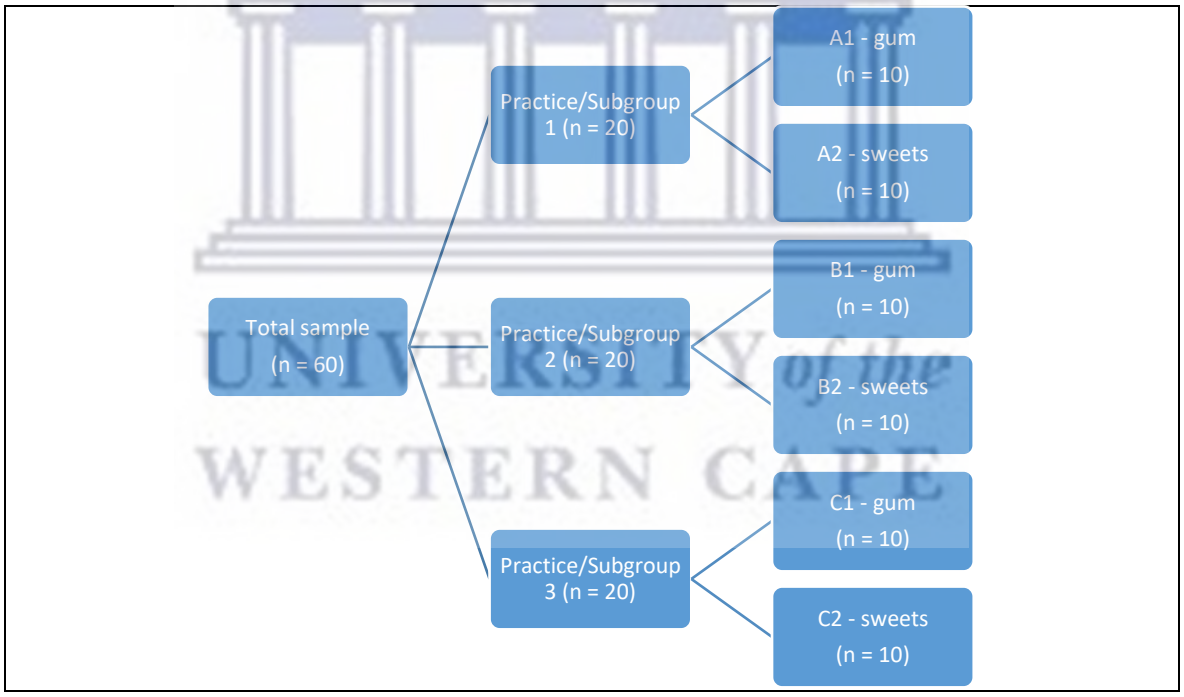


**Figure 3.1: Sample distribution**

The orthodontic system used for treatment in each practice during the study is described below:

Practice 1 – Specialist practice: Participants (n = 20) received treatment using the MBT™ Edgewise bracket system, 022 bracket slot size, starting with 0.014 NiTi initial arch wires.

Practice 2 – Specialist practice: Participants (n = 20) received treatment using the Damon™ passive self-ligating bracket system, 022 bracket slot size, starting with 0.014 Cu NiTi initial arch wires.

Practice 3 – General practice: Participants (n = 20) received treatment using the MBT™ Edgewise bracket system, 018 bracket slot size, starting with super elastic 0.012 NiTi initial arch wires.

### 3.6 Data collection tool

Data collection was achieved through self-administered questionnaires (Annexure D) incorporating VAS. The questionnaire was completed by the participant over a 48-hour period following the placement of a fixed orthodontic appliance.



### 3.7 Data collection process / Outcome measures

The questionnaires were structured in the form of a diary to make it more personal for the patient to monitor their own pain experience and to ensure that adequate data was captured over time. The self-administered questionnaires incorporated both open- and closed-ended questions. Participants were given a letter seeking permission from their school for them to participate in the study (Annexure E).

For the purpose of this review, pain in the 'initial phase' following placement of the fixed bracket appliance was examined. This initial phase is associated with the highest incidence of orthodontic pain. It has been well documented that pain begins 4–12 hours after applying orthodontic force, peaks at 24 hours and gradually diminishes over 3−7 days (Marković *et al.*, 2015).

The first objective was to measure the intensity of pain experienced by the participants in the experimental group and the placebo group following the placement of fixed orthodontic appliances. Additional objectives were to note and describe whether gender and different bracket systems or techniques had any influence on pain scoring.

The outcome measure for pain in the total sample was indicated by the patient at specified intervals using the VAS (Likert-type scale) for pain assessment.

The initial time interval, time interval 0 (T0), was four hours following the initial placement of the fixed appliance; this formed the baseline score for pain without an intervention. Time interval 1 (T1) was 8 hours following the initial placement of the fixed appliance and recorded the first pain scoring after the use of an intervention medicament. Time interval 2 (T2) was recorded at 24 hours following the initial placement of the fixed appliance to draw comparisons with similar studies in which maximum orthodontic pain (with no intervention) was experienced (Ertan Erdinç & Dinçer, 2004). Time interval 3 (T3), the last interval in this experiment, was 48 hours after the initial placement of the fixed appliance to coincide with the beginning of pain resolution, as mentioned in the literature (Ertan Erdinç & Dinçer, 2004; Marković *et al.*, 2015).

The chosen VAS (Figure 3.2) incorporated a linear numerical measure that was scaled from 0 cm to 10 cm (1 cm intervals) with facial diagrammatic representation in order to engage with the participants visual interpretation of pain. In addition, typical Likert word descriptions were employed that categorised pain in segmented scoring: No pain (score 0 cm), Mild pain (score 1–2 cm), Moderate pain (scores 3–4 cm and 5–6 cm) and Severe pain (scores 7–8 cm and 9–10 cm), where 10 cm was recorded as 'Worst possible pain'. Concurring with the scientific literature, linear numerical readings were used to measure the pain scores in this study (Hjermstad *et al.*, 2011).

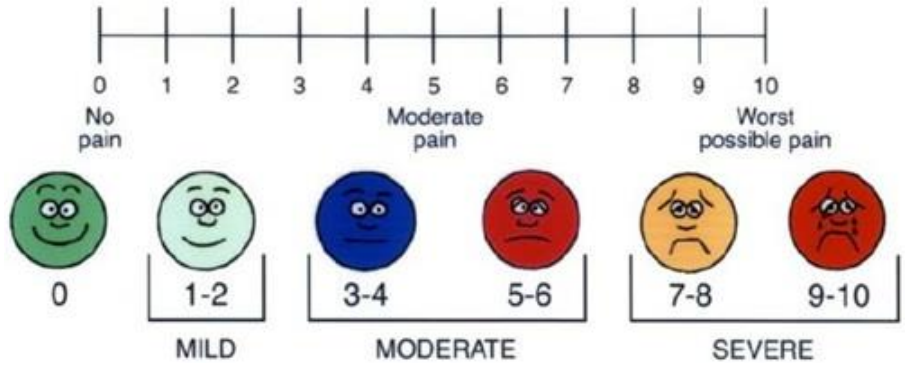


**Figure 3.2: Visual analogue scale for pain scoring**

## 3.8 Reliability

Assessing the reliability of the study findings requires one to make judgements about the consistency of the research in relation to the application and appropriateness of the methods undertaken and the integrity of the final conclusions. To decrease the risk of error in the results, it is important that the researcher ensures that the measurement tools are valid and reliable. Ultimately, an independent researcher should be able to arrive at similar or comparable findings (Noble & Smith, 2015).

The 'soundness' of the methods and results in this thesis was based on the standardisation of the assessment tool; a modified VAS incorporating numerical ratings, worded descriptions and diagrammatic representation. The VAS was used to assess all the participants across the research setting. The use of this assessment tool is well documented in pain studies. Furthermore, both intervention groups were required to fill in their questionnaires at the same time intervals while using the same brand of allocated medicament in all subgroups (see Figure 3.5). Clear instructions on how and when to use the medicament were given to each participant (see Annexure C).

## 3.9 Validity

Validity refers to the precision with which the findings accurately reflect the data. Validity recognises that multiple realities exist due to the researcher's personal

experiences and viewpoints, and these may have resulted in methodological bias (Noble & Smith, 2015).

In this thesis, validity of the data collection was ensured through double-blinding techniques; the researcher and the participant were blinded to the interventions that were allocated. Furthermore, the participants were blinded to which intervention was experimental and which was a placebo. The results were made available to the researcher only once the statistician had recorded the findings.

Interactions between variables were tested through a repeated measures ANOVA test and cross-checked using (post-hoc) pairwise comparisons, thus further ensuring the validity of the data acquired. Any discrepancies between ANOVA and the pairwise comparisons were accurately documented and discussed further.

## 3.10 Randomisation

### *3.10.1 Sequence generation*

Two unmarked medicaments were used in this study: Conventional sugar-free chewing gum (experimental) and sugar-free sweets (placebo) Figure 3.5.

Even amounts of each medicament were distributed among Practice 1, Practice 2, and Practice 3. See groups A1, A2, B1, B2, C1 and C2 in Figure 3.1.

Ten unmarked envelopes were filled with conventional sugar-free chewing gum and ten unmarked envelopes were filled with sugar-free sweets by the independent record keeper. A total of 20 envelopes were then randomly allocated a number using a mobile random number generator application (Random UX) (see Figure 3.3). The envelopes were then distributed to Practice 1 (envelopes 1–20). The sequence was repeated congruently for Practice 2 (envelopes 21–40) and for Practice 3 (envelopes 41–60), ensuring that each practice received an even number of experimental and placebo medicaments.

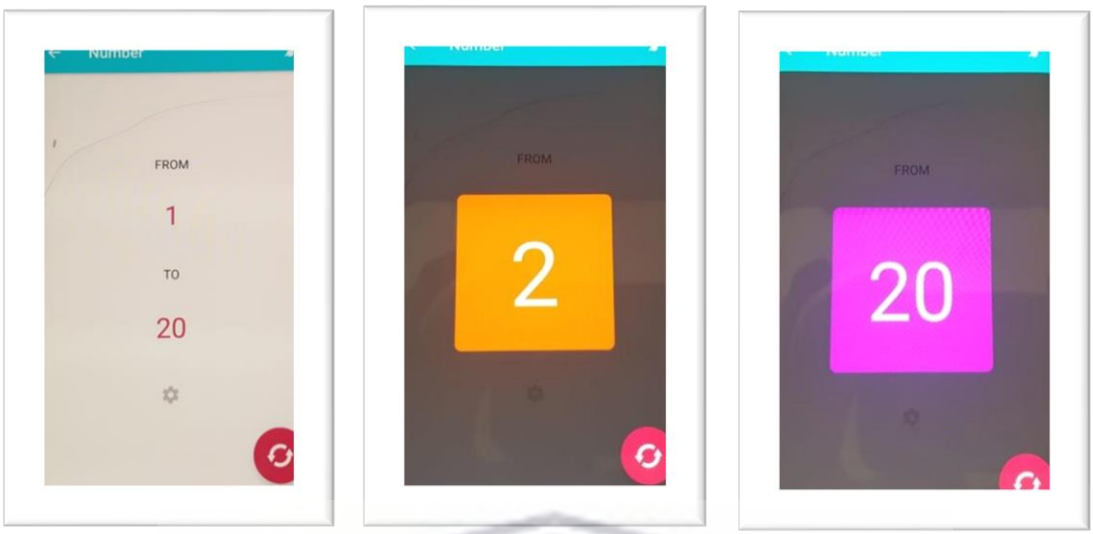


**Figure 3.3: Random number generator (Random UX)**

### *3.10.2 Allocation concealment mechanism*

The unmarked medicaments were removed from the original packaging and resealed in sterile pouches. Each sterile pouch contained either ten conventional sugar-free chewing gums or ten sugar-free sweets to last the duration of the experiment.

Thereafter, the sterile pouches were sealed in a brown envelope with the instruction for the patient (Annexure C) either to chew gently (chewing gum) for five to ten minutes or to suck (sweets) until completely dissolved (approximately five minutes). Each envelope had an identification number, and this was recorded with the relevant medicament that it contained by the independent record keeper prior to distribution to the practices.

### *3.10.3 Implementation*

The medicaments were purchased by the researcher and handed to the independent record keeper who followed the process outlined above. The envelope number was recorded with the corresponding medicament by the record keeper onto an Excel spreadsheet, which was kept confidential from all other parties involved in the research process. The envelopes were then sealed and distributed to each practice. Each practice had a designated field worker (practice manager) who oversaw the experiment, taking

responsibility for the process outlined in Figure 3.4. In addition, the designated field worker ensured that all questionnaires were returned to the researcher. The sample size was conveniently determined due to time limitations and availability of the practices. At this stage, all participants' responses were captured onto an Excel spreadsheet by the designated data capturer. The final blinded information was entered onto an Excel data-capturing sheet and sent to the statistician for statistical analysis. The researcher remained blinded until the results from the statistician were analysed and presented.

### *3.10.4 Blinding*

Both the researcher and the patient were blinded to the allocated contents in the envelopes. Furthermore, patients were blinded to whether they were receiving the experimental medicament or the placebo medicament; the patient could have perceived the placebo as being the sugar-free sweet or the conventional chewing gum. The independent record keeper ensured that an even number of experimental and placebo medicaments reached each of the three practices. The flow chart below (Figure 3.4) explains the step-by-step process that was followed.

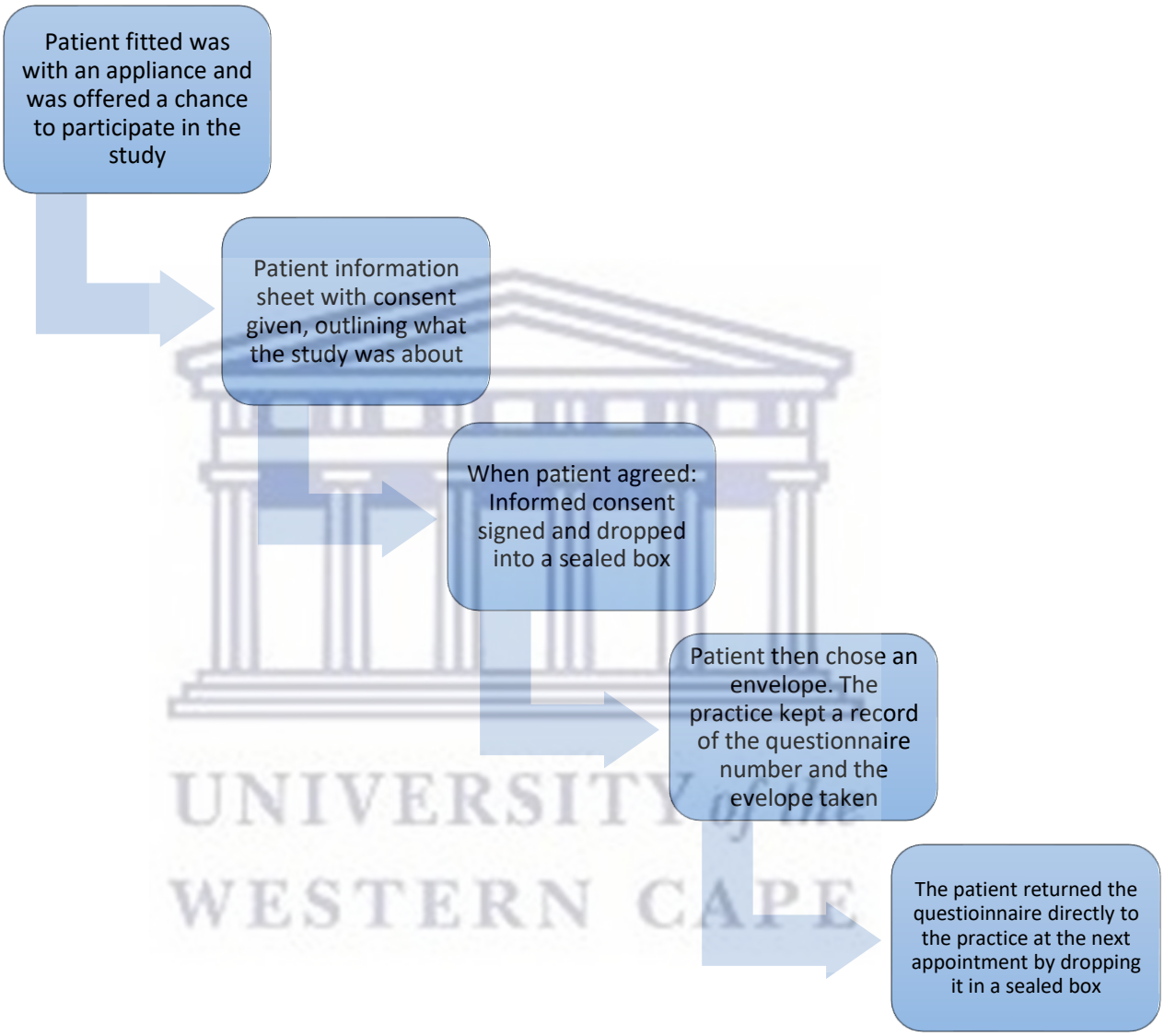


**Figure 3.4: Sequence of steps used for randomisation and blinding**


**Figure 3.5: Medicaments used in the study**

Left: Sugar-free sweets (placebo)

Right: Conventional sugar-free chewing gum (experimental)

Written informed consent (Annexure B) was obtained from all participants after they had read the Patient Information Sheet (Annexure A). This was a voluntary study and anonymity was preserved regarding the feedback given by the participants. Participants did not record their names on the questionnaires; however, their personal details, questionnaire number and random envelope numbers were kept in a register held at each treating practice/subgroup. At the end of the experiment, the register was matched with the records kept by the official record keeper to correlate the responses with the respective medicaments that were given. The names of the practice and the medicaments were kept confidential for ethical reasons.

### 3.11 Statistical methods

All data was captured by the data capturer, recorded onto an Excel spreadsheet, and transferred to StataCorp. 2017, *Stata Statistical Software: Release 15*.

The statistician used the StataCorp LLC statistical package for the analysis. Descriptive statistics were used to describe patient characteristics. Histograms, bar graphs and

box-and-whisker plots of the data from the different groups were examined to make comparisons.

A repeated measures ANOVA was used to determine

(i) if there was an interaction between the intervention and the level of pain experienced over time.
(ii) if there was an interaction between gender and the level of pain experienced over time; and
(iii) if there was an interaction between the bracket systems and techniques used and the level of pain experienced over time.

Post-hoc testing and pairwise comparisons were used to support ANOVA testing. Any differences in the test results were discussed accordingly. Descriptive statistics were presented as mean and standard deviation unless otherwise specified.

### 3.12 Ethics considerations

Ethics considerations refer to the practices that must be conducted in the clinical management of participants in a study and the ethics protocol that must be maintained during all RCTs.



The treatment of all the participants in this study followed the principles that govern the actions of all healthcare practitioners treating any patient in South Africa. These guidelines, as stipulated by the Health Professions Council of South Africa (HPCSA), ensured that all participants received treatment that was necessary and was independent of the objectives of the current study.

A research proposal was submitted to the Faculty of Dentistry and to the Senate Research Committee of the University of the Western Cape prior to the commencement of the study. Ethics approval was applied for and granted by the Biomedical Research Ethics Committee (BMREC) of the University of the Western Cape (BMREC Approval Number BM17/7/11).

Anonymity and confidentiality of all information recorded during the study was assured, and study subjects were advised that they could withdraw from the study at any point without penalty or prejudice. All research activities conducted followed strict ethical principles in honour of the Declaration of Helsinki (Skierka & Michels, 2018).

# CHAPTER 4: RESULTS

## 4.1 Introduction

This chapter presents the findings of the study. It begins with a description of the time frame for the recruitment process, including when the investigation was terminated. The flow of the chapter follows the recommendations of CONSORT for reporting randomised trials (Moher *et al.*, 2010).

The chapter describes the baseline demographic data and thereafter reports on the pain scores associated with the intervention groups, the pain scores related to gender and lastly, the pain scores associated with different orthodontic techniques and bracket systems.

Each outcome on 'Pain Reporting' includes a table of mean pain scores, a profile plot, a box-and-whisker plot, a repeated measures ANOVA test and a table showing pairwise comparisons (post-hoc testing).

The chapter concludes with a summary of the results.

## 4.2 Recruitment

Following the granting of ethics clearance, 60 participants with a mean age of 14.82 years (SD4.02) were recruited for the study. There were no losses or exclusions incurred during the trial, and all questionnaires were returned to the treating practices before being handed over for data capturing. The recruitment process for this study took place between July 2018 and January 2019. The trial was concluded on 31 January 2019 once all 60 questionnaires had been returned. As mentioned previously, the sample was a convenient size that was determined due to time constraints within the research setting.

### 4.3 Baseline demographic data

Most of the participants in this investigation were aged between 12 years and 15 years (62%) with a mean age of 14.82 years (SD4.02). Only 10% of the sample was over 20 years of age (see Table 4.1).

**Table 4.1: Age and gender demographics**

| | **Gender** | | |
|---|---|---|---|
| | Female | Male | Total |
| **Age category** | | | |
| **<15 years** | 23 | 14 | 37 |
| **15–19 years** | 8 | 9 | 17 |
| **>20 years** | 5 | 1 | 6 |
| | 36 | 24 | 60 |

A greater proportion of females were recruited (60%) overall in the study, with the mean age of females and males being similar: 14.92 years (SD4.01) for females and 14.67 years (SD3.96) for males (Figure 4.2).

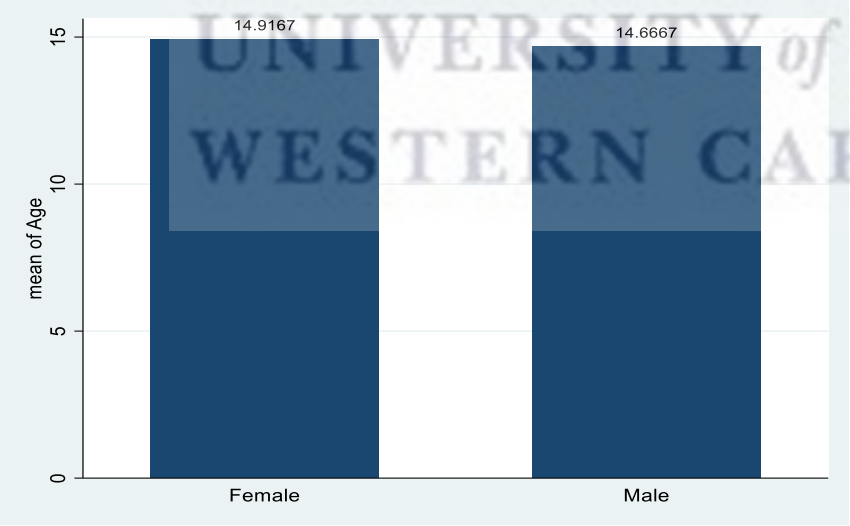


**Figure 4.1: Mean age of participants by gender**

An identical number of experimental (chewing gum) medicaments and placebo (sweets) medicaments were used in the sample (n = 30 for each). The distribution of the experimental (chewing gum) medicament between male and female participants was similar (17 and 13 respectively), with the female participants using a higher percentage of the placebo medicament (77%) due to more females participating in the study than males (Table 4.2).

**Table 4.2: Gender and medicament distribution**

| | **Gender** | | |
|---|---|---|---|
| | Male | Female | Total |
| **Medicament** | | | |
| **Chewing gum** | 17 | 13 | **30** |
| **Sweets/placebo** | 7 | 23 | **30** |
| | 24 | 36 | **60** |

## 4.4 Pain reporting

### *4.4.1 Medicament (gum vs sweets) influence on pain scores over time*

The mean (standard deviation) pain scores recorded at specific intervals (T0, T1, T2 and T3) show that the participants using the experimental medicament (gum) had lower pain scores at each time interval except at T1 (8 hours) when the mean scores were equal to the placebo medicament (sweets) (Table 4.3 and Figure 4.2).

In addition, the profile plot presented in Figure 4.2 demonstrates

- the lower mean pain scores in gum throughout the experiment.
- the decline in mean pain scores for both medicaments (experimental and placebo) over time, except at T1 (8 hours) where the experimental medicament (gum) showed a slight elevation in mean pain scores equal to that of the placebo medicament (sweets); and
- a greater decrease in mean pain scores in the gum group towards T2 (24 hours), followed by a noticeably rapid decline in pain when compared with the placebo medicament (sweets) towards the end of the experiment (T3; 48 hours).

**Table 4.3: Summary of mean pain scores and standard deviation for the experimental (gum) and placebo (sweets) medicaments over time**

| | | T0 | T1 | T2 | T3 |
|---|---|---|---|---|---|
| **Medicament** | **Pain scores over time intervals** | | | | |
| **Gum** | n | 30 | 30 | 30 | 30 |
| | **Mean** | **4.6** | **5** | **4.1** | **1.4** |
| | SD | 1.73 | 1.44 | 1.27 | 0.98 |
| **Sweets** | n | 30 | 30 | 30 | 30 |
| | **Mean** | **5.2** | **5** | **4.6** | **3.6** |
| | SD | 2.01 | 1.49 | 1.44 | 1.39 |
| **Total Pain** | n | 60 | 60 | 60 | 60 |
| | Mean | 4.9 | 5 | 4.4 | 2.5 |
| | SD | 1.88 | 1.46 | 1.37 | 1.61 |

SD: Standard deviation

Where:

T0 = 4 hours post the placement of the fixed appliance; no intervention (start of the experiment)

T1 = 8 hours post the placement of the fixed appliance

T2 = 24 hours post the placement of the fixed appliance

T3 = 48 hours post the placement of the fixed appliance (end of the experiment)

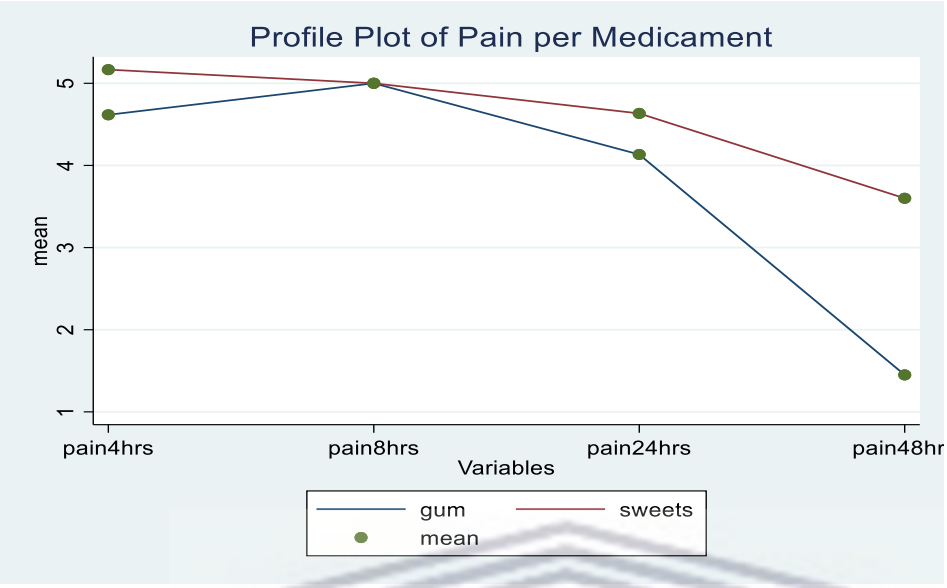


**Figure 4.2: Mean pain trend of the experimental (gum) and placebo (sweets) medicaments over time**

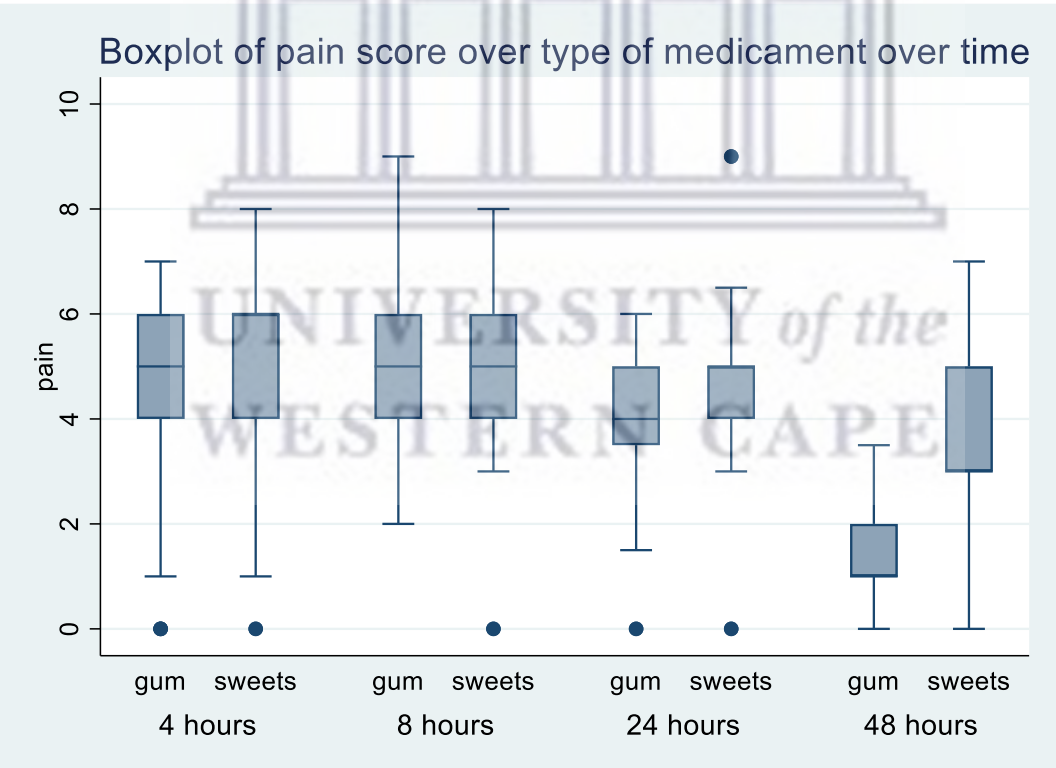


**Figure 4.3: Pain variation including the median pain score over time for the experimental (gum) and placebo (sweets) medicaments**

A boxplot representation of the survey data (Figure 4.3*)* showed generally higher levels of pain with the placebo medicament (sweets) than the experimental medicament (gum) over time, except at time interval T1 (8 hours) where gum scored a maximum pain level of 9 compared with sweets for which the maximum recorded pain was 8. The interquartile range (IQR) and median between the groups were the same at this time interval. 'No pain' or 0 score was recorded at all time intervals and presented as outliers at 4 hours, 8 hours, and 24 hours and as a lower fence or minimum score at 48 hours. Interestingly, the maximum pain recording for gum at 48 hours was just slightly more than the median and first quartile recording of sweets, which is further reflected in the statistical difference detected when comparing the means of both groups ($p<0.001$) (Table 4.3).

A repeated measures ANOVA showed there was a statistically significant interaction between the medication and time on pain scores, $F(3, 174) = 8.19$, $p<0.001$.

A further post-hoc analysis using a pairwise comparison (Table 4.4) allow intercomparing of the pain scores of the two treatment groups. At the beginning of the experiment (4 hours) and at 8 hours and 24 hours, there was no statistically significant difference between sweets and gum ($p>0.05$). However, at 48 hours, pain was significantly lower in the gum group (1.45; 0.98) than the sweet group (3.6; 1.39) with a difference of 2.15, 95% CI (1.54 to 2.76) ($p<0.001$).

The positive contrast recording at each comparison (sweet vs gum) is indicative of mean pain scores always being higher in the placebo (sweets) group than the experimental (gum) group at each time interval.

**Table 4.4: Pairwise comparison (post-hoc) showing mean difference between sweets and gum over time**

| Pairwise comparison: Medicament and pain | Contrast (Mean difference) | Standard error | 95% Confidence Interval for Mean Difference | | p-value |
|---|---|---|---|---|---|
| | | | Lower Bound | Upper Bound | |
| Sweet vs Gum at T0 (4 hrs.) | 0.55 | 0.484 | -0.398 | 1.498 | 0.255 |
| Sweet vs Gum at T1 (8 hrs.) | 4.44e-15 | 0.379 | -0.743 | 0.743 | 1.000 |
| Sweet vs Gum at T2 (24 hrs.) | 0.5 | 0.351 | -0.189 | 1.189 | 0.155 |
| Sweet vs Gum at T3 (48 hrs.) | 2.15 | 0.310 | 1.541 | 2.759 | <0.001 |

### *4.4.2 Comparison of gender on pain scores over time*

The mean (standard deviation) pain scores recorded at specific intervals (T0, T1, T2 and T3) show that the male participants and the female participants reported equal (T0 and T2) or similar pain scores. However, at the end of the experiment (T3), the male participants scored a significantly lower mean pain score 2.0 (1.39)] than the female participants (2.9 [1.59]). See Table 4.5 and Figure 4.4.

In addition, the profile plot (Figure 4.4) demonstrates the following:

- Female mean pain scores remained constant across the first two-time intervals (T0 and T1), followed by a steady decline in the gradient at T2 and a further decline at T3.
- Male mean pain scores increased slightly from the start of the experiment and followed a steeper decline towards the end of the experiment than the female mean pain scores.

**Table 4.5: Summary of mean pain scores and standard deviation for females and males over time**

| | | T0 | T1 | T2 | T3 |
|---|---|---|---|---|---|
| **Gender** | **Pain scores over time intervals** | | | | |
| **Male** | n | 24 | 24 | 24 | 24 |
| | **Mean** | **4.9** | **5.1** | **4.4** | **2.0** |
| | SD | 2.01 | 1.49 | 1.44 | 1.39 |
| **Female** | n | 36 | 36 | 36 | 36 |
| | **Mean** | **4.9** | **4.9** | **4.4** | **2.9** |
| | SD | 2.11 | 1.64 | 1.55 | 1.59 |
| **Total Pain** | n | 60 | 60 | 60 | 60 |
| | Mean | 4.9 | 5 | 4.4 | 2.5 |
| | SD | 1.88 | 1.46 | 1.37 | 1.61 |

SD: Standard deviation

Where:

T0 = 4 hours post the placement of the fixed appliance; no intervention (start of the experiment)

T1 = 8 hours post the placement of the fixed appliance

T2 = 24 hours post the placement of the fixed appliance

T3 = 48 hours post the placement of the fixed appliance (end of the experiment)

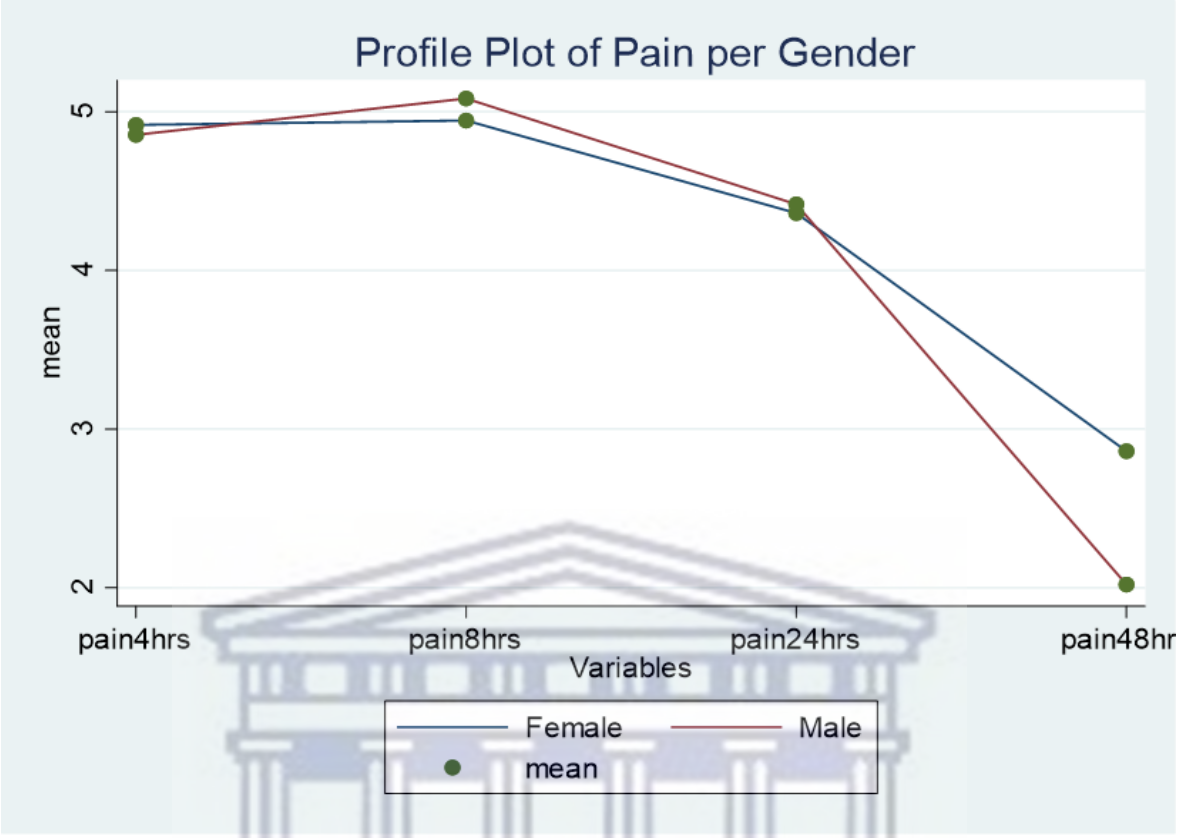


**Figure 4.4: Mean pain trend for female and male participants over time**

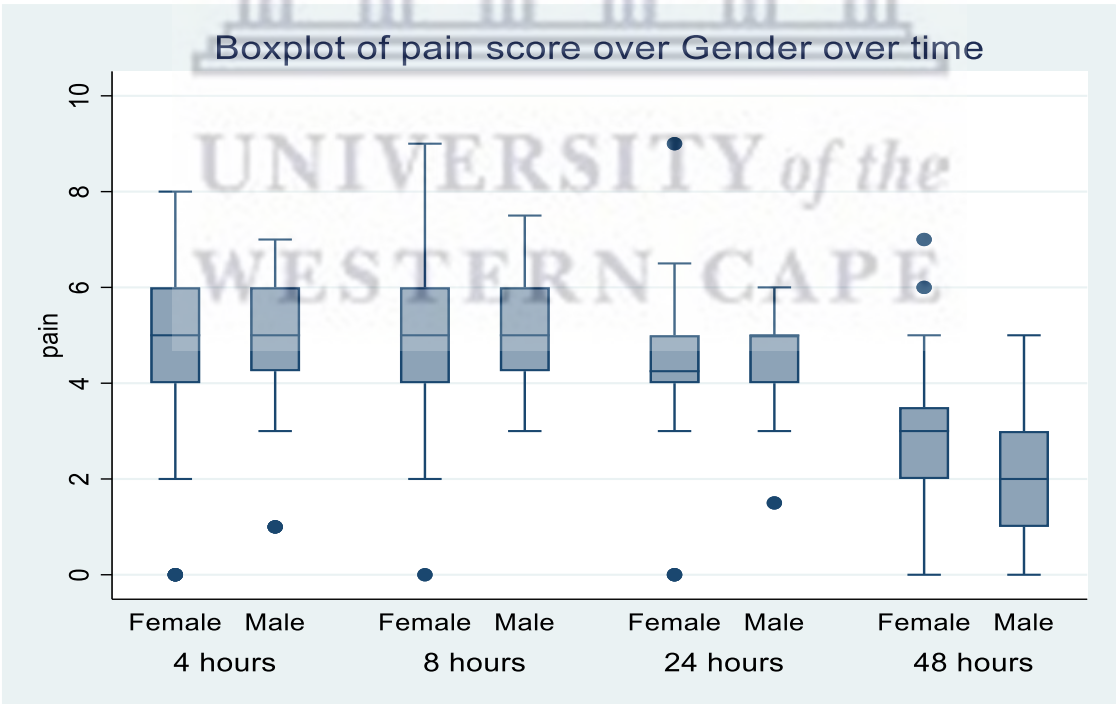


**Figure 4.5: Pain variation including median pain score over time for female and male participants**

A boxplot representation of the survey data (Figure 4.5) showed female participants displayed more varied pain scoring than male participants at the start of the study (T0) and at 8 hours, at which time the median pain scores were congruent. The IQRs were similar for both females and males at these time intervals. However, the maximum and minimum scores were further apart from the median for the female participants, and outliers were present.

There were recordings of 'No pain' or 0 score at all time intervals for the female participants, presenting as outliers at 4 hours, 8 hours, and 24 hours and as a lower fence or minimum score at 48 hours. At the end of the experiment, both female and male participants had minimum scores that were equal (0 or 'No pain'). However, there were female participants who still had high pain scores present as outliers. Interestingly, 50% of male pain scores were equal to the lower 25% (first quartile) of female scores.

A repeated measures ANOVA showed no statistically significant interaction between gender and time on pain: $F$ (3, 174) = 1.64, p=0.18. In addition, there was no statistically significant difference between male participants and female participants: $F$ (1, 174) = 0.38, p=0.5421. There was, however, a statistically significant difference at the different time intervals: $F$ (3, 174) = 46.17, p<0.001.

A further post-hoc analysis using a pairwise comparison allowed the intercomparing of gender (male and female) pain scores over time (see Table 4.6). At the beginning of the experiment and at 8 hours and 24 hours, there was no statistically significant difference between the male participants and the female participants on pain scores (p>0.05). However, at 48 hours, pain was significantly less in the male participants (2.02 [1.52]) than in the female participants (2.86 [1.59]), with a difference of -0.84, 95% CI (-1.65 to -0.29), p=0.042. This was in contrast to the ANOVA test result.

**Table 4.6: Pairwise comparison (post-hoc) showing mean difference on pain scores between male and female participants over time**

| Pairwise comparison: Gender and pain | Contrast (Mean difference) | Standard error | 95% Confidence Interval for Mean Difference | | p-value |
|---|---|---|---|---|---|
| | | | Lower Bound | Upper Bound | |
| Male vs Female at T0 (4 hrs.) | -0.06 | 0.499 | -1.041 | 0.916 | 0.9 |
| Male vs Female at T1 (8 hrs.) | 0.14 | 0.386 | -0.62 | 0.896 | 0.719 |
| Male vs Female at T2 (24 hrs.) | 0.06 | 0.365 | -0.66 | 0.771 | 0.879 |
| Male vs Female at T3 (48 hrs.) | -0.84 | 0.414 | -1.65 | -0.029 | 0.042 |



### *4.4.3 Comparison of techniques[1] on pain scores over time*

The mean (standard deviation) pain scores recorded at specific intervals (T0, T1, T2 and T3) (see Table 4.7 and Figure 4.6) show that all practices reported similar scores over time.

[1] The orthodontic systems used for treatment in each practice during the study have been described in Chapter 3: Methodology on page 29

The mean pain scores of Practice 3 were lower than those of Practice 1 and Practice 2 for all time intervals, except at the start of the experiment (T0) where Practice 3 had a slightly higher mean pain score of 4.9 (1.63) than the other practice groups.

Practice 1 and Practice 2 showed an increase in mean pain at time interval T1 (8 hours), followed by a decline towards T2 (24 hours) and T3 (48 hours), whereas Practice 3 showed a decline in mean pain scores across all time intervals.

In addition, the profile plot (Figure 4.6) demonstrates the following:

- All practices showed a rapid decrease in mean pain scores between T2 (24 hours) and T3 (48 hours).
- Practice 2 showed a steeper decline in mean pain values between time intervals T1 (8 hours) and T3 (48 hours) than Practice 1 and Practice 3, which demonstrated a gradual decline in mean pain values after time interval T1 (8 hours) followed by a more rapid decline after time interval T2 (24 hours), as mentioned in the point above.

**Table 4.7: Summary of mean pain scores and standard deviation for the different practices/techniques over time**

| | | T0 | T1 | T2 | T3 |
|---|---|---|---|---|---|
| **Practice/bracket system and technique** | **Pain Scores over time intervals** | | | | |
| **Practice 1** | n | 20 | 20 | 20 | 20 |
| | **Mean** | **4.7** | **5** | **4.5** | **2.7** |
| | SD | 2.15 | 1.72 | 2.04 | 1.66 |
| **Practice 2** | n | 20 | 20 | 20 | 20 |
| | **Mean** | **5.2** | **5.4** | **4.3** | **2.6** |
| | SD | 1.89 | 1.59 | 1.04 | 1.66 |
| **Practice 3** | n | 20 | 20 | 20 | 20 |
| | **Mean** | **4.9** | **4.7** | **4.3** | **2.3** |
| | SD | 1.63 | 0.92 | 0.77 | 1.58 |
| **Total Pain** | N | 60 | 60 | 60 | 60 |
| | **Mean** | **4.9** | **5** | **4.4** | **2.5** |
| | SD | 1.88 | 1.46 | 1.37 | 1.61 |

SD: Standard deviation



Where:

T0 = 4 hours post the placement of the fixed appliance; no intervention (start of the experiment)

T1 = 8 hours post the placement of the fixed appliance

T2 = 24 hours post the placement of the fixed appliance

T3 = 48 hours post the placement of the fixed appliance (end of the experiment)

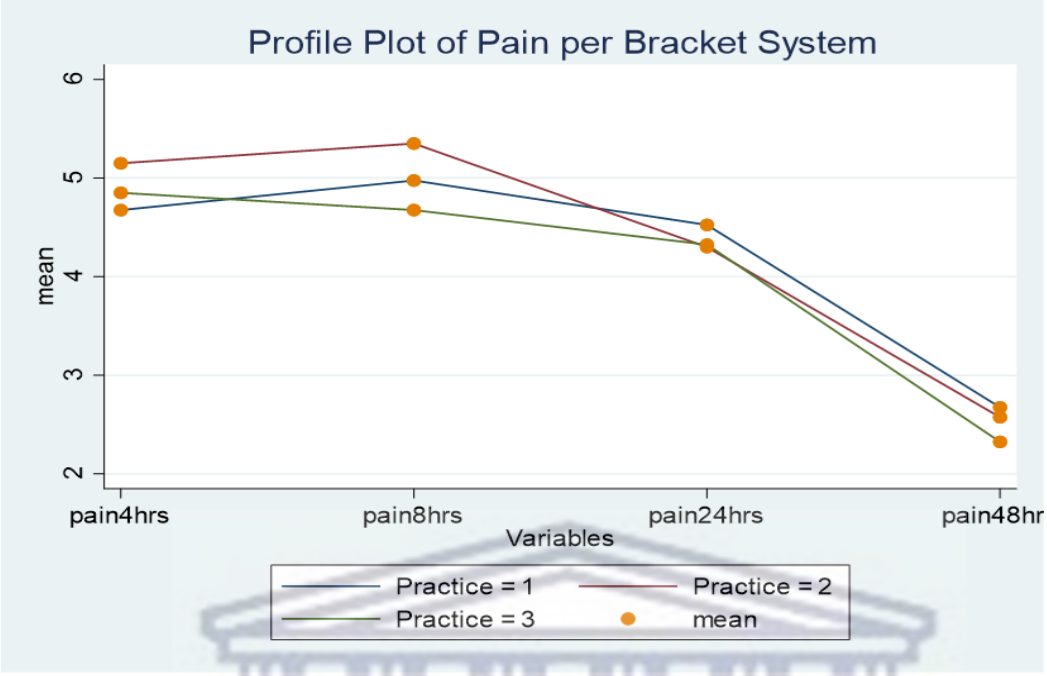


**Figure 4.6: Mean pain trend for the different practices/techniques over time**

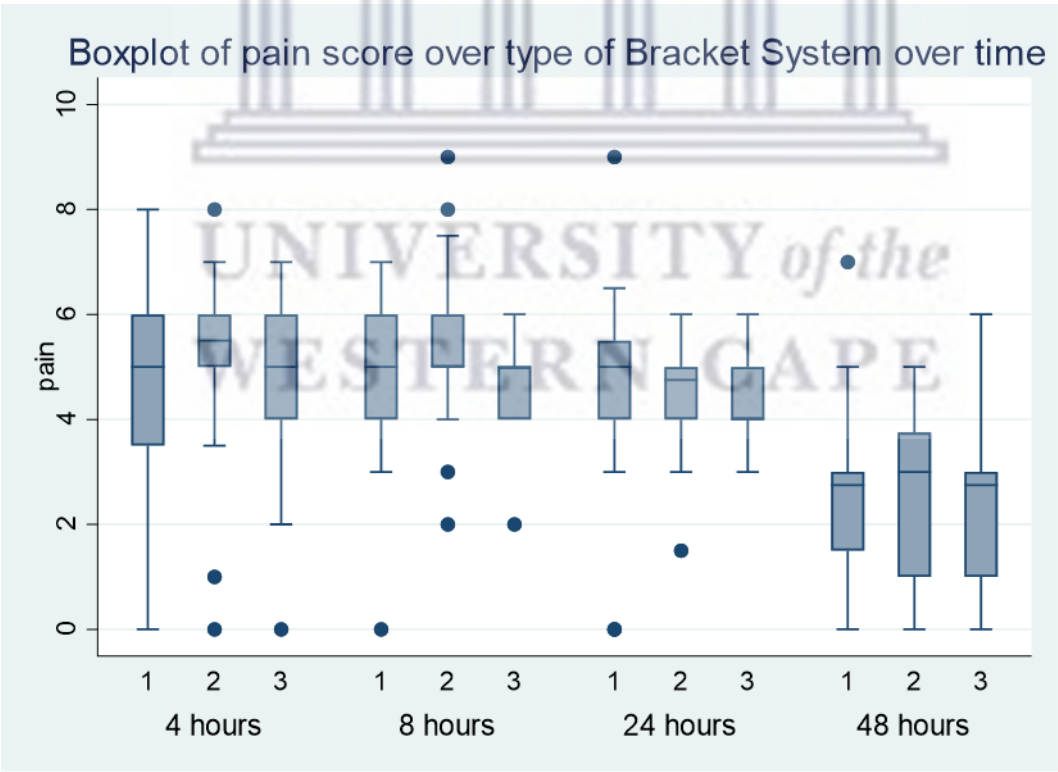


**Figure 4.7: Pain variation including the median pain score over time for the different practices/techniques**

A boxplot representation of survey data (Figure 4.7) indicates that at the start of the experiment (T0; 4 hours)

- The median pain scoring for Practice 1 and Practice 3 was equal to the first quartile (lower 25%) of Practice 2 scoring.
- Practice 2 displayed the smallest IQR; however, outliers in the lower and upper pain extremities were noted.
- There were scores of 'No pain' (0 score) noted for all three practices at the start of the experiment.

At the end of the experiment (T3; 48 hours)

- The distribution of pain scores for all three practices were similar, with Practice 1 having an outlier score of 7 or 'Severe pain.
- The median pain scores for all practices were similar.
- The lower fence / minimum score for all three practices was 0 (No pain).

A repeated measures ANOVA showed no statistically significant interaction between the different practices/techniques used and time, on mean pain scores: $F$ (6, 171) = 0.47, p=0.8279. In addition, there was no statistically significant difference between the three practices/techniques used, $F$ (2, 171) = 0.37, p=0.6906. There was, however, a statistically significant difference at the different time intervals: $F$ (3, 171) = 43.4, p<0.001.

A further post-hoc analysis using a pairwise comparison (Table 4.8) allowed the intercomparison of the pain scores of the three practices / techniques used over time and thereafter, a comparison of these findings with the ANOVA results. The pairwise comparison confirmed that at the beginning of the experiment and at 8 hours, 24 hours and 48 hours (end of the experiment), there was no statistically significant difference between the three practices / techniques used on the mean pain scoring (p>0.05).

**Table 4.8: Pairwise comparison (post-hoc) showing mean difference on pain scores between the three practices (brackets/techniques used) over time**

| Pairwise comparison: Gender and pain | Time interval | Contrast (Mean difference) | Standard error | 95% Confidence Interval for Mean Difference | | p-value |
|---|---|---|---|---|---|---|
| | | | | Lower Bound | Upper Bound | |
| Practice 2 vs Practice 1 | T0 – 4 hours | 0.48 | 0.601 | -0.703 | 1.653 | 0.429 |
| Practice 3 vs Practice 1 | | 0.18 | 0.601 | -1.003 | 1.353 | 0.771 |
| Practice 3 vs Practice 2 | | -0.3 | 0.601 | -1.478 | 0.878 | 0.618 |
| Practice 2 vs Practice 1 | T1 – 8 hours | 0.38 | 0.46 | -0.526 | 1.276 | 0.415 |
| Practice 3 vs Practice 1 | | -0.3 | 0.46 | -1.201 | 0.601 | 0.514 |
| Practice 3 vs Practice 2 | | -0.68 | 0.46 | -1.576 | 0.266 | 0.142 |
| Practice 2 vs Practice 1 | T2 – 24 hours | -0.23 | 0.440 | -1.088 | 0.638 | 0.609 |
| Practice 3 vs Practice 1 | | -0.2 | 0.440 | -1.063 | 0.663 | 0.650 |
| Practice 3 vs Practice 2 | | 0.03 | 0.440 | -0.838 | 0.888 | 0.955 |
| Practice 2 vs Practice 1 | T3 – 48 hours | -0.1 | 0.516 | -1.112 | 0.912 | 0.846 |
| Practice 3 vs Practice 1 | | -0.35 | 0.516 | -1.362 | 0.662 | 0.498 |
| Practice 3 vs Practice 2 | | -0.25 | 0.516 | -1.262 | 0.762 | 0.628 |

## 4.5 Summary of results

The dependent variable of 'pain' was measured against three groups of independent variables:

1. Medicaments (experimental medicament [chewing gum] vs placebo [sweets]):

Pain was significantly lower in the gum group (1.45 [0.98]) than the sweet group (3.6 [1.39]) after 48 hours ($p<0.001$).

2. Gender (male vs female):

Pain was significantly less in the male participants (2.02 [1.52]) than in the female participants (2.86 [1.59]) after 48 hours ($p=0.042$).

3. Bracket system / techniques used (Practice 1 vs Practice 2 vs Practice 3)

There was no statistically significant difference between the three practices / techniques used on mean pain scoring throughout the experiment ($p>0.05$).

# CHAPTER 5: DISCUSSION

## 5.1 Introduction

Chapter 5 evaluates and discusses the results obtained in the present study. Where possible, comparisons with other research trials were considered to demonstrate the similarities and differences in the findings. This chapter focuses primarily on the objectives, strengths and limitations of the methods and other relevant issues to highlight factors that may have influenced the results. Statements concerning the experimental hypothesis are made when relevant.

Pain is a common side effect of orthodontic treatment. Despite this, most orthodontists do not follow a protocol at the initial consultation and fitting of fixed appliances regarding pain management. Advice on pain is usually given post-procedurally when requested and includes the prescription of NSAIDs and other analgesic medication as the gold standard (Krishnan, 2007; Shedam, 2015). The side effects of non-steroidal anti-inflammatory medication is highlighted in the literature (Harirforoosh, Asghar & Jamali, 2013). More importantly, there is little information regarding preventative treatment options and minimal advice on the management of orthodontic pain.

The introduction of conventional sugar-free chewing gum at the onset of orthodontic treatment has been suggested for reducing the pain experience due to the ability of gum to suppress nociceptive responses via serotonergic (5-HT) descending inhibitory pathways (Kamiya *et al.*, 2010). In addition, it is possible that conventional gum may activate other endogenous mechanisms as part of a 'placebo effect' (Weijenberg & Lobbezoo, 2015). No other study to date has compared the effects of conventional sugar-free chewing gum with a placebo medicament. The discussion formulated in this thesis is based on how the results related to similar studies on chewing gum and orthodontic pain. The effects of placebos and the 'placebo effect' played a central role in the thesis and, therefore, much of the argument was a balance between the available scientific information and suggestions for future research. This is due to paucity in the available literature.

## 5.2 Limitations of the study

### *5.2.1 Sampling limitations*

The limitation of this study was the sample size of 60 participants. The study of Ireland *et al.* (2016), as discussed in subsection 5.4.1 below, included a large sample size of 826 participants, and a similar study in Pakistan in the same year comprised 250 participants (Waheed-Ul-Hamid *et al*., 2016). Although both these comparative studies displayed larger sample sizes, they had other limitations, including bias (through non-blinding techniques) and smaller variables for observational scrutiny.

The study of Shedam (2015) investigated the effects of sugar-free chewing gum in orthodontic pain and reported a similar sample size to the current study. There were, however, other methodological differences, including a less complex distribution of the sample into smaller subgroups than that of the current study. The total sample of 60 participants in the current investigation was determined from three practices (yielding subgroups containing 20 participants each). This was further divided into participants who received conventional sugar-free chewing gum as an intervention and those who received the placebo medicament (n = 10 each). Comparisons across subgroups did not yield inferential data, possibly due to the small numbers in each group and category and, therefore, descriptive comments were made in these instances.

The recruitment of participants was slow because it was a voluntary trial with no remuneration for participation. The recruitment of participants relied solely on the treating practitioner informing patients who conformed to the inclusion criteria about the study. This was not always followed through since the busy schedules of the practices limited transfer of relevant information pertaining to the study. Additionally, not all informed orthodontic patients who conformed to the inclusion criteria were willing to participate.

This study is unique in that it investigated both the physiological effect and the ‘placebo effect’ involved in reducing orthodontic pain; the limitations encountered are a minor component in comparison with the information gained. The results prompt further exploration in the usefulness of placebos and ‘placebo effects’ in orthodontics.

### *5.2.2 Bias*

Bias was limited in a few ways during the study. Participants were blinded and randomly allocated, using a random number generator software program (Random UX), and the research was conducted according to CONSORT principles. This is the optimum way to ensure significant outcome measures that can ultimately convert to clinical suggestions (Moher *et al.*, 2010). Bias was also minimised by the standardised procedure of measurement using a simple-to-understand VAS with specific time intervals set in the form of a diary so that patients of all ages could complete the questionnaires easily.

A potential bias may have arisen since the researcher was a treating clinician of some of the participants in one of the trial subgroups, which unintentionally could have influenced recruitment. This was, however, ethically matched with the researcher being blinded to the raw data and the results obtained until the full analyses by the statistician were documented. The use of an independent record keeper and double blinding reduced the bias regarding the observations that were recorded.

Other biases may have included the use of multiple variables. The subjective reporting of pain could have been affected by a combination of age, gender, bracket system fitted, the psychological state of the participant and the medicament allocated. This could have had an impact on the primary outcome measure of pain. In addition, the objectives were based on research questions and the factors influencing orthodontic pain and clinically, each objective highlighted in the thesis does not occur in isolation. A holistic approach is needed when managing pain in an orthodontic patient, while bearing in mind that numerous factors may influence their perceived pain.

The VAS is commonly used in pain studies to evaluate the pain experienced as a linear numerical value. Diagrammatic and worded descriptions may also be included. The values obtained are based on the subjective perception of pain rather than a physical measurement. This can be seen as a reliability bias. However, according to the definition of pain, if an experience is regarded as pain and if it is reported in the same way as pain caused by tissue damage, it should be accepted as pain (IASP, 1994). In addition, studies using brain mapping to understand pain further highlight the complexity of factors

affecting pain, pain perception and pain modulation (Bantick *et al.*, 2002). Therefore, no single assessment tool can be considered fully accurate.

### *5.2.3 Control omission*

A limitation of this study acknowledged retrospectively was the lack of a true control group (i.e. a group that received no intervention). As decided during the protocol phase, the control in this study was the use of a placebo. Although a placebo medicament is intended to have no clinical effect, an updated review of the literature during the thesis together with the results obtained proved that the 'placebo effect' does exist and in fact, reduces the total pain experienced (Bantick *et al.*, 2002; Benedetti, 2015). A 'no intervention' or true control group would have helped in establishing a baseline for orthodontic pain, allowing for better comparisons between the experimental group and the group receiving the placebo medicament and determining the overall 'placebo effect' in both groups receiving an intervention. Nonetheless, comparisons with the available scientific literature (mean and median pain scores in studies with no intervention) formed part of the discussion of this thesis. The study in India by Shedam (2015) demonstrated higher pain scores in the control group (no intervention) than the scores in both intervention groups of the current study. Some participants in the control group in the Indian study still reported pain after a week (Shedam, 2015). The benefits of the interventions in this study are discussed in Section 5.4.2 below.

The lack of a post-trial questionnaire to determine whether the participants believed they had received the experimental medicament, or the placebo medicament may be a limitation. This may have quantified the extent of the 'placebo effect' in pain regulation. However, such a questionnaire would have compromised the anonymity of the patient, raised ethical concerns by participants who felt pain during the experiment, and introduced bias.

## 5.3 Generalisability

As mentioned in the literature review, many factors influence pain perception, including the psychological state of the participant at the time. To differentiate the physiological effect from the placebo effect of conventional sugar-free chewing gum and its associated effect on pain levels is not easy. The thesis makes observations and remarks based on the sample population investigated and appreciates that data surrounding the whole pain experience is complex. The findings of this investigation form the foundation for further research in the effects of both physiological pain reduction and placebo-driven management. Larger sample sizes are needed to make inferences regarding gender and pain and different orthodontic techniques and pain.

## 5.4 Interpretation of results

This subsection initially discusses the sample population characteristics by comparing the baseline demographics with the relevant literature. Thereafter, pain reporting is discussed to fulfil the aim and the objectives of the study.

### *5.4.1 Sample population characteristics, bias, and assessment*

As mentioned in Chapter 3, the sample size was determined retrospectively. This was primarily done for the convenience of the three subgroups/practices. Due to slow recruitment and busy practice schedules, it was decided to terminate the study when a satisfactory sample size was reached, which concluded with 20 participants (n = 20) for each of the three practices. One-half of the participants received the experimental medicament and the other half received the placebo medicament, giving a total sample size of 60 participants (n = 60) (Figure 3.1).

Although a power calculation for this sample size was not electively done, the results pertaining to the number of participants for the primary outcome measure were comparable with similar studies that assessed chewing gum and orthodontic pain, allowing descriptive analyses and comparisons to be discussed. The study by Shedam (2015) in India recruited a congruent number of participants (n = 60) as the present study

and divided the sample population into two groups of 30 participants each. One group received the intervention of chewing gum and the other group received no intervention (control). Similarities between the study of Shedam (2015) and the current study were the inclusion criteria, recruiting patients between the ages of 13 years and 30 years with no gender preference and the use of VAS at similar time intervals to determine mean pain scores. The core differences in the methods of both studies were the sample distribution and the interventions. The current study introduced more variables (different subgroups using various orthodontic treatment protocols). In addition, the current study used two interventions groups (chewing gum and sweets) whereas the Indian study had one intervention group (experimental chewing gum) and one control group that received nothing. The current study compared the effects of chewing gum with a placebo and in doing so introduced the concept of 'placebo effects' in the management of orthodontic pain. The discussion on 'Pain Reporting' demonstrates the usefulness of this concept and helps to further the interest in this research field.

Two studies that investigated the effects of chewing gum on orthodontic pain used larger sample sizes than the current study. The Pakistan study of Waheed-Ul-Hamid *et al.* (2016) included 250 patients who were divided into two groups. One group received chewing gum as a means of pain control while the other received ibuprofen. The patients were required to take their prescribed pain control at the initial arch wire insertion and thereafter at 8-hour intervals until the seventh day. All patients were asked to complete a VAS questionnaire at 24 hours and after each arch wire change (Waheed-Ul-Hamid *et al.*, 2016). The study conducted in South West England by Ireland *et al.* (2016) across nine sites recruited 1 000 patients who were randomly assigned to a chewing gum or ibuprofen (control) group. The male-to-female ratios were similar in both groups, with patients aged 11–17 years forming the eligibility criteria (Ireland *et al.*, 2016).

Compared with the current study, the key features of the aforementioned studies included larger sample sizes and the use of NSAIDs (ibuprofen) as the alternative medicament or control instead of a placebo intervention. The participants of the study in Pakistan were given either chewing gum or ibuprofen at regular intervals and asked to evaluate pain scores after 24 hours (Waheed-Ul-Hamid *et al.*, 2016). The participants of the study in England were given either ibuprofen alone (control group) to use when necessary or were

given chewing gum and ibuprofen as a backup (experimental group) to use if they felt the chewing gum was ineffective in providing sufficient analgesia (Ireland *et al.*, 2016). A criticism of the method employed by Ireland *et al.* (2016) was the introduction of bias by allowing participants in the intervention group to use backup medication (ibuprofen) if they felt it was needed. While this may have been more ethically acceptable, it does not scientifically answer whether chewing gum alone was effective in managing pain since the participants were preconditioned to a backup. One could argue that this could have had a negative 'placebo effect' on the participants at the onset of the investigation, with the participants believing that chewing gum alone was ineffective. In contrast, the current study blinded participants to the intervention they received. Participants were more likely to have positive 'placebo effects' with either intervention, albeit through distraction.

The researcher and the participants in the Pakistan study of Waheed-Ul-Hamid *et al.* (2016) were blinded to the intervention, which is comparable with the current study in which the blinded information was only released once the results had been processed by a statistician. In contrast, the study by Ireland *et al.* (2016) did not include any blinding techniques, which increased the risk for bias despite the much larger sample size.

The reporting of clinical trials has come under scrutiny over the years where bias can have a damaging influence on treatment outcomes. The current study followed CONSORT guidelines in reporting both the methodology and the results obtained (Moher *et al.*, 2010). Proper randomisation was achieved using a random number generator software program (Random UX). There was, in addition, proper concealment of medicaments from the researcher, enrollers and participants, thus ensuring proper blinding.

Age effects on pain scoring did not form part of the assessed outcomes of this thesis. The thesis incorporated an inclusion criterion for age, and most patients undergoing fixed orthodontic treatment in this study were approximately the same age. The majority of participants in this investigation were between 12 years and 15 years of age (62%), with a mean age of 14.82 years (4.02) for all participants in the sample. Only 10% of the sample was over 20 years of age. Although ageing may change the way that pain is perceived, according to a general pain study (Eltumi & Tashani, 2017), an orthodontic

study that examined pain scores found that age did not affect the level of discomfort experienced by subjects undergoing fixed appliance treatment (Rahman *et al.*, 2016).

The current study used the VAS as a method of assessing orthodontic pain. According to the literature, verbal rating scales appear to have better response rates (Hjermstad *et al.*, 2011); however, compliance was not an issue in this study since all 60 questionnaires were returned. The VAS is widely accepted as a standard assessment tool (Klimek *et al.*, 2018). Similar chewing gum studies such as those of Ireland *et al.* (2016), Waheed-Ul-Hamid *et al.* (2016) and Shedam (2015) used VAS as a method for orthodontic pain assessment.

Other methods of assessing pain include brain imaging. However, analysing pain through imaging is not a simple process; pain is multimodal and often involves input and modulation for different areas in the brain (Bantick *et al.*, 2002).

### *5.4.2 Effects of medicaments on pain*

Conventional sugar-free chewing gum is an inexpensive and convenient option to consider for orthodontic pain management but requires further investigation. It is hypothesised that chewing gum reduces ischaemia in the periodontal ligament space by mechanical stretching; this suppresses nociceptive responses via serotonergic (5-HT) descending inhibitory pathways and thus reduces the initial pain response (Kamiya *et al.*, 2010).



The added benefits of gum emanate from its ability to improve oral hygiene (Imfeld, 1999) and to decrease anxiety through various psychosomatic pathways (Kamiya *et al.*, 2010; Weijenberg & Lobbezoo, 2015), possibly reducing or replacing NSAIDs as a treatment option for patients undergoing fixed appliance therapy (Ireland *et al.*, 2017).

All previous theories surrounding the ability of chewing gum to reduce orthodontic pain focused on its mechanical effects on the periodontal ligament, which is a physiological process. There have been no orthodontic studies investigating 'placebo effects' as a mechanism of reducing pain.

The ‘placebo effect’ is a psychobiological phenomenon that can be attributable to different mechanisms, including an expectation of clinical improvement (Benedetti *et al.*, 2005). It has been shown that patients can improve their pain experience by simple distractions (Finniss *et al.*, 2010).

The current study considered two philosophies, the physiological effects of conventional chewing gum and the ‘placebo effect’. Both intervention groups of the study were susceptible to this ‘effect’ due to blinding.

The primary outcome measure of the study was to compare the effect of the experimental medicament (conventional sugar-free chewing gum) with the effect of a placebo medicament (sugar-free sweets) on orthodontic pain scores following the placement of a fixed appliance.

Table 4.3 and Figure 4.2 (the profile plot) demonstrate that the mean overall orthodontic pain decreased over time in both intervention groups. Mean pain scores in the gum group were always lower than the placebo medicament, except at 8 hours (T1) where the mean pain scores were equal in both groups. The boxplot (Figure 4.3) showed a greater spread of pain data at T1 for the chewing gum group, with greater upper and lower limits. The IQR and median pain scores were, however, equal for both intervention groups at T1, which further emphasised that the slight upward trend in the profile for gum was not statistically or clinically significant. At the end of the experiment (T3 = 48 hours), it was shown that participants in the chewing gum group had the greatest reduction in mean pain scores compared with the placebo group, with a difference of 2.15, 95% CI (1.54 to 2.76), which was statistically significant ($p<0.001$).

The majority of the participants in the chewing gum group reported pain scores less than 2 on the VAS at the end of the experiment, while most participants in the placebo group still reported scores between 2.5 and 3.5, with the highest recording being 6.5. This suggests moderate pain in the placebo group even at the end of the experiment (Figure 4.3).

This study, therefore, suggests that both conventional sugar-free chewing gum and the placebo, sugar-free sweets, reduce orthodontic pain over time, but that chewing gum is

more effective at reducing pain and significantly reduces pain between 24 hours and 48 hours.

As seen in the profile plot (Figure 4.2), both medicaments possibly have positive placebo effects on pain reduction. The rapid reduction in the mean pain scores of the chewing gum group at the time interval (T2–T3) suggests that chewing gum has both a positive psychological effect and a positive biological or physiological effect on pain relief and that these effects are superior to those of the placebo. These effects are supported in the literature. Long *et al.* (2016) describe the complex physiological process that is involved when an orthodontic force is applied to a tooth. This process includes a vascular, cellular and chemical response, which can be modulated along various points of the central nervous system (Long *et al*., 2016). Kamiya *et al.* (2010) postulated that chewing gum physically reduced pain by stretching the periodontal ligament and suppressing nociceptive responses. Ireland *et al.* (2016), Shedam (2015) and Waheed-Ul-Hamid *et al.* (2016) all showed the pain-reducing effects of chewing gum in orthodontic treatment. Furthermore, the literature demonstrates that although the onset of pain relief with chewing gum is slightly delayed, it is more effective in reducing pain once it takes effect (Ireland *et al.*, 2016).

Orthodontic studies have not reported the usefulness of placebo treatments in pain reduction. However, in general pain studies, chewing gum has been shown to be beneficial as a distractor, demonstrating positive 'placebo effects' in lowering perceived pain (Kamiya *et al.*, 2010). This effect is seen in the current study in which the mean baseline scores (T0) and the subsequent mean pain scores (in both intervention groups) are lower than the mean pain scores at similar time intervals in other studies that compared the effects of sugar-free chewing gum or controls on orthodontic pain (Ireland *et al.*, 2016; Shedam, 2015; Waheed-Ul-Hamid *et al.*, 2016).

Waheed-Ul-Hamid *et al*. (2016) reported mean baseline scores for chewing gum intervention at a level of 7.72 (1.49) and a control (ibuprofen) mean baseline score of 7.78 (1.28) using similar VAS scales to the current study. In comparison, the current study showed mean baseline scores of 4.6 (1.73) for chewing gum and 5.2 (2.01) for the placebo (sweets) medicament. The lower pain scores in this study than in the Pakistan study of Waheed-Ul-Hamid *et al.* (2016) are most likely due to a positive 'placebo effect' that

participants may have experienced, especially since the other comparative variables such as age, gender distribution and time intervals were similar for both studies. Similar remarks can be made when comparing the current study with the study of Shedam (2015). As discussed in Section 5.2.3 above, the current study displayed lower pain scores in both intervention groups than the control group in the Indian study (Shedam, 2015). This shows that both conventional chewing gum and placebo medicaments are effective in lowering pain scores compared with the natural regression of pain displayed in the control groups with no intervention (Shedam, 2015).

The study of Eslamian, Dehghani and Amraie (2016) compared a medicated (ketoprofen) gum with conventional gum and an anaesthetic gel. The study showed that participants in the ketoprofen gum group reported mean pain scores that were slightly lower than participants in the conventional gum and anaesthetic gel groups, but the scores were not statistically or clinically significant (Eslamian, Dehghani & Amraie, 2016). There is a lack of evidence in the efficacy of medicated gum. Furthermore, side effects are still unknown. The hypothesis that chewing gum reduces orthodontic pain through mechanical effects holds true if one looks at the similar pain scores of conventional gum and medicated gum in the study of Eslamian, Dehghani and Amraie (2016) (Kamiya *et al.*, 2010).

Orthodontic pain is known to start shortly after a fixed appliance has been fitted (Ertan Erdinç & Dinçer, 2004). This holds true for the current study in which pain was high at the start of the experiment (T0). According to Bergius, Kiliaridis and Berggren (2000), pain peaks at 24 hours following the placement of fixed appliances with no intervention. In contrast, the current study showed a decline in mean pain scores for both intervention groups over time. The mean pain scores of participants with gum were always lower than the mean scores of participants with the placebo, except at (T1) where the scores were equal. There was also no 'Peak pain' noted in this study (see Figure 4.2*)*. At 24 hours, both intervention groups showed a marked decrease in mean pain scores compared with other studies (Krishnan, 2007). This shows that conventional chewing gum and the placebo medicament are effective in reducing orthodontic pain. The physiological and psychosomatic effects of conventional gum significantly reduced orthodontic pain at 48 hours when compared with the placebo, making conventional gum a more effective

medicament in reducing orthodontic pain. The experimental/alternative hypothesis (H1) is, therefore, accepted: There will be a significant difference between the analgesic effects of conventional sugar-free chewing gum and a placebo medicament (sugar-free sweets) in pain resolution following the placement of fixed orthodontic appliances. This was seen at 48 hours.

### *5.4.3 Role of gender (male and female) on pain*

Pain is influenced by a multitude of factors. The literature regarding gender and pain perception is scanty. According to studies, more females receive treatment for pain-related conditions than males. Females also report more severe pain, more frequent pain and pain of longer duration than males (Dao & LeResche, 2000). Other reviews have also claimed that post-operative and procedural pain may be more severe among women than men, including greater pain sensitivity among females than males for most pain modalities (Fillingim *et al.*, 2009).

Orthodontic pain is a unique 'pressure-related pain' induced by an inflammatory cascade (Long *et al.*, 2016). Chesterton *et al.* (2003) found that healthy females exhibited a significantly lower mean PPT than males. This is similar to the findings of Racine *et al.* (2012) who found that females and males have comparable thresholds for cold and ischaemic-type pain, while PPTs are generally lower in females (Racine *et al.*, 2012).

The current sample comprised 60% female participants (Table 4.1) and, therefore, information regarding gender and pain prompted the researcher of this study to examine if there were any significant differences on how males and females reported orthodontic pain.

This study found that the mean pain scores (Table 4.5 and Figure 4.4) for male and female participants were equal at T0 and T2. However, at T3, the male participants scored a significantly lower mean pain score (2.0 [1.39]) than the female participants (2.9 [1.59]). This was confirmed with post-hoc pairwise comparisons (Table 4.6), with a difference of -0.84, 95% CI (-1.65 to -0.29) ($p<0.001$).

Similar mean pain scores reported across time intervals T0, T1 and T2 do not support the arguments of Chesterton *et al*. (2003) and Racine *et al*. (2012) that PPTs are lower in females than males. According to these arguments, the female participants in the current study should have reported higher pain scores in the earlier intervals of the experiment. Hence, the results obtained may be attributed to other variables affecting the mean pain scores such as the medicaments used by the participants. Chewing gum reduces nociceptive responses via serotonergic (5-HT) descending inhibitory pathways and thus reduces the initial pain response (Kamiya *et al.*, 2010). A positive 'placebo effect' may also reduce pain perception (Enck, Benedetti & Schedlowski, 2008). A combination of both these effects may have contributed to similar pain reporting by both the male and female participants during the initial time intervals. Of the population in the current study, 77% of the female participants received the placebo medicament and despite this, pain reporting remained similar for both sexes in the first 24 hours of the experiment, which is contradictory to the current literature in which females are expected to report higher pain scores (Averbuch & Katzper, 2001; Racine *et al.*, 2012). This suggests that in this population, the female participants were initially more affected by 'positive placebo effects' than their male counterparts.

At 48 hours, there was a significant difference in mean pain reporting, with females reporting more pain than males ($p<0.001$). This supports the current literature that females have a lower threshold for pain and report pain for a longer duration (Dao & LeResche, 2000; Chesterton *et al.*, 2003; Racine *et al.*, 2012). This could be due to the 'placebo effect' wearing off in the 77% of female participants who received the placebo medicament. The placebo medicament initially had a positive 'placebo effect' but eventually allowed the process to follow a natural progression over time. This is further supported by Aslaksen *et al.* (2011) who claim that women are less susceptible to 'placebo-related effects' than men in experiencing pain. As discussed in the 'medicament vs pain' section above, chewing gum was shown to reduce mean pain scores significantly. Most male participants (71%) used chewing gum and, therefore, displayed lower pain scores than the female participants (77%) who mainly used the placebo medicament.

Enck, Benedetti and Schedlowski (2008) indicated that gender cannot be assessed in complete isolation when comparing pain and 'placebo effects'. Other factors such as

menstrual cycle variation, age, maturation, trust perceptions and adjunct medications may have compounding effects on pain reporting. These factors could have affected the results in the current study. Further research is required, including measuring pain for more than 48 hours, before suggesting that females report more pain and are less affected by placebo treatment than males (Enck, Benedetti & Schedlowski, 2008).

### *5.4.4 Techniques (bracket systems) and pain reporting*

As a marketing strategy, there are individual claims that certain bracket systems are of superior quality. The current study investigated orthodontic pain and how different techniques and/or bracket systems may have influenced such reporting. The sample population was stratified in three subgroups or practices, as mentioned in Chapter 3 and Chapter 4. Practice 1 and Practice 3 used similar techniques (MBT/Edgewise brackets) with conventional ligation. Practice 1 (specialist practice) used brackets with a 022 slot size and commenced treatment with 0.014 NiTi initial wires, while Practice 3 (general dental practice) used smaller bracket slot sizes (018), commencing with 0.012 NiTi initial wires. Practice 2 (specialist practice) employed a self-ligating (Damon™ passive) bracket system with 022 bracket slots and commenced treatment with 0.014 Copper NiTi initial wires.

Self-ligating brackets have become increasingly popular in practice, which can be attributed to claims that their advantages over conventional appliance systems lie in their ability to reduce frictional resistance, overall treatment time and subjective pain and discomfort (Miles, 2009). Fleming and Johal (2010) demonstrated that by 2008, 42% of American practitioners had incorporated a self-ligating system in their practice compared with 9% in 2002. Despite this, the MBT™ system is equally preferred due to a more desired increased palatal and lingual torque of incisors (Moesi, Dyer & Benson, 2013).

Using repeated ANOVA measures for orthodontic pain, the current study found no statistically significant differences between the bracket systems / techniques used and the mean pain scores over time ($p>0.5$). The information in the literature regarding bracket systems, techniques and pain is both scanty and controversial. Miles, Weyant and Rustveld (2006) reported that initially, participants expressed less pain with the Damon

SLBs but significantly more pain than conventional brackets when engaged with a 0.016 NiTi wire ten weeks later. The study minimised bias by following a split-mouth technique (Miles, Weyant & Rustveld, 2006).

On close inspection of the related boxplot (see Figure 4.7), it can be seen that the median pain scoring for Practice 1 and Practice 3 (conventional MBT ligation) was equal to the first quartile (lower 25%) scoring of Practice 2 (Damon self-ligating). Practice 2 displayed the lowest IQR; however, outliers in the lower and upper pain extremities were noted. This result (see also Figure 4.6) indicates that participants in the current study with SLBs (Practice 2) demonstrated slightly higher pain scores initially, although this was not statistically significant. Rahman *et al.* (2016) support this finding; the participants in their study also reported higher levels of initial pain with 0.014 arch wires ligated to SmartClip™ SLBs than the Victory™ conventional MBT™ Edgewise system.

The current findings are, however, debatable. A review by (Fleming & Johal, 2010).and Miles, Weyant and Rustveld (2006) concluded that in the initial phase of treatment, patients with SLBs reported lower pain scores than patients with conventional brackets. It is, however, important to note that Fleming *et al.* (2009) and (Fleming & Johal, 2010).clearly stated that the difference in pain reporting of conventional brackets versus SLBs was not statistically significant, which correlates with the findings of the current study. Further review with larger sample sizes and less compounding variables to evaluate whether bracket choice and techniques play a significant role in orthodontic pain is needed.

There are no studies documented that assess the difference in mean pain reporting between participants receiving treatment at a specialist orthodontic practice versus a general dental practice. However, the findings in the current study indicate that participants in the general dental practice reported slightly lower pain scores throughout the experiment, except at the initial interval with no intervention. The lower pain scores could be due to treatment commencing with a super elastic 0.012 NiTi initial wire compared with the specialist practice specialist practice that used a similar system (MBT) but with a slightly larger, conventional NiTi initial wire. Although these differences were not statistically significant, they may have clinical implications. Fernandes, Ogaard and Skoglund (1998) compared initial pain between super elastic NiTi arch wires and

conventional NiTi in a study with 128 participants over three sites. The results showed that during the first ten hours, it was apparent that the pain experienced after placement of a super elastic NiTi arch wire was less than that found with a conventional NiTi arch wire, although a significant difference was only found at 4 hours (Fernandes, Ogaard and Skoglund, 1998). This supports the evidence in the current study, although no significant differences were found at any time interval or between any of the systems. Other studies have investigated whether the size and the material of the initial arch wire play a significant role in orthodontic pain. As mentioned in Chapter 2, there are limited published reports that assess arch wire types and associated pain as an isolated topic. The systematic review by Wang *et al.* (2018) consisted of 12 trials and considered different initial arch wires and the effects that they had on rate of alignment, root resorption and pain. The review found moderate quality evidence that there is no difference in pain at Day 1 between multistrand stainless steel arch wires and super elastic NiTi arch wires following placement of a fixed appliance. There was also insufficient evidence to determine whether any specific arch wire material proved superior in terms of alignment rate, time to alignment, pain and root resorption (Wang *et al.*, 2018).

The current study found that there is no significant difference in pain scores associated with a specific orthodontic bracket system or technique. The results in literature that compare pain reporting with self-ligating systems and conventional brackets using the MBT technique are debatable. One can infer that the lowering of pain scores in this study was more closely related to the medicaments used by the participants than to any specific technique.

# CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

Chapter 6 concludes the findings and discussion of the thesis. The objectives of the study were achieved satisfactorily. Clinical implications and suggestions for future research are presented.

The current study found that conventional sugar-free chewing gum was effective in reducing orthodontic pain associated with fixed orthodontic treatment when compared with a placebo medicament. Both conventional sugar-free chewing gum and the placebo medicament reduced orthodontic pain over time; however, at 48 hours, chewing gum significantly reduced pain when compared with the placebo ($p<0.001$). This is most likely due to the combined physiological and 'placebo effect' of conventional sugar-free chewing gum. The experimental hypothesis is, therefore, accepted. In addition, the mean pain scores in both intervention groups throughout the study were lower than the pain scores in the intervention and control groups (no intervention) documented in similar studies.

Regarding gender and pain, male participants showed significantly lower mean pain scores after 48 hours than female participants, which is supportive of the literature.

All practices showed a decrease in mean pain scores over time. However, there was no significant differences between the different orthodontic systems in reducing orthodontic pain. The reduction of pain over time was more closely related to the medicaments used than the techniques employed.

Orthodontic pain is complex and 'placebo effects' require further review. The benefits of conventional sugar-free chewing gum have been demonstrated, and clinical use is recommended either in combination with other medicaments or alone.

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# ANNEXURES

## Annexure A: Patient Information Sheet


UNIVERSITY *of the*
WESTERN CAPE

**UNIVERSITY OF THE WESTERN CAPE**

**BIOMEDICAL RESEARCH ETHICS COMMITTEE**

**APPLICATION FOR ETHICS APPROVAL**

**For research with human participants (Biomedical)**



**Information Sheet to Participate in Research**

Date: May 2017

Dear Patient

My name is Dr Yolin Govender. I work as a sessional staff member in the Department of Orthodontics and Oral Surgery, at the Faculty of Dentistry, University of the Western Cape, South Africa. I also work in private practice at Medicross Tableview. I am a registered Masters (MSc) student (2382468) at the University of the Western Cape.

Contact Details:

Phone: 021 5571614 (w)

Email: yolingovender@yahoo.com

You are being invited to consider participating in a study that involves assessing and managing pain during orthodontic treatment. The aim and purpose of this research is to help assess what level of pain patients experience during orthodontic treatment and if certain interventions influence those levels. The study is expected to enroll 60 patients, 20 patients will be treated at this orthodontic practice and 40 patients will be treated at 2 other practices. It will involve patients undergoing fixed orthodontic treatment. If you agree to participate in the study, you will be randomly selected to either be part of a control group or experimental group. For the validity of the results, you will not be aware of which group you belong to. Two medicaments are being tested. The one medicament will be chewed for 5- 10 mins and then discarded, while the other medicament will be sucked till it is completely dissolved. You will only receive one medicament. A questionnaire to rate pain will need to be completed by yourself. The experiment lasts 48 hours. The instructions on when to take the medicament are outlined in the questionnaire. This study will be funded by myself, and there will be no financial commitments from you, regarding the purchase of the medicaments.

The study is using medicaments that have minimal side effects such as an increase in bowel movement (laxative effect). You will also be required to use the medicaments gently to avoid any breakage to your braces. We hope that the study will give us a guideline on how to manage orthodontic pain. If you experience any discomfort that you feel you cannot manage, you must contact your orthodontic practice immediately for further advice and you will possibly receive alternative treatment for pain.

This study has been ethically reviewed and approved by the UWC Biomedical Research Ethics Committee (approval number BM17/7/11).

This is a voluntary study, done at your own risk, and the treating practitioner and researcher cannot accept responsibility for any injury occurred during the participation in the study. Anonymity will be preserved with regards to the feedback, given. The practice names and medicament names will also be kept confidential for ethical reasons.

The name and telephone number of patients agreeing to participate will be kept in a confidential file; no other information will be kept, and the file will be discarded once the feedback boxes are collected by the researcher.

In the event of any problems or concerns/questions you may contact the researcher at (yolingovender@yahoo.com) or the UWC Biomedical Research Ethics Committee, contact details as follows:

**BIOMEDICAL RESEARCH ETHICS ADMINISTRATION**
University of the Western Cape
Research Office
New Arts Building
C-Block, Top Floor, Room 28.
Western Cape, SOUTH AFRICA

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## Annexure B: Informed Consent


UNIVERSITY *of the*
WESTERN CAPE

**INFORMED CONSENT FORM**

I (Name) _____ have been informed about the study by Dr Yolin Govender.

I understand the purpose and procedures of the study.

I have been given an opportunity to ask questions about the study and have had answers to my satisfaction.

I declare that my participation in this study is entirely voluntary and that I may withdraw at any time without affecting any treatment or care that I would usually be entitled to.

I have been informed about any available compensation or medical treatment if injury occurs to me, as a result of study-related procedures.

If I have any further questions/concerns or queries related to the study I understand that I may contact the researcher at (yolingovender@yahoo.com).

If I have any questions or concerns about my rights as a study participant, or if I am concerned about an aspect of the study or the researcher then I may contact:



**BIOMEDICAL RESEARCH ETHICS ADMINISTRATION**
University of the Western Cape
Research Office
New Arts Building
C-Block, Top Floor, Room 28.
Western Cape, SOUTH AFRICA
Tel: 27 21 9592988

_____ _____
**Signature of Participant** **Date**

_____ _____
**Signature of Witness** **Date**
**(Where applicable)**

_____ _____

**Signature of Translator** **Date**

**(Where applicable)**

**Annexure C: Patient Instructions for Medicament Use**

The instructions below were provided in the sealed envelope retained by the patient when leaving the treating practice. Only 1 of the instructions appeared in any single given envelope:

## Patient Instructions

***Instruction for use***

***The medicament contained in this envelope should be chewed GENTLY for a TOTAL of 5 to 10 mins;***

***Chew on your Back teeth (Right Side 2 – 4 mins, Left Side 2 – 4 mins) and Front teeth (1 – 2 mins)***

***Use only 1 medicament at a time, when you are instructed by the Questionnaire/Diary.***

***OR***

***Instruction for use***

***The medicament contained in this envelope should be sucked until completely dissolved. This will usually take 5 – 10 mins on average.***

***Use only 1 medicament at a time, when you are instructed by the Questionnaire/Diary.***

**Annexure D: Self-Administered Questionnaire**

## Questionnaire NUMBER:_____

Thank you for agreeing to participate in this study. After you have read the *Patient Information* sheet and signed the Informed Consent form, you may complete the Questionnaire. The questionnaire, in part, follows the format of a diary. Please read the questionnaire beforehand so that you will know how to plan to complete it. Answer the questions and follow the step by step instructions. The Questionnaire runs over 48 hours from the time you have your braces fitted.

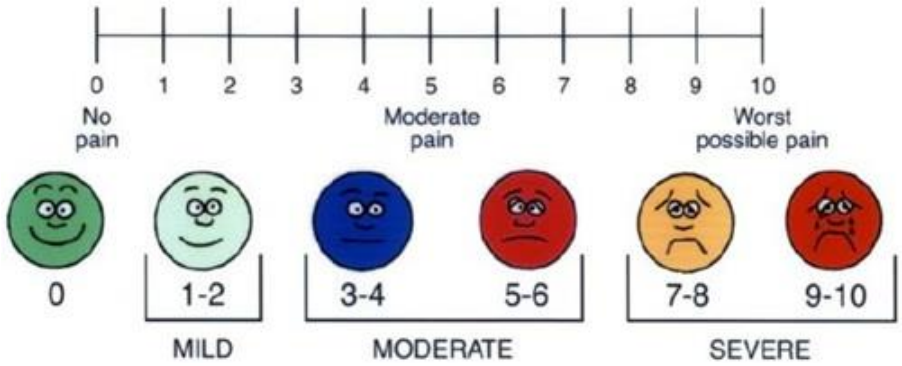
---

1) Age:_____
2) Gender: ☐ M
   ☐ F
3) Why are you getting braces?:
   _____
4) What Date and Time did you have you braces fitted?
   _____

**WAIT 4 HOURS after getting your braces before you continue with the next instruction :**



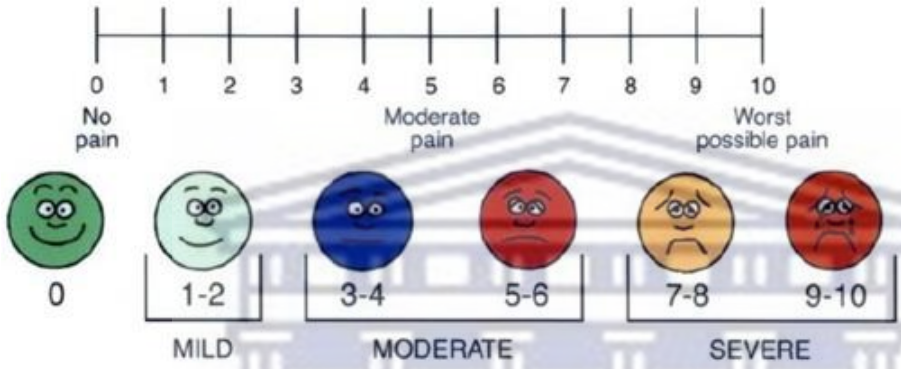
4.1) Mark your level of pain (with a single visible dot) at this point **on the chart below.**




**Wait 4 hours and continue with the next instruction**

**After answering question 4.1, <u>take the medicament</u> you were given <u>immediately</u> and use it according to the instructions given in the envelope. Then continue to answer 5.1 - 5.3**

5.1) Mark your level of pain (with a single dot) at this point **<u>on the chart below</u>**




5.2) Did you use the medicament according to the instructions given in the envelope?
_____

5.3) Record the time now . *eg 6pm in the evening* _____

# DAY 2

**GOOD MORNING**

6.1) Did you take ANY medication during the night (including the medicament which we are testing) ? If so, Record the name of the medication and the time at which you took it:

_____

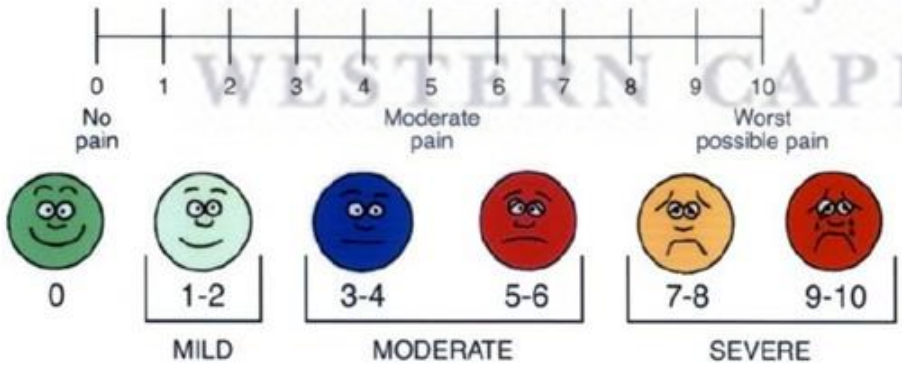
**Wait until its 24 hours since your braces were fitted and continue with the next question**

*If you are going to school /work today, remember to take the questionnaire and medicaments in the envelope with. If you are in school, take the letter explaining that you are part of a study.*

---

**After answering question 6.1, take the medicament you were given immediately and use it according to the instructions given in the envelope. Then continue to answer 6.2 - 6.4**

6.2) Mark your level of pain (with a single dot) at this point **on the chart below.**




6.3) Did you use the medicament according to the instructions given in the envelope?

_____

6.4) Record the time now . *eg 10am in the morning*

_____

**Wait until its 48 hours since your braces were fitted and continue with the next question**

# DAY 3

**GOOD MORNING**

7.1) Did you take ANY medication (including the medicament we are testing) during the night? If so, Record what you took and at what time.

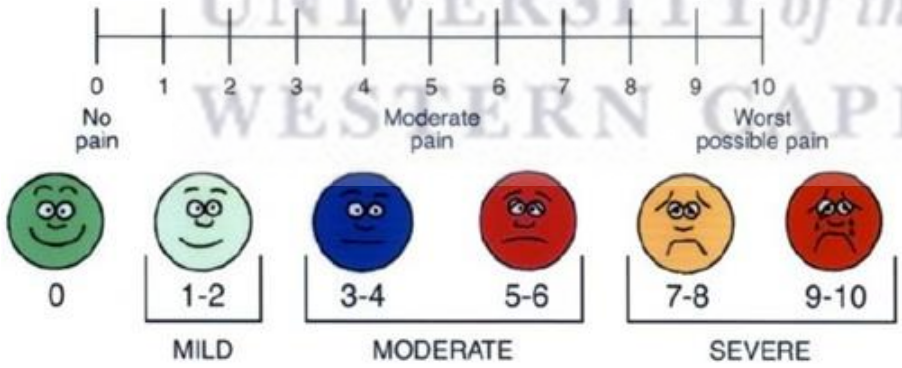
---

*If you are going to school /work today, remember to take the questionnaire and medicaments in the envelope with. If you are in school, take the letter explaining that you are part of a study.*

---

**After answering question 7.1, take the medicament you were given immediately and use it according to the instructions given in the envelope. Then continue to answer 7.2 - 7.4**

7.2) Mark your level of pain (with a single dot) at this point **on the chart below.**




7.3) Did you use the medicament according to the instructions given in the envelope?

_____

7.4) Record the time now . *eg 10am in the morning*

_____

**Thank you for being a part of this study.**

**Annexure E: Letter of Participation (for school)**


UNIVERSITY *of the*
WESTERN CAPE

May 2017

My name is Dr Yolin Govender. I work as a sessional staff member in the Department of Orthodontics and Oral Surgery, at the Faculty of Dentistry, University of the Western Cape, South Africa. I also work in private practice at Medicross Tableview. I am a registered Masters (MSc) student at the University of the Western Cape.

Contact Details:

Phone: 021 5571614 (w)

Email: yolingovender@yahoo.com

The student presenting this letter is part of a clinical research trial regarding orthodontic pain and anxiety. They have been asked to use a medicament (which needs to be chewed or sucked) at specific intervals and to provide feedback in a questionnaire, structured like a diary, for 48 hours.

Please accomodate the student during the experiment, by allowing them to use the medicament when needed. Their participation in this study is valuable and could benefit other patients undergoing orthodontic treatment

If you have any concerns or questions, please feel free to contact me.

Regards

Dr Y Govender

BChD (Stell, wc), PDD (Orthodontics), PDD (Minor Oral Surgery)