PAIN ASSOCIATED WITH INVISALIGN VERSUS CLEAR TRADITIONAL BRACKETS: A RANDOMIZED, PROSPECTIVE TRIAL

A Thesis

by

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ABSTRACT

The purpose of the present study is to compare the pain levels, analgesic consumption, and sleep disturbances associated with Invisalign aligners (Align Technology, Santa Clara, Calif) and traditional fixed appliances at multiple time points.

A prospective, randomized cohort study was conducted that included 41 adult patients who were treated with either traditional fixed appliances (6 males and 12 females) or aligners (11 males and 12 females). Patients completed a daily discomfort initially following bonding or delivery of the aligners, after one month, and after two months. At each occasion, patients were asked to record their analgesic consumption, sleep disturbances, along with their pain at rest, while chewing, while biting on their front teeth, and when biting on their back teeth.

Both treatment modalities demonstrated similar pain values at baseline. There were no significant sex differences. Patients in the traditional fixed appliances group consistently reported higher pain scores than the patients in the Invisalign aligners group. Depending on the question, the treatment group differences were statistically significant ($p<0.05$) most days during the first week. Aligner patients also reported significantly lower pain than the traditional treated patients after the first and second months. Pain scores after the subsequent adjustments were consistently lower than after the initial bonding or aligner delivery. A higher percentage of patients in the fixed appliances group reported taking analgesics during the first week for dental pain, but only the difference on day 2 was statistically significant.

Aligner treatment is significantly less painful than traditional fixed appliances. Patients treated with aligners consume fewer analgesics than patients treated with traditional appliances.

DEDICATION

I would like to dedicate this thesis to my wonderful wife, Bonnie White, and to our two daughters, Audrey and Eliza White. They have supported me from the beginning and have made a lot of sacrifices to help me get to this point. I would also like to dedicate this thesis to my parents, Ronald White and Barbara Snider. Both of them have done everything possible to help me succeed in life.

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NOMENCLATURE

CNS	Central Nervous System
CuNiTi	Copper Nickel Titanium
GCF	Gingival Crevicular Fluid
IASP	International Association for Pain
IL-1β	Interleukin 1 beta
IL-6	Interleukin 6
LLLT	Low Level Laser Therapy
NiTi	Nickel Titanium
NRS	Numeric Rating Scale
NSAID	Non-steroidal Anti-inflammatory Drugs
PDL	Periodontal Ligament
PGE2	Prostaglandin E_2
PGI2	Prostaglandin I_2
TENS	Transcutaneous Electrical Nerve Stimulation
TNF-α	Tumor Necrosis Factor alpha
VAS	Visual Analog Scale
VRS	Verbal Rating Scale

TABLE OF CONTENTS

Page

ABSTRACT ii

DEDICATION iv

ACKNOWLEDGEMENTS v

NOMENCLATURE vi

TABLE OF CONTENTS vii

LIST OF FIGURES viii

LIST OF TABLES ix

CHAPTER I INTRODUCTION AND REVIEW OF THE LITERATURE 1

Introduction 1
Review of the Literature 4

CHAPTER II PAIN ASSOCIATED WITH INVISALIGN VERSUS CLEAR TRADITIONAL BRACKETS: A RANDOMIZED, PROSPECTIVE TRIAL 24

Introduction 24
Materials and Methods 25
Results 29
Discussion 32

CHAPTER III CONCLUSIONS AND CLINICAL APPLICATIONS 38

Conclusions 38
Clinical Applications 38

REFERENCES 39

APPENDIX A 46

APPENDIX B 58

LIST OF FIGURES

Page

Figure 1. Diagram of patient flow through the study 46

Figure 2. Patient treatment and daily diary timeline 47

Figure 3. Median pain levels for Invisalign and traditional treatment groups in response to the question: “Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign.” 50

Figure 4. Median pain levels for Invisalign and traditional treatment groups in response to the question: “Rate how much discomfort you experienced the last time that you chewed.”..50

Figure 5. Median pain levels for Invisalign and traditional treatment groups in response to the question: “Rate how much discomfort you are experiencing when you bite down on your back teeth?”..51

Figure 6. Median pain levels for Invisalign and traditional treatment groups in response to the question: “Rate how much discomfort you are experiencing when you bite down on your front teeth?” 51

Figure 7. Median pain levels for traditional treatment patients at rest and while chewing. 52

Figure 8. Median pain levels for traditional treatment patients while biting down on the front and back teeth...52

Figure 9. Median pain levels for Invisalign patients at initial bonding, 1 month adjustment and at the 2 month adjustment in response to the question: “Rate how much discomfort you are experiencing when you bite down on your front teeth?” 55

Figure 10. Median pain levels for traditional patients at initial bonding, 1 month adjustment and at the 2 month adjustment in response to the question: “Rate how much discomfort you are experiencing when you bite down on your front teeth?” 55

Figure 11. Percentages of patients who took medications for tooth pain during the first week after the initial appliance placement or Invisalign delivery.............55

Figure 12. Percentages of patients who had sleep disturbance from tooth pain during the first week after the initial appliance placement or Invisalign delivery.......57

LIST OF TABLES

Page

Table 1. Pain [medians (Med) and interquartile ranges] associated with Invisalign and traditional orthodontic treatment at initial delivery or appliance placement. ...48

Table 2. Pain [medians (Med) and interquartile ranges] associated with Invisalign and traditional orthodontic treatment for the first month adjustment......................53

Table 3. Pain [medians (Med) and interquartile ranges] associated with Invisalign and Traditional orthodontic treatment for the second month adjustment................54

Table 4. Percentages of patients who took medications for tooth pain after the first, second, and sixth month adjustments. 56

Table 5. Percentages of patients who had sleep disturbance from tooth pain after the first, second, and sixth month adjustments. 57

CHAPTER I

INTRODUCTION AND REVIEW OF THE LITERATURE

INTRODUCTION

Pain and discomfort are common side effects of orthodontic treatment. According to a study by Scheurer et al. conducted on 170 patients, 95% of the patients reported feeling pain within 24 hours of insertion of orthodontic appliances.[1] They reported that the average pain level was 42% of maximal pain. Kvam et al. confirmed the high prevalence of pain in orthodontics when they evaluated the experience of patients treated in both private practice and a graduate program in Oslo, Norway.[2] Of the 161 patients, 95% had experienced pain during treatment and 11% maintained that they were constantly in pain. Approximately 85% of the patients felt as though the pain only lasted two to three days. Another study conducted in Singapore found that 91% of 368 Chinese patients experienced transient pain and 39% experienced pain with each new archwire or elastic force application.[3]

The main factor causing pain has been shown to be the initial application of orthodontic forces.[2, 4-6] There are also other situations and appliances that have been shown to stimulate painful responses in orthodontic patients. While Kvam et al. demonstrated that archwire changes were the most painful part of their orthodontic treatment, they also showed that approximately 76% of patients had some form of oral ulceration during treatment.[2] 2.5% of their patients described the ulcers as being "very painful." Similarly, Otasevic et al. found oral ulcers in 42% of their sample of orthodontic patients.[7] Rapid maxillary expanders have also been shown to cause pain in 85% of patients over the entire course of treatment.[8] Most patients reported pain between the 4th to the 7th day of expansion. The Herbst appliance, which is commonly used in class II dentoskeletal corrections, has been reported to be a potential cause of pain in the masticatory system.[9] Lastly, 16% of patients with a class III skeletal pattern who were treated with chin cup therapy developed symptoms of temporomandibular joint disorder.[10] Deguchi et al. theorized that posterior positioning of the condyle caused anterior displacement of the disk, which led to both pain and clicking upon opening.

As members of a health-care profession, orthodontists traditionally are concerned about their patient's well-being. They desire to provide necessary treatment in a time appropriate manner, while attempting to minimize painful side effects. In addition to this motivation, orthodontists should be very concerned about causing pain in their patients, because it alters patients' behaviors in ways that often lead to negative consequences. Even before treatment begins, fear of pain is one of the primary reasons that patients fail to seek orthodontic care.[11] O'Connor conducted a study that found that injury from wires sticking out and dental pain are the 2nd and 4th most commonly selected fears of patients prior to starting orthodontic treatment.[12] He also found that pain was the greatest dislike during treatment, above even appearance, headgear, or waiting-room delays.

During treatment, orthodontic pain has numerous negative effects on both the patient and the treatment outcomes. Jones and Chan found that 22% of patients reported that pain disturbed their sleep.[13] This was supported by Scheurer et al., who reported that 18% of patients claimed to have been awoken by pain during the first night after fixed appliance placement.[1] Patients often have trouble eating the foods they are accustomed to while undergoing orthodontic treatment. Otasevic et al. found that 54% of the patients in their study reported difficulties eating and chewing that led to a change in diet.[7] As treatment continues and patient's begin to resent being in pain, their compliance to treatment starts to decrease. Sergl et al. found that compliance is negatively associated with increasing complaints of pain.[14] Krukemeyer et al. stated that pain from orthodontic treatment had a negative effect on both oral hygiene efforts and was a major factor in patient's missing appointments.[15] Ultimately, some patients tire from being in pain and seek to end treatment early. Patel reported that almost 1 out of every 10 patients will interrupt their treatment early due to painful experiences. Haynes suggested that pain from orthodontic appliances and its effect on a patient's daily life were major reasons for discontinuance of treatment.[16]

Invisalign aligners have been used as a treatment modality since 1998 for those patients who desire an esthetic orthodontic appliance. Since they were brought to the market, there have been very few studies which have compared the effects of Invisalign to traditional fixed appliances.[17-19] The purpose of this study was to evaluate specifically the differences in pain levels and analgesic consumption between the two treatment modalities at multiple time points. The hypothesis is that Invisalign aligners will produce less pain than traditional fixed appliances, due to its nature as a removable appliance that provides intermittent forces. The study will help orthodontists to be able to correctly inform patients on the positives and negatives of both treatment options.

The review of the literature will start with an overview of the pain pathway from sensation at the receptor to perception in the brain. Second, the orthodontic pain cascade will be outlined, focusing on the role of inflammatory mediators in the process. Next, both the treatment and measurement of orthodontic pain will be examined. This will be followed by an analysis of how variable forces affect pain perception by patients. Lastly, the literature evaluating Invisalign aligners and the studies comparing Invisalign aligners to traditional fixed appliances will be evaluated.

REVIEW OF THE LITERATURE

Pain Sensation to Perception

Pain plays an important role in the survival of individuals. Melzack described it as a "warning signal" that enables an organism to sense impending tissue damage and thus avoid harm.[20] The International Association for the Study of Pain (IASP) has defined pain as: "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[21] The painful response of individuals has been described as consisting of four stages: signal transduction, transmission, modulation, and perception.[22]

The first responder to a painful stimulus is the primary afferent neuron located at the site of injury.[22] Primary afferent neurons are composed of a cell body, dendrites, and axons. The cell body contains the nucleus and much of the cellular organelles. The dendrites role is to detect and transduce the stimulus, while the axon transmits the electrical stimulus to the next neuron. The dendritic end of a primary afferent neuron contains specialized receptors that are able to identify various external stimuli. For example, Ruffini corpuscles are able to detect changes in light touch or pressure and Krause corpuscles respond to cold temperatures. Polymodal nociceptors are specialized receptors that recognize a variety of noxious stimuli, such as physical, thermal or chemical trauma to a tissue.[23] They are able to convert, or transduce, the initial stimulus to an electrical current that rapidly passes down the primary afferent cell's axon to the second-order neuron, which transmits it eventually to the central nervous system (CNS). The speed at which the nerve impulse is conducted by the neuron depends upon the size of the nerve axon and whether or not the axon is myelinated.

The two most common types of neuron cell fibers in the orofacial complex that transmit pain are the large Aδ (1-20 μm) and smaller C (0.5-1.0 μm) fibers.[22] The faster Aδ fibers usually transmit pain that is localized and described as being sharp or bright. While the slower C fibers transmit pain that is more diffuse and is thought to be dull or aching. While there are exceptions, for the most part in the body, pain is transmitted through a set of three neurons on its way to the somatosensory cortex of the brain. The cell bodies for the primary afferent sensory neurons in the orofacial complex are mostly located in the trigeminal ganglion near the apex of the petrous part of the temporal bone. When a painful stimulus in the mouth activates these neurons, they transfer the signal to the secondary neurons, which are located in the trigeminal spinal tract nucleus of the brainstem. These neurons then relay the message to the tertiary cell bodies located in the thalamus, which ultimately communicate with neurons located in the somatosensory cortex. It is in the somatosensory cortex that the pain signal is interpreted and an appropriate response is initiated.

In order to better explain many of the phenomena related to pain sensation and why it is so varied between individuals, Melzack and Wall suggested what has become known as the gate control theory.[24] Sensory impulses being relayed from peripheral receptors to the CNS first must pass through a gating mechanism located in the dorsal horn of the spinal cord for most of the body. The gating mechanism either inhibits or allows the impulse to pass up to higher relay stations located in the thalamus.[25] In the orofacial region the anatomy is slightly different. The impulses are transported by the trigeminal nerve to the brain stem pons where the trigeminal spinal nucleus is located. The trigeminal spinal nucleus acts much like the spinal cord dorsal horn. This system allows the mind to shut down or minimize certain signals from receptors.

Another way that pain signals are modulated is through sensitization of pain receptors and the neurons that compose the pain signal pathway. When cells are subjected to brief physical or chemical trauma, and either Aδ or C fibers are activated, there is a transient pain signal that serves as a physiological warning to the individual. [26] Part of the body's reaction to the damaging stimulus is to activate the inflammatory response, which serves to remove the stimuli and begin the healing process. The damaged cells release a variety of inflammatory mediators, such as: ions (e.g. K^+, H^+), bradykinin, histamine, ATP and nitric oxide. [23] Immune cells are recruited by the initial release of these chemical messengers. They subsequently release a host of cytokines and growth factors, for example: interleukin 1 β (IL-1β), interleukin 6 (IL-6), tumor necrosis factor α (TNFα), and nerve growth factor .[23] When released, these cytokines can induce powerful hyperalgesia.[26] Hyperalgesia has been defined by the IASP as: "an increased response to a stimulus which is normally painful."[27] In addition to the release of all of these inflammatory cytokines, the arachidonic acid pathway is activated, leading to the synthesis of prostaglandins from the cyclooxegenase enzymes COX-1 and COX-2.[23] Prostaglandin E_2 (PGE_2) and prostaglandin I_2 (PGI_2) are the lipid metabolites that have the greatest impact on pain signal modulation.[28]

The many inflammatory mediators previously mentioned have a varied and profound effect upon the primary afferent neuron's activity. Some of them serve to directly activate the nociceptors, which causes spontaneous pain. Others indirectly increase the rate and intensity of the signal by sensitizing the receptor to respond to either a lower stimulus or a normally non-painful stimuli.[26] When the painful response is increased by sensitization, it is called hyperalgesia. Whereas, when a normally harmless stimulus causes pain, it is known as allodynia. The inflammatory mediators initiate these effects on the neurons by either changing the sensitivity of the actual receptor molecules or by modulating the activity of voltage-gated ion channels that are responsible for transmitting the signal. [23]

Pro-inflammatory cytokines, such as TNF-α and IL-1β, play a crucial role in initiating and maintaining the inflammatory process by helping communication between cells. In the short term, they increase sensitization by activating receptor-associated kinases and ion channels. In the long term or chronic situations, they induce the transcriptional up-regulation of receptors.[29] All of these effects serve to increase hyperalgesia in an individual. Neuropeptides such as substance P and calcitonin-gene related protein (CGRP) work synergistically to initiate pro-inflammatory actions: vasodilation, extravasation of plasma, and degranulation of mast cells. [26] Neuropeptides are released at the peripheral junction of neurons and trigger sensitization of other neurons.[22] Prostaglandins (e.g. PGE2 and PGI2) are some of the most active molecules causing inflammatory hyperalgesia. They play a role in reducing the activation threshold, sensitizing the sensory neurons, and increasing their response to additional stimuli.[26] They are thought to reduce the activation threshold of Na^+ channels, which help propagate the signal from the receptor to the CNS. [30] Local anesthetics used in dentistry, such as lidocaine, work by blocking these very same Na^+ channels.

In order for a noxious stimulus to be perceived as pain, it must be greater than the pain threshold, or the least experience of pain which a subject can recognize.[27] There is a significant amount of variation between individuals in the stimulus and the pain experienced. This is partly due to the variable pain thresholds that occur in each individual based on a multitude of factors: patients psychological well-being, sex, age, race/culture. The combination of all of those factors makes it very difficult to predict the response of any individual to a specific stimulus as well as the patient's pain tolerance. The IASP defined pain tolerance level as "the maximum intensity of a pain-producing stimulus that a subject is willing to accept in a given situation."[27]

According to Klinberg et al., 3-21% of children and adolescents visiting a dentist reported being fearful or anxious.[31] This is important, because there have been multiple reports that increased levels of anxiety leads to greater reactions to painful stimuli.[32-34] Commonly, this is because of past experiences and the expectation of that painful experience to reoccur.[35] A review of pain and anxiety in the dental setting concluded that anxiety can lower the pain threshold in patients and cause them to react to non-painful stimuli as being painful.[36] This has been supported in the orthodontics literature by Sergl et al., who proposed that psychological well-being of an individual affected pain perception more than even force levels. Both personalized phone calls and text messages from the orthodontists have been shown to decrease pain reports and anxiety in patients. [37, 38]

There are reports that the pain threshold, in general, increases along with age. In a study looking at 520 individuals, aged 5 to 105, cutaneous pain thresholds were measured using a constant-current electrical stimulator.[39] The researchers found that pain thresholds rapidly increase until the age of 25 years, and then following a plateau, increased only slightly until 75 years. The orthodontic literature is somewhat divided on whether adolescents or adults report higher levels of pain. Jones and Chan found a significant association between the age of an orthodontic patient and the subsequent arch wire pain, with greater ages being associated with greater pain.[13] However, all of their patients were less than 17 years of age. This was supported by Fernandes et al., who also found a significant association between age and level of pain or discomfort while comparing superelastic nickel-titanium wires with nitinol wires in patients less than 17 years of age.[5] Lower pain scores were attributed to younger patients. Jones found that those older than 16 were significantly more likely to report pain than those under 16.[6] Conversely, Brown and Moerenhout found that adolescents (aged 14-17) reported higher levels of pain and lower levels of psychological well-being than pre-adolescents and adults.[4] Other studies have found no significant difference in age groups. Ngan et al. stated that there was no significant difference in pain reports when comparing patients less than 16 years of age and those that were greater than 16.[40] The conflicting reports of age being a factor in pain levels, can be explained by the fact that adults and adolescents often have very different treatment plans involving different appliances.

In general, the orthodontic literature does not demonstrate a correlation between gender and perception of orthodontic pain. Multiple studies have failed to show a significant difference between the two sexes. Jones and Chan found no significant differences in pain reports between males and females.[13] Erdinc and Dincer stated that gender differences were not shown to be statistically significant in the perception of orthodontic pain.[41] However, some studies have shown that females report more pain/discomfort than males. Kvam et al. showed that girls were more likely to report oral ulcerations than boys.[2] Scheurer et al. administered a series of eight questionnaires to 170 patients (93 females, 77 males) and found that girls report greater levels of general pain intensity, analgesic consumption, and pain while chewing than boys.[1] They believed that some of the variation between their findings and much of the published literature could be explained by differences in culture. Their sample was drawn from a predominantly German-speaking region of Switzerland.

There is evidence that while some aspects of pain perception are universal, other aspects are culture-specific.[42] People of Italian or Jewish descent are more likely to report pain than people of Northern European descent, and to tolerate less intense pain levels.[43] Also, studies over the last 50 years have generally shown that non-Hispanic Caucasians have a higher pain tolerance and threshold than African Americans and Hispanics.[44-46] This demonstrates that certain aspects of pain perception are learned behaviors. Stoicism is encouraged by some cultures during painful experiences, while other cultures reinforce pain expression by providing sympathy and attention.

The Orthodontic Pain Cascade

Before discussing how orthodontic forces initiate pain in a patient, it is necessary to have an understanding of the basic anatomy of a tooth and its surrounding structures. Each tooth is separated from the surrounding alveolar bone by a densely collagenous tissue called the periodontal ligament (PDL). [47]. The PDL is approximately 0.5 mm thick and inserts into the cementum covering the tooth root and into the dense bone immediately surrounding the root. It contains both cellular elements and tissue fluids, each of which plays an important role in orthodontic tooth movement. The cells found in the PDL are predominantly undifferentiated mesenchymal cells and their offspring: fibroblasts/fibroclasts and osteoblasts/osteoclasts. These cells play an integral role in the remodeling process by removing both collagen and bone in the direction of force application, and then laying down collagen and bone behind the tooth. Blood vessels and nerve endings are also found in the PDL space. The nerve endings are either of the unmyelinated variety that sense pain, or they are of the more complicated type that differentiates pressure and positional information.

The pressure tension theory is the classical theory in orthodontics used to explain how tooth movement occurs.[47] When an orthodontic force is applied to a tooth in a certain direction, the tooth shifts positions. This results in compression of the PDL in some areas and tension of the PDL in others. On the compression side, pressure builds in the decreased PDL space, which occludes blood vessels in this area. However, on the tension side, the reverse occurs; blood flow is either maintained or increased. Changes in blood flow rapidly lead to adjustments in the chemical composition of the PDL environment. For example, decreased oxygen levels and increased levels of inflammatory mediators are found on the compression side. All of these effects serve to activate cells involved in bone and tissue remodeling, but they also form the basis for orthodontic pain.

As has been previously discussed, inflammatory mediators increase pain by either direct activation of nociceptors or indirectly by lowering the activation threshold. Orthodontic forces have been shown to produce mechanical damage and inflammation in the periodontium.[48] Numerous studies have looked at the inflammatory metabolites and chemical mediators that are present in the PDL and gingival crevicular fluid. Most of them concur that orthodontic pain is a consequence of an inflammatory reaction initiated by changes in blood flow following orthodontic force application.

Beginning in 1975, Davidovitch and Shanfield looked at biochemical changes in mechanically stressed bone in cats, who were orthodontically treated anywhere from 1 hour to 28 days. They found elevated levels of cyclic adenosine monophosphate (cAMP, a second messenger important in many biochemical processes, and suggested that this rise was due to an increase in bone remodeling activity in the compression sites. Then in 1985, Oliver and Knapman discovered increased levels of PgE and IL-1β immediately after an increase in pressure.[11] This was supported by the work of Grieve et al., who used a split-mouth design to evaluate PgE and IL-1β levels drawn from gingival crevicular fluid (GCF) during human orthodontic tooth movement.[49] The GCF levels of PgE and IL-1β were significantly elevated, while the levels on the control side remained the same as the baseline. Uemastsu et al. assessed a host of cytokines found in the GCF of orthodontic patients using an enzyme-linked immunosorbent assay. They found elevated levels of IL-1β, IL-6, TNF-α, epidermal growth factor, and β_2-microglobulin in the experimental side when compared to the control side.[50]

Nicolay et al. used a cat model to evaluate neurotransmitters in the PDL following orthodontic forces.[51] While substance P levels were relatively low before application of the forces, the density of the positive staining for substance P increased markedly from 24 hours to 14 days. They hypothesized that substance P may be an initial trigger for a biochemical cascade that comprised the activation of various cell types in the PDL. In a review of the literature on the cellular and tissue level reactions to orthodontic force, Krishnan and Davidovitch concluded that force-induced tissue strain produces local alterations in vascularity, which leads to the synthesis of various neurotransmitters, cytokines, growth factors, and metabolites of 13ignificant acid.[52]

As has been discussed previously, these molecules are all involved in initiating and propagating a painful response to a patient.

Treatment of Orthodontic Pain

As Scheurer et al. demonstrated, around 90-95% of orthodontics patients experience pain while in treatment.[1] Based on how many negative consequences result from this experience, it is imperative that orthodontists find ways of decreasing their patients' pain. Non-steroidal anti-inflammatory drugs (NSAIDS) are the most commonly used method of treating patients for pain. Ibuprofen was found to be more effective at controlling pain than aspirin in patients who were treated with both separators and orthodontic wire changes.[53] Young et al. evaluated the best time to administer NSAIDS.[54] He split up three groups of adult patients, and asked them to score the amount of pain that they felt after the initial arch wire was placed. The first group received 40 mg of Valdecoxib, an NSAID, 30 minutes prior to arch wire placement; the second group received it 2 hours after arch wire placement, and the third group received a placebo control. The study showed that 1 day after initial arch wire placement, the group that received the 40 mg of Valdecoxib 30 minutes before arch wire placement had the lowest pain scores. Even though NSAIDs have been shown to be effective in pain management, they are only being used by 13-16% of patients during the peak pain periods of 1-2 days.[1]

There are three other modalities that have been studied for their ability to manage pain: low level laser therapy (LLLT), mastication, and transcutaneous electrical nerve stimulation (TENS). LLLT has been shown to have both anti-inflammatory properties as well as regenerative effects. Turhani et al. found a significant difference in pain levels between a group treated with a low level laser and a control group.[55] However, the operator was not blinded and could differentiate between the laser and the control. It has been theorized that chewing on gum or a plastic wafer during the first few hours after orthodontic forces would decrease patient's pain levels by moving the teeth enough to allow blood flow through compressed areas. This would permit the removal of metabolic byproducts that have previously been discussed to increase sensitization to pain. White had 93 patients with full appliances chew on two pieces of Aspergum and report whether they felt more, the same, or less pain than their normal adjustments.[56] Fifty-eight patients (63%) reported that they had a decrease in discomfort, while 24 (25%) said that they experienced no difference, and only 11 (12%) said that they felt an increase in their discomfort. Hwang et al reported that chewing on something hard, such as a therabite wafer for 10-12 minutes after an adjustment may reduce pain.[57] While 56% of their sample reported a decrease in pain, the other 44% found it to be more painful. Lastly, Roth and Thrash evaluated whether TENS was able to reduce periodontal pain following separator placement mesial and distal to first molars.[58] Patients were asked to report their pain every 12 hours for the four days. They found a significant decrease in pain at the 24, 36, and 48 hour time frames in the treatment group.

Measurement of Orthodontic Pain

Pain is a subjective experience, and therefore difficult to quantify accurately. Pain intensity is influenced by the meaning of the pain to the patients and its expected duration, along with a host of other factors.[20] There are many pain rating scales that have been devised and are used in the literature. However, in orthodontics the three most commonly used scales are the numerical rating scale (NRS), verbal rating scale (VRS), and the visual analog scale (VAS).

A NRS has a patient rate their pain on a scale of 0-10 or 0-100, where 0 represents no pain and 10 or 100 represents the worst pain imaginable.[24] While it is not commonly used in orthodontics, it is an interval level scale and can provide data to which parametric tests can be applied.[59] The VRS provides a list of adjectives that describe various levels of pain intensity and asks the patient to select the best response. The list typically consists of words that describe the extremes and then some of the gradations in between (e.g. no pain, mild, moderate, and severe pain).[59] These are assigned numbers, but it would be incorrect to assume that the intervals in between each response are equal, which is not the case according to Jensen et al.[60] VRS data is ordinal and therefore can only be analyzed by non-parametric tests.[59]

The VAS is the most commonly used scale in orthodontic literature today, because it has been shown to be the most accurate and reliable. It consists of a 10 cm line that is anchored on both ends by verbal descriptors (e.g. no pain, worst pain imaginable). The patient marks a line through the area that represents the pain level that they are currently experiencing. This allows for 1001 gradations if measurements are taken to the nearest $1/10^{th}$ of a mm. Even young children have been shown to understand it and respond to the questions.[41] According to Krishnan, VAS has two main advantages. First, it provides freedom to select the exact intensity of pain, and second, it allows for maximum expression of an individual response style.[61] VAS has ratio properties, but it is not always normally distributed.[62] If the data is normally distributed, Williamson et al. suggest the use of parametric statistical analysis.[59] Similarly, if it is not normally distributed, then non-parametric tests should be used. Therefore, normality should be determined prior to running any statistical tests.

Variable Orthodontic Forces and their Effects on Pain

Pain during orthodontic treatment is the result of compression of the periodontal ligament and the changes in blood flow that result. There is still some debate, however, as to how force levels are related to pain. Burstone devised a classification system that differentiated painful responses based upon either the relationship of the force application or the timing of onset.[63] In terms of force application, there are three degrees. With first degree the patient doesn't perceive pain unless the doctor is pushing on the teeth. Second degree is when the patient feels pain when he or she is clenching. Third degree is when patients have difficulty eating foods of normal consistency. In terms of the timing of onset, the pain can either be immediate or delayed. Immediate is characterized by abrupt heavy forces placed on the teeth, while delayed is produced by various force levels which create hyperalgesia of the PDL space.

The current goal of orthodontists is to provide the optimum force level to produce fast tooth movement, while limiting tissue damage and maximizing patient comfort. Traditionally, orthodontic forces have been classified as either being "heavy" or "light". Most experts advocate using light forces, because they are thought to be more physiologic than heavy forces and therefore less painful.[47] It is believed that heavy, sustained forces cause necrosis and hyalinzation of cells in the PDL. This causes less efficient bone remodeling called undermining resorption. Lighter forces are believed to lead to healthy cellular activity in the PDL along with efficient and relatively painless remodeling of the alveolar bone, known as frontal resorption. Luppanapornlarp et al. tested this theory using a split mouth design while retracting canines with either a 50 g or 150 g nickel-titanium coil spring. They found that the mean VAS score was significantly higher in the 150 g control side than the 50 g experimental side.[64] However, Andreasen et al. also used a split mouth design to evaluate heavy (400-450g) and light (100-150g) forces between canines and first molars and found no significant differences in pain levels reported.[65] Jones and Richmond also failed to find a correlation between pain and applied forces, using severity of crowding as an indicator of applied forces.[66]

In an effort to minimize orthodontic pain, other researchers have investigated different wire types and removable appliances. Wires made from a nickel-titanium alloy have been shown to provide lighter and more constant force levels than stainless steel wires.[67] Miura et al. found that Japanese NiTi wires exhibited super-elastic properties, indicating definite stress levels with increasing amounts of strain. A three-point bending test showed that initial super-elastic NiTi wires (e.g. 0.016 in.) generate forces in the range of 140-170 grams. When comparing NiTi wires to a multistranded stainless steel wire, Jones and Chan found similar levels of pain intensity and pain duration.[13] Superelastic NiTi wires have also been reported to cause lower pain values when compared with conventional nitinol wires.[5]

Traditional fixed appliances generate constant forces while removable appliances inherently provide intermittent forces. Studies have looked at the effects of the different types of appliances on pain levels. On one hand, Oliver and Knapman found no significant differences in patient discomfort between fixed and removable appliances.[11] However, Sergl et al. found that the severity of pain and discomfort was significantly higher in patients treated with functional or fixed appliances than in those treated with removable plates.[14] Stewart et al. also concluded that fixed appliances were more painful than removable.[68]

Invisalign Clear Aligners

The first mention of using small sequential tooth positioners to make major changes to the occlusion came almost 70 years ago by Kesling. He recognized the potential for tooth alignment, but understood that it was not feasible in 1945.[69] At the time, impressions of the dentition were poured up in plaster and the teeth were separated and then individually moved to their desired locations. A one-piece pliable rubber appliance was made to adapt to each surface of the teeth and patients were instructed to wear it full time. However, the tooth positioning appliances were limited to correcting slight rotations and making minor modifications to the arch form and axial position of teeth. Over the following decades, numerous authors wrote about using plastic overlay appliances to act as invisible retainers and to make minor tooth movements.[70-74] Raintree Essix (New Orleans, LA) developed a technique to use aligners with small “divots” to put pressure on teeth and move them into spaces, called “windows.”[75]

However, these aligners were limited to tooth movements that were no greater than two to three mm.

Around the year 2000, Align technologies introduced the Invisalign system, which utilized computer-aided-design-computer-aided-manufacturing technology to manufacture clear aligners from stereolithography models.[75] After creating a digital representation of a patient's dentition from either a polyvinyl siloxane impression or from a 3D digital scan, Align technology fabricates a set of clear plastic aligners to slowly move the teeth to the desired location. Each plastic aligner is 0.030" thick and allows for minor tooth movements, around 0.25-0.33 mm per tray.[76] The number of trays produced depends on the number of stages required to move the teeth to their final position. They are traditionally worn for two weeks before switching to the new set of aligners.[77] In a recent study by Simon et al., they found that the forces generated by the Invisalign system are "within the range of orthodontic forces."[78] Specifically, intrusion and distalization movements by Invisalign aligners produced forces between 0.5 to 1.0 newtons (N) or around 50-100 grams.

Invisalign Compared to Traditional Braces

Since Invisalign has only been in existence for a little over a decade, there are limited studies investigating the patient experiences and clinical outcomes. Nedwed and Miethke were the first to evaluate patient acceptance of Invisalign and the quality of life of patients undergoing treatment. They administered a questionnaire with twelve questions to fifty-four consecutively treated Invisalign patients after three to six months of treatment. The patients were limited to only three verbal answer choices for each question. The question concerning pain found that 35% had no pain, 54% had minimal pain, and 11% had severe pain. There were several flaws with their study design. Not only are verbal rating scales limited, but Nedwed and Miethke did not even provide a fourth answer choice for moderate pain. This could have skewed the responses towards minimal pain. The surveys were only administered after 3-6 months of treatment. This only provides a brief look at the patient's experience and fails to reliably express the pain levels at different stages of treatment, especially at the beginning.

The first study to actually evaluate differences in pain levels between an Invisalign sample and one treated with traditional braces was by Miller et al. in 2007.[17] They administered a daily diary to 60 patients from offices in Florida, Arizona, Kentucky, Texas, and at the University of Florida. The diary was to be completed every day for the first week and was to assess treatment effects including functional, psychosocial, and pain-related outcomes. Four of the questions addressed the pain experienced by the patients. Three of them were Likert style questions, while the other was a visual analog scale based question. The results show that at baseline there was no significant difference. Both groups show a dramatic increase during the first day and then a gradually return to baseline over the course of the week. The results indicated both a significant treatment group and treatment day effect, with Invisalign patients demonstrating lower pain levels at each of the seven days. At 24 hours, the fixed group had a mean VAS score of approximately 50/100, while the Invisalign group had a mean VAS score closer to 40.

Shalish et al. performed a similar study, however, they included a sample of patients wearing lingual brackets.[18] Sixty-eight patients filled out a health related quality of life questionnaire composed of numeric rating scale questions for the first week after initial appliance placement and then again on day 14. While the pain levels were consistently higher in the Invisalign group than in the buccal fixed group, the differences were not statistically significant. These are opposite results from those found by Miller et al. They stated that the difference could have been due to the greater mechanical force that the Invisalign technique applies early in treatment. They also hypothesized that the wire's flexibility may result in a more gradual and lighter force in the buccal fixed group.

More recently, a group from Japan performed a study comparing the pain levels of patients treated with Invisalign aligners and fixed edgewise appliances.[19] Fujiyama et al. administered a VAS style survey to a sample consisting of 55 adult patients in the fixed appliances group and 38 adult patients in the Invisalign group. Patients were asked to report their pain at multiple time points during the first week and then again at 3 weeks and 5 weeks after appliance placement or delivery of aligners. They found that while patients reported more pain with fixed appliances, the difference was only significant at a couple of time points during each stage. Similar to prior studies, they failed to randomly assign patients to specific treatment categories.

All of the studies evaluating differences between Invisalign and traditional braces had flaws in their research design. None of them randomly assigned the patients to their prospective treatment modality. Shalish et al. claimed that adult patients, who are often concerned with esthetics, would be unwilling to comply with random assignment.[18] They recognized that lack of randomization was a weakness, because allowing the patients to choose treatments may provide results that reflect personality traits rather than true appliance differences. In addition, Miller et al. and Shalish et al. only looked at the first week or two of treatment, and thereby failed to evaluate treatment effects at any other point in treatment. There is a possibility that pain levels early in treatment could be very different at other time points. Lastly, Miller et al. and Shalish et al. used questions from inferior rating scales. Miller et al. used some Likert style questions, while Shalish et al. used a NRS for their pain questions.

CHAPTER II

PAIN ASSOCIATED WITH INVISALIGN VERSUS CLEAR TRADITIONAL BRACKETS: A RANDOMIZED, PROSPECTIVE TRIAL

INTRODUCTION

Pain and discomfort are common side effects of orthodontic treatment.[1-3] Because orthodontists are concerned about their patients' well-being, they want to minimize any painful side effects. Orthodontists should also be concerned about causing pain, because it alters their patients' behaviors in ways that often lead to negative consequences. Fear of pain is one of the primary reasons that patients fail to seek orthodontic care.[11] Sergl et al. found that compliance during treatment is negatively associated with increasing complaints of pain.[14] Therefore, it would be beneficial to be able to provide treatment modalities that produce the least amount of pain possible.

There are numerous reports describing the pattern of pain associated with traditional fixed appliances.[1, 13, 40] For example, Scheurer et al. found that pain peaked at 42% of maximum pain around 24 hours after initiation of orthodontic treatment, and decreases thereafter.[1] Subsequent reports confirmed that pain decreases during the first week after initial bonding, returning to baseline values. While the first week of treatment has been extensively studied, few studies have evaluated the pain and discomfort experienced by patients further into treatment. This is important, because pain reported at future time points could be different than during the first week.

Since their introduction to the market in 1997 by Align technologies, clear aligners have quickly become one of the preferred orthodontic appliances for patients who are concerned with esthetics. Given how popular aligners have become, there is surprisingly little research comparing the treatment effects and outcomes of aligners to traditional braces. The first study to evaluating the differences in pain found that traditional braces were significantly, approximately 25%, more painful than Invisalign.[17] However, this study was conducted at multiple locations and was only conducted during the first week after treatment started. This was followed by a study from Shalish et al. that reported the exact opposite effect.[18] They utilized the inferior numeric rating scale and also failed to evaluate pain months after initiation of treatment. Recently, Fujiyama et al. confirmed the results of Miller et al. and found that traditional fixed appliances were significantly more painful than Invisalign aligners.[19] Importantly, none of the previous articles randomly assigned treatment modality, which increases the possibility of biased comparisons.

The purpose of this study was to compare the pain levels produced by traditional fixed appliances and Invisalign aligners at multiple time points. Secondarily, the study sought to compare their effects on pain medication usage and sleep disturbances.

MATERIALS AND METHODS

A power analysis determined that ideally the sample needed to consist of 80 adult (males > 19 years old and females > 17 years old) patients recruited from advertisements at the Graduate Orthodontic Clinic of Baylor College of Dentistry. Of the 240 people who were screened, 199 of them did not qualify for the study or declined to participate (Figure 2.1). Currently there are 41 patients admitted to the study (17 males, 24 females). This study was approved by the Texas A&M University Baylor College of Dentistry IRB (IRB approval # 2012-21-BCD). Informed consent was obtained from all of the subjects.

The patients were randomly divided into one of the two treatment groups using a randomization table created using Microsoft Excel. The experimental group consisted of 23 patients treated with Align Technology's Invisalign appliance, while the control group consisted of 18 patients treated using conventional fixed appliances (clear in maxillary arch, stainless steel in the mandibular arch) as described in detail below. In order to qualify for the study, patients had to fulfill the following selection criteria:

Inclusion Criteria

1. Class I molar and canine relationships
2. Non-extraction treatments
3. Mandibular crowding of 4 mm or less
4. No missing teeth (from second to second molar)

Exclusion Criteria

1. Anterior or posterior crossbites
2. Anterior or lateral open bites
3. Maxillary overjet exceeding 3 mm
4. Impacted teeth

All patients were seen at Texas A&M University Baylor College of Dentistry and treated by one of two clinicians, Dr. Katie Julien DDS, MS or Dr. Helder Jacob DDS, PhD. Following randomization and the obtainment of informed consent, initial diagnostic records were taken (intra and extraoral photographs, lateral cepholagrams, panoramic radiographs, Blu-Mousse® bite records, and plaster models) at the first appointment. Subsequent appointments were dependent on whether the patient was in the experimental group or the control group. The sequence of appointments adhered to the timeline found in Figure 2

Patients in the Invisalign group had either a polyvinylsiloxane impression made or the dentition was scanned using an iTero scanner®. The records were then sent to Align Technology. A series of removable polyurethane aligners were fabricated based on the treatment plan determined using Align Technology's proprietary ClinCheck® software. All composite attachments were placed at the initial aligner delivery appointment. Patients were given two sets of aligners and instructed to wear them twenty-two hours per day for two weeks and to change to the new set of trays on the 15th day. Patients were scheduled every 4 weeks for evaluation appointments and were given two new sets of trays at each appointment.

Traditional fixed appliances consisted of American Orthodontics' Radiance clear brackets in the maxillary arch, and stainless steel brackets in the mandibular arch. The brackets used were a 0.018" X 0.028" Alexander prescription (American Orthodontics, Sheboygan, WI). Brackets and tubes were bonded to the maxillary and mandibular arch from second molar to second molar. A sequence of NiTi (.016" and .017"x.025") and stainless steel (.016”x.022” and .017”x.025”) wires were used according to the malocclusion and the progress of correction. To monitor the progress of treatment, patients were scheduled for appointments every four weeks.

This was a randomized, prospective, clinical trial that assessed patients’ pain and analgesic consumption using a daily diary. The patients completed a daily discomfort diary at four different occasions during treatment. The first was completed immediately following initial bonding or delivery of Invisalign to create a baseline, and each day thereafter during the first week (Appendix) They also completed diaries on the day of and for 4 days following each of the next two adjustment appointments (4 and 8 weeks). Four days was considered to be adequate because patients have been shown to adapt to the pain and discomfort of orthodontics within the first 3-5 days.[2, 14, 24] The patients were seen every 4 weeks for adjustment appointments or delivery of new aligners.

The daily discomfort diary consisted of eight questions (Appendix). The first five questions asked about their discomfort under certain circumstances. The responses were recorded on a 10 cm VAS, using *No Discomfort* and *Worst Discomfort* as the anchors. The final three questions determined whether the patient’s sleep was affected (Did discomfort caused by your orthodontic appliance interfere with your sleep?) and the frequency of analgesic consumption (Did you take medication to relieve tooth pain?). The daily diaries were collected at the adjustment appointments following a recorded occasion. The examiner of the surveys was blinded as to which treatment the patients had received. If a patient failed to bring the daily diary form in to the appointment, they were asked to either bring it to the next appointment or mail it in a self-addressed and stamped envelope. Four out of one hundred thirty two surveys were either lost or not returned. After all of the diaries had been collected, they were measured by the principal investigator, who was blinded as to the treatment modality, to the nearest 0.01 mm using a digital caliper. The data were transcribed into a Microsoft Excel spreadsheet, using a numeric label to identify the patients.

Statistical Analysis

All statistics were calculated using SPSS version 18 software (SPSS Inc., Chicago, Illinois). Due to skewness and kurtosis of the results, medians and interquartile ranges were used to describe the results and group differences were compared using the non-parametric Mann-Whitney test. Significance for all tests was set at $P < 0.05$.

RESULTS

Based on the first question from the daily diary, both treatment groups demonstrated strong rating reliability with an intraclass correlation coefficient of 0.917-0.986, depending on the assessment period.

Initial Adjustment

Traditional braces produced a similar pattern of pain for each of the four questions. At baseline, or immediately following appliance placement, the patients reported a low level of pain (Table 1). This was followed by a dramatic and statistically significant ($p < 0.05$) increase in pain response (300 – 500%) that peaked between the first and third day (Figures 3-6). The highest peak pain scores were reported when chewing (VAS score = 46.91) and biting down on the front teeth (VAS score = 50.43). Following the peak, there was a gradual reduction in pain over the next 4-5 days, ending with a pain level similar to or slightly above those reported at baseline. Patients in the traditional treatment group reported significantly higher pain while chewing than at rest during most of the first week (Figure 7). They also reported higher pain at the front teeth than the back teeth for the first few days, but the differences were not statistically significant (Figure 8).

Invisalign also produced a similar pattern of pain for each of the VAS questions. Initially, patients reported low levels of pain that were followed by slight increases (50 – 100 %), peaking after the first or second day (at VAS pain scores around 15-20) (Figures 3-6). Pain levels then decreased slowly over the rest of the first week. By day 7, patients in the Invisalign treatment group experienced minimal pain levels, lower than those reported on day 0.

Both treatment groups reported similar levels of pain on day 0, with no statistically significant group differences (Table 1). Between day 1 and day 7, the traditional group consistently demonstrated higher pain levels than the Invisalign group (Figures 3-6). Depending on the question, the pain values in the traditional group were found to be significantly higher during the majority of the first week. Due to high variability between subjects, there were no statistically significant group differences initially. After day 2 or day 3, group differences were mostly statistically significant at a p level < 0.05 (Table 1).

Subsequent Adjustments

Pain after the first and second month adjustments was also consistently less for Invisalign than traditional treatments. Many of the group differences after the first month adjustment were statistically significant ($p < 0.05$) and all of the others closely approached significant levels (Table 2). Significant group differences were found on days 0, 1, 2, and 3. For both groups, the pain levels reported at subsequent adjustments peaked at much lower levels than during the first week after the initial bonding or Invisalign delivery.

The first month and second month Invisalign adjustments showed a similar pain response pattern for each of the VAS questions. At day 0, the pain scores were generally lower than those reported at the initial delivery and then slowly decreased over the next four days (e.g. Figure 9). With traditional treatment group, the pain scores at day 0 were generally higher than at the initial bonding (e.g. Figure 10). Like the Invisalign group, the pain values decrease gradually over the next four days. However, unlike during the first week of treatment, there was not a drastic increase in pain values following the adjustment at months 1 and 2. The pain scores after the initial bonding were significantly higher than the first month adjustments for both the Invisalign and traditional groups (Figures 9-10)

Analgesic Consumption

The percentage of patients in the traditional group taking medication to relieve tooth pain increased by approximately 45% during the first two days, and then decreased steadily during the remaining five days (Figure 11). In the Invisalign group, the percentage taking medication increased by 11% during the first day, and then decreased steadily thereafter. While the percentages of patients taking medication was consistently greater in the traditional than Invisalign group, only the 50% difference that occurred on day two was statistically significant ($p < 0.05$). Medications taken after the first and second adjustments showed no clear pattern and no statistically significant differences between the traditional and the Invisalign treatments (Table 3.5).

Sleep Disturbance

There was no consistent pattern of group difference and no statistically significant group difference in the percentage of patients who had sleep disturbances during the first week (Figure 3.10). The frequency of patients reporting sleep disturbances decreased from approximately 30% on the first day to 15% on the seventh day. There also were no significant group differences in the proportion of patients reporting sleep disturbances during the first and second adjustments (Table 3.6).

DISCUSSION

Patients treated with traditional fixed appliances show a dramatic increase in pain over the first 24 hours after appliance placement; pain peaks after 24-48 hours, and then decreases steadily to baseline values over the remainder of the first week. Previous studies evaluating orthodontic pain during the first week of treatment have also shown sharp pain increases during the first 24 hours, followed by gradual decreases over the subsequent 6-7 days to values similar to those observed at appliance placement.[1, 13, 17, 19, 40] Regardless of the amount of crowding or degree of malocclusion, this pattern of pain appears to be consistent. The large increase in pain over the first 24 hours correlates with an acute inflammatory response [52] Initial orthodontic forces cause pain through compression of the PDL, which leads to ischemia, edema, and the release of pro-inflammatory mediators during the first 24-48 hours. The inflammatory mediators, such as prostaglandins (e.g. PgE) and interleukins (e.g. IL-1β), sensitize nociceptors in the PDL and lower the pain threshold.[26, 29] The levels of PgE and IL-1β found in gingival crevicular fluid (GCF) peak 24 hours after initiation of orthodontic force and fall to baseline after 7 days.[49] As such, the gradual reduction in pain observed over the course of the first week can be attributed to the decrease of inflammatory mediators in the PDL.

The amount of peak pain during the first week that occurs with traditional fixed appliances appears to depend on the initial archwire used. Patients in the traditional fixed appliances group reported that pain peaked at approximately 33% of the worst pain imaginable. This peak pain value closely approximates the value found by a study that used superelastic NiTi (29%) and is less than a study that used nitinol (42%).[1, 13] The differences could be due to the material used. Initial nitinol archwires have been shown to produce higher peak pain than superelastic NiTi archwires.[5] This could be due to the fact that nitinol produces a greater amount of force.[79] The current study used 0.016 in. copper NiTi (CuNiTi) archwires, which is a type of superelastic archwire. When loaded 2 mm, CuNiTi generates a force of 47 grams while unloading. Classic nitinol generates a force of 180 grams when loaded under the same conditions.[79]

Patients treated with traditional fixed appliances experience significantly more pain during the first week of treatment than patients treated with Invisalign aligners. While both treatment groups reported similar baseline values, pain from days 2 through 7 was consistently and significantly higher in the traditional group, regardless of the question being asked. Significantly less pain among patients treated with Invisalign aligners compared to those treated with fixed appliances has been previously reported.[17, 19] The lower pain reported by Invisalign patients could be due the fact that it is a removable appliance. Removable appliances are generally less painful than fixed appliances.[14, 68] The difference could be due to the fact that removable appliances provide intermittent forces, while fixed appliances provide continuous forces. Thilander proposed that interrupted or intermittent forces are advantageous, because they allow the tissues enough time to reorganize before the compression force is reapplied.[80]

The difference in pain between Invisalign and traditional fixed appliances does not seem to be attributed to the extent of force applied. Invisalign aligners produce forces between 0.5-1.0 N, or around 50-100 g, for intrusion and distalization movements.[78] Conversely, initial leveling and aligning archwires, such as the 0.016 in CuNiTi used in this study generate forces between 47-77 g.[79] Therefore, Invisalign aligners and NiTi archwires produce similar forces that cannot explain the difference in pain observed between Invisalign and fixed appliances.

After the first and second month of treatment, patients also reported that Invisalign was less painful than traditional fixed appliances. One other study that evaluated pain 3 and 5 weeks after appliance delivery showed similar differences.[19] The reduced pain reported by Invisalign patients can be explained by the role of pro-inflammatory mediators, such as IL-1β. Over the short term, they increase sensitization by activating receptor-associated kinases and ion channels. Over the long term, or in chronic situations, they induce the transcriptional up-regulation of receptors, leading to hyperalgesia in an individual.[29] If fixed causes greater initial pain due to an increased inflammatory response, then it is possible that patients with fixed appliances have more sensitized nociceptors, which affects their pain perception during following adjustments.

Invisalign's new SmartTrack® (Align Technology, Santa Clara, Calif) material appears to be less painful for patients than previous clear aligner materials manufactured by Invisalign. Patients in the Invisalign treatment group reported small increases in pain that peaked at 13.6% of maximum during the first 24 hours and then decreased gradually to pain values below baseline by day seven. Miller et al., who found a similar pattern of slight pain increase followed by a steady pain decrease to values below baseline by the end of day seven, reported peak pain values at 40% of maximum pain for the original material.[17] Although more studies are needed, this supports Invisalign's claims that SmartTrack® provides greater patient comfort than the original material. [81]

In comparison to pain values during the first week of treatment, both treatment modalities demonstrated significantly less pain at the subsequent adjustment. Fujiyama et also found lower levels of pain for Invisalign and fixed appliances at subsequent adjustments.[19] Soltis et al. showed that there is a decrease in the pain threshold immediately after orthodontic forces are placed, but that after a period of time, the pain threshold returns to its original level.[82] Therefore, the same stimulus will generate a less painful signal months into treatment than immediately after appliances are placed.

For patients in the traditional group, pain while chewing was significantly higher than pain at rest for most of the first week. Inflammatory mediators, such as substance P, have been shown to be present in the PDL following the initiation of orthodontic forces.[51] These mediators are believed to sensitize the nociceptors in the PDL.[24] It is possible that chewing compresses previously sensitized nociceptors in the PDL and stimulates a more painful signal than at rest. Importantly, this phenomenon was only evident in the traditional group, which exhibited a more painful response to orthodontic forces. The nociceptors in the PDL of patients in the traditional group may have been more sensitized than those in the Invisalign group, due to the continuous nature of the forces used, making them more susceptible to variations in compression of the PDL.

Patients treated with traditional fixed appliances report that their front teeth are more sensitive than their back teeth while chewing, but the differences were not found to be statistically significant. This is supported by the published literature.[1, 40, 41] Scheurer et al. hypothesized that this difference depends on how involved anterior teeth are during leveling and aligning, as well as to their smaller root surface.[1] According to the principles of static equilibrium, the forces exerted on the anterior teeth during initial leveling stage must be equal to the forces exerted on the posterior teeth.[83] Anterior teeth could be more painful during chewing, because forces are distributed over smaller root surface areas than posterior teeth.

Patients treated with fixed appliances are more likely to take pain medication than Invisalign patients. The pattern of analgesic consumption closely mirrored the pattern of pain at rest during the first week of treatment. There was an increase in analgesic consumption during the first 24-48 hours, and then a gradual return to baseline levels by day 7. A correlation between pain medication intake and pain levels throughout the first week has been previously demonstrated.[17] Patients with fixed appliances have been shown to have been in more pain than their Invisalign counterparts, and accordingly, they reported taking more pain medication during the first week. Interestingly, this phenomenon was not present at subsequent adjustments. This could be due to the fact that patients, in general, were in less pain at subsequent adjustments and didn't require pain control.

CHAPTER III

CONCLUSIONS AND CLINICAL APPLICATIONS

CONCLUSIONS

1) Invisalign treatment is significantly less painful than traditional fixed appliances.
2) Patients treated with both Invisalign and traditional fixed appliances report significantly less pain at subsequent adjustments than at the initial bonding.
3) Chewing is significantly more painful than when a patient is at rest for patients treated with traditional fixed appliances.
4) Consumption of analgesics closely mirrored the levels of pain reported by patients and was predominantly during the first week of treatment.

CLINICAL APPLICATIONS

While the first week of treatment may be mildly to moderately painful for patients with Invisalign or traditional fixed appliances, following appointments will produce less pain. Invisalign may be an alternative treatment option for patients that are hesitant to start treatment due to fear of pain. Patients should be warned that biting with the front teeth is more painful than chewing on the back teeth. Patients should also be aware that analgesics may be needed during the first week of treatment, but are traditionally not as necessary after subsequent adjustments.

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APPENDIX A

FIGURES AND TABLES

Figure 1. Diagram of patient flow through the study

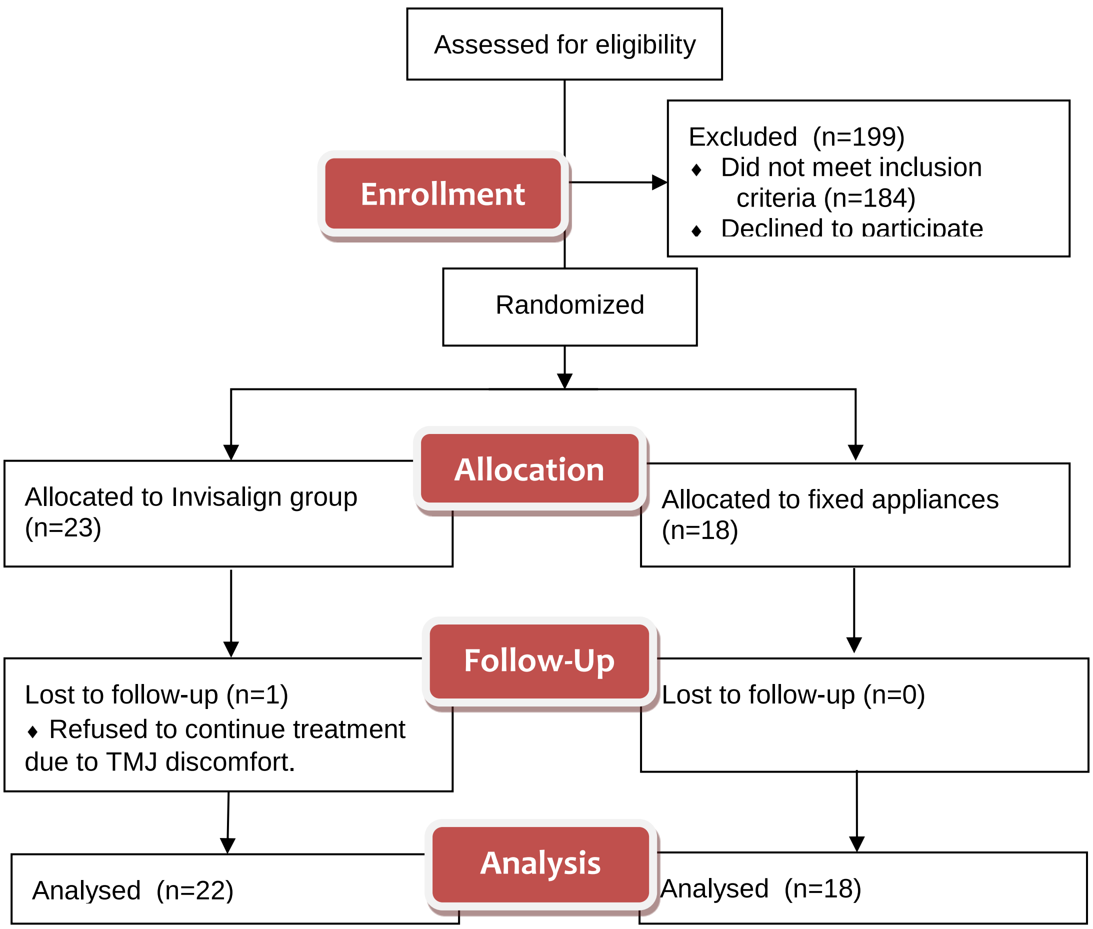


Figure 2. Patient treatment and daily diary timeline

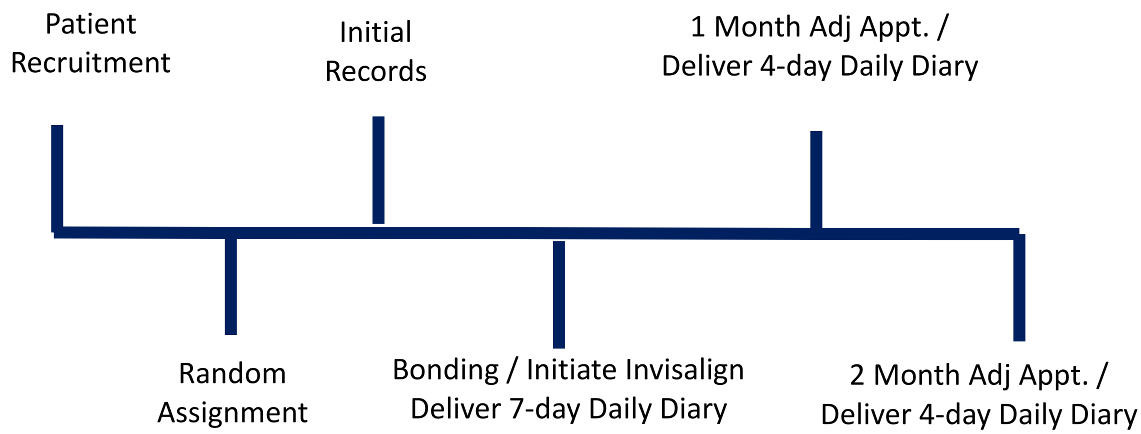


Table 1. Pain [medians (Med) and interquartile ranges] associated with Invisalign and traditional orthodontic treatment at initial delivery or appliance placement.

	Day	0			1			2			3		
Question		25%	Med	75%	25%	Med	75%	25%	Med	75%	25%	Med	75%
Current Discomfort	Invisalign	3.3	11.87	17.1	7.1	13.59	36.9	8.3	13.08	36.7	4.6	**10.68**	39.2
	Traditional	4.6	10.62	22.1	21.0	26.79	46.4	26.8	28.92	46.7	17.0	**32.85**	53.0
	Prob.		.564			.138			.073			**.039**	
Last Time Chewed	Invisalign	1.5	7.57	19.1	8.5	13.41	27.1	8.0	**15.58**	42.2	2.0	**9.01**	44.2
	Traditional	3.1	8.59	24.8	30.6	43.00	60.6	31.6	**39.20**	70.4	21.7	**46.91**	65.1
	Prob.		.780			.051			**.043**			**.023**	
Back Teeth	Invisalign	2.1	9.84	15.7	6.6	**10.78**	30.3	8.7	14.34	35.3	2.1	**10.12**	23.4
	Traditional	4.5	14.85	22.2	25.8	**37.11**	57.8	27.3	30.78	42.6	22.1	**30.75**	56.7
	Prob.		.138			**.026**			.051			**.012**	
Front Teeth	Invisalign	1.6	12.70	23.2	10.0	21.19	61.8	11.9	20.33	57.6	4.3	**13.12**	58.5
	Traditional	4.4	20.18	29.5	38.6	50.43	60.3	26.0	48.26	66.0	23.4	**46.53**	58.8
	Prob.		.423			.188			.078			**.043**	

Table 1 cont. Pain [medians (Med) and interquartile ranges] associated with Invisalign and traditional orthodontic treatment at initial delivery or appliance placement.

4			5			6			7		
25%	Med	75%	25%	Med	75%	25%	Med	75%	25%	Med	75%
6.1	**11.31**	20.4	0.0	**5.70**	11.2	0.2	**5.54**	16.7	0.0	**3.19**	13.1
12.8	**26.85**	54.2	13.7	**17.83**	36.8	10.3	**15.03**	26.3	77.0	**13.80**	26.5
	.029			**.004**			**.011**			**.008**	
0.9	**10.28**	36.4	0.0	**4.32**	17.7	0.2	**4.00**	15.7	0.0	**3.20**	10.4
12.5	**34.76**	66.5	14.9	**24.05**	54.9	14.5	**21.67**	34.5	11.4	**18.80**	29.2
	.015			**.002**			**.010**			**.001**	
0.7	**9.13**	19.7	0.0	**4.94**	12.3	0.2	**5.62**	12.8	0.0	**3.23**	10.8
10.5	**33.82**	44.5	11.4	**24.18**	38.6	9.7	**20.52**	30.5	6.2	**18.75**	26.8
	.021			**.002**			**.012**			**.010**	
0.5	11.04	35.0	0.0	**8.36**	18.0	0.3	**6.63**	19.9	0.0	**2.92**	13.3
13.0	23.84	64.0	15.7	**22.64**	49.1	5.8	**18.16**	44.1	7.0	**18.08**	32.4
	.056			**.043**			**.043**			**.011**	

Figure 3. Median pain levels for Invisalign and traditional treatment groups in response to the question: "Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign."

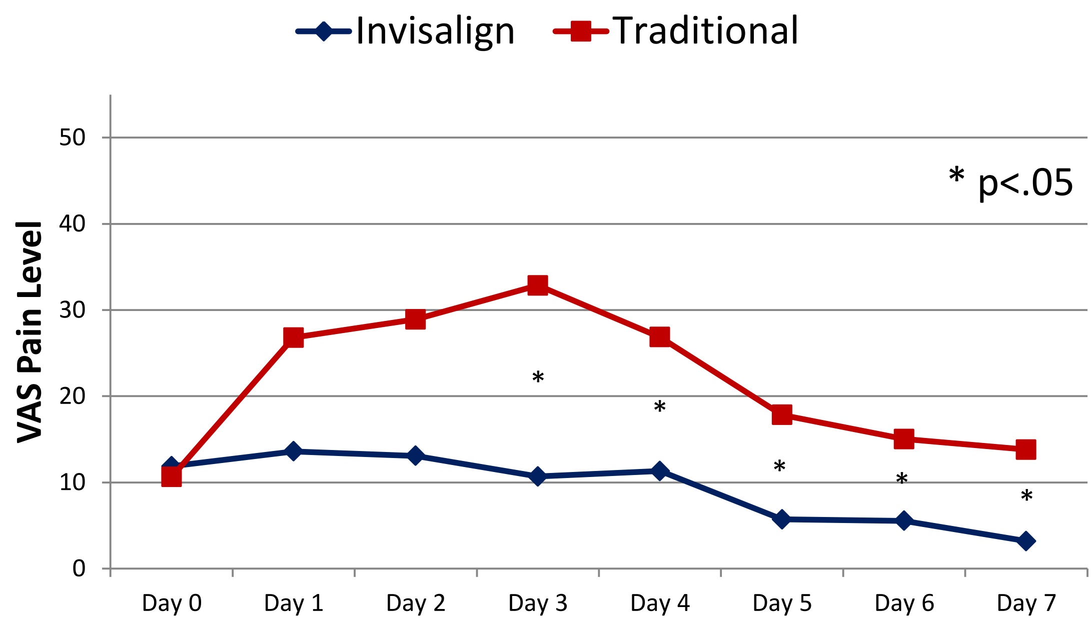


Figure 4. Median pain levels for Invisalign and traditional treatment groups in response to the question: "Rate how much discomfort you experienced the last time that you chewed."

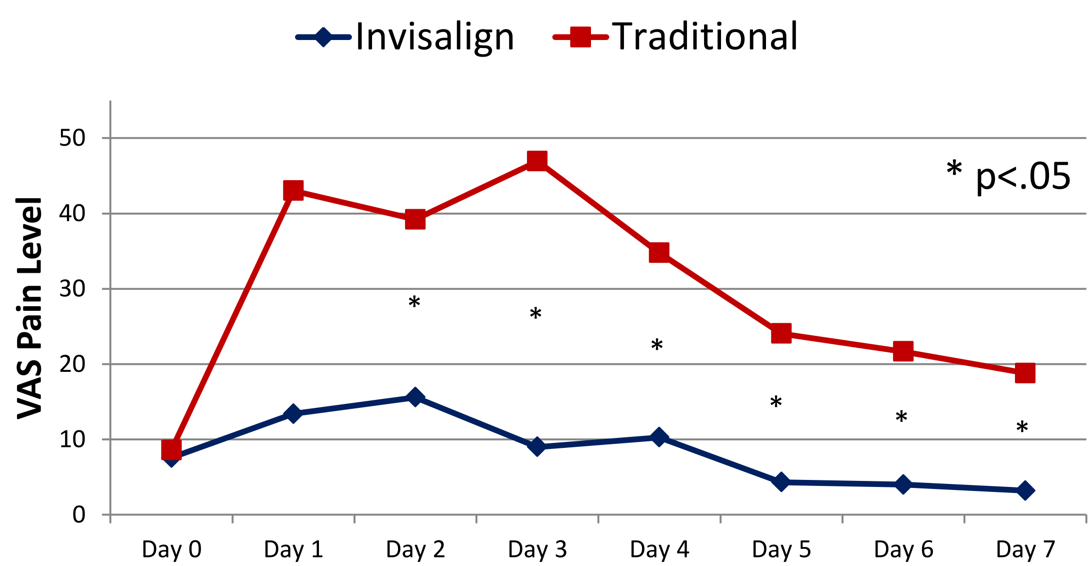


Figure 5. Median pain levels for Invisalign and traditional treatment groups in response to the question: "Rate how much discomfort you are experiencing when you bite down on your back teeth?"

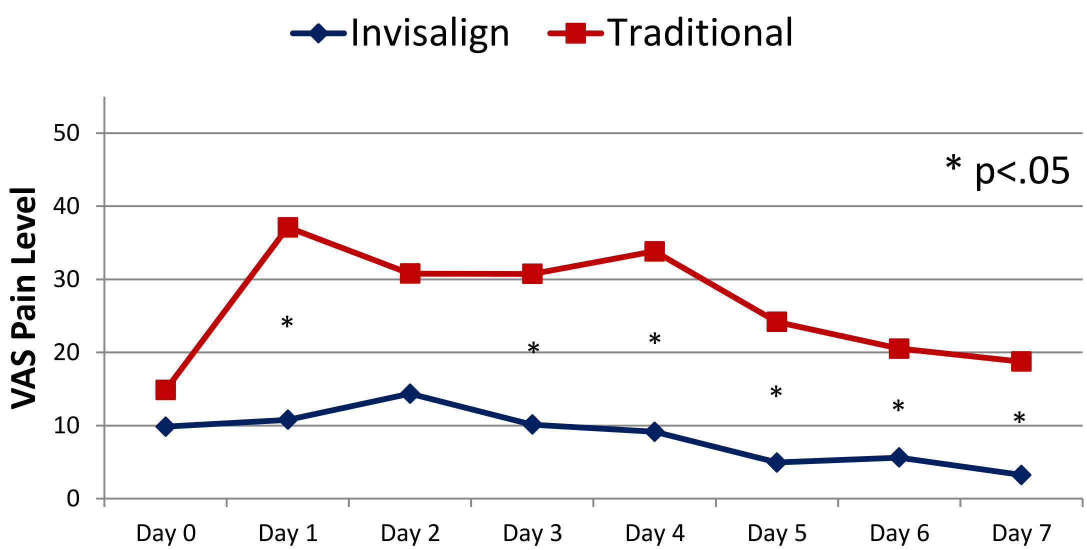


Figure 6. Median pain levels for Invisalign and traditional treatment groups in response to the question: "Rate how much discomfort you are experiencing when you bite down on your front teeth?"

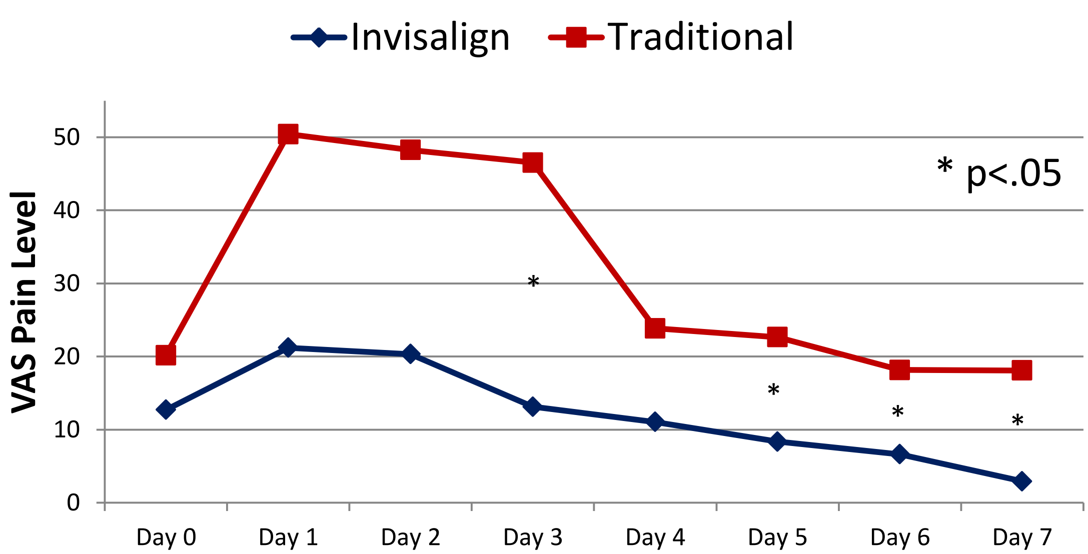


Figure 7. Median pain levels for traditional treatment patients at rest and while chewing.

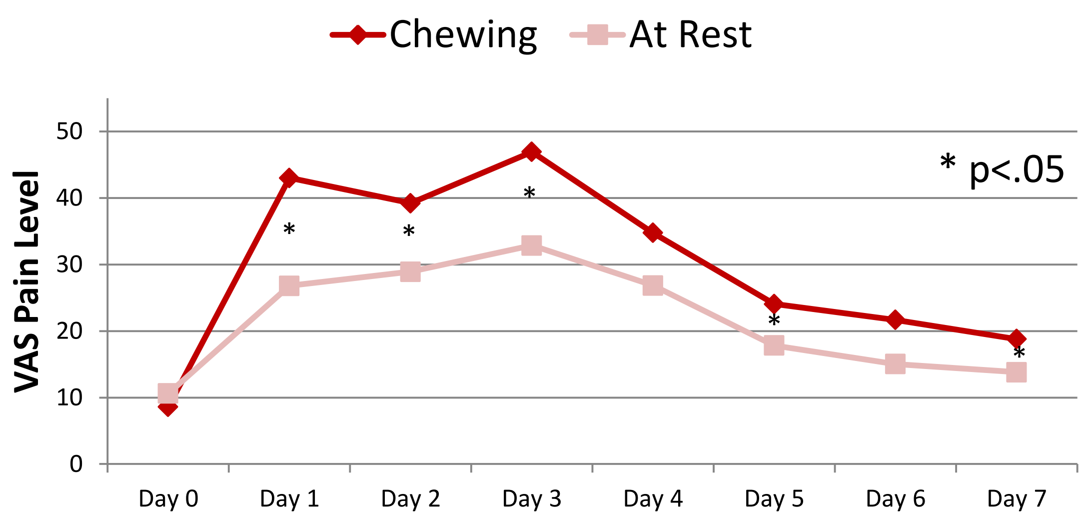


Figure 8. Median pain levels for traditional treatment patients while biting down on the front and back teeth.

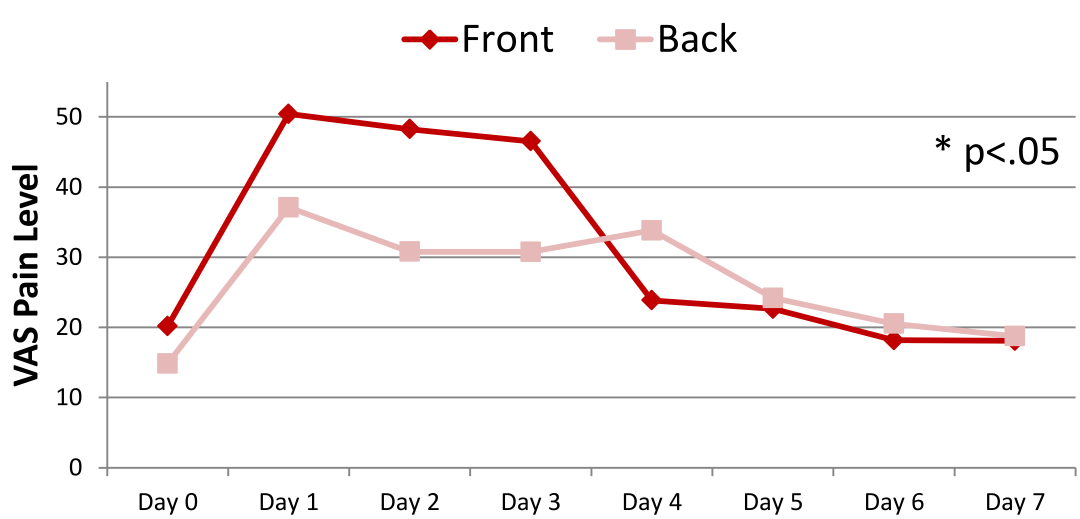


Table 2. Pain [medians (Med) and interquartile ranges] associated with Invisalign and traditional orthodontic treatment for the first month adjustment.

	Day	0			1			2			3			4		
Question		25%	Med	75%	25%	Med	75%	25%	Med	75%	25%	Med	75%	25%	Med	75%
Current Discomfort	Invisalign	1.07	6.37	36.53	0.33	**5.05**	29.27	0.17	**4.19**	23.46	0.00	3.56	16.58	0.00	2.40	17.85
	Traditional	7.62	16.17	37.32	10.83	**16.87**	33.13	12.81	**19.64**	29.27	6.67	10.58	19.73	8.38	16.33	21.94
	Prob.		.081			**.045**			**.041**			.087			.119	
Last Time Chewed	Invisalign	1.19	**5.58**	34.07	1.16	**5.16**	42.76	0.17	**4.19**	23.46	0.00	3.58	16.58	0.00	2.40	17.85
	Traditional	9.91	**23.04**	40.88	12.15	**20.72**	37.42	11.33	**20.84**	33.25	7.59	12.93	19.62	9.37	12.70	22.93
	Prob.		**.037**			**.049**			**.049**			.063			.056	
Back Teeth	Invisalign	0.36	**5.64**	16.08	0.29	**3.72**	22.84	0.28	**3.48**	13.01	0.00	**2.94**	11.59	0.00	2.96	12.55
	Traditional	6.73	**17.49**	34.46	11.33	**20.62**	32.49	10.48	**21.27**	27.49	7.90	**11.08**	17.01	8.84	12.91	20.65
	Prob.		**.049**			**.014**			**.034**			**.041**			.051	
Front Teeth	Invisalign	1.68	6.35	38.21	1.77	3.86	41.01	1.70	4.01	21.38	0.17	4.67	11.37	0.30	4.91	15.17
	Traditional	7.30	22.33	44.31	8.63	16.14	43.39	11.07	20.13	30.48	8.29	10.64	23.50	8.53	14.85	23.37
	Prob.		.127			.146			0.127			.102			.110	

Table 3. Pain [medians (Med) and interquartile ranges] associated with Invisalign and Traditional orthodontic treatment for the second month adjustment.

	Day	0			1			2			3			4		
Question		25%	Med	75%	25%	Med	75%	25%	Med	75%	25%	Med	75%	25%	Med	75%
Current Discomfort	Invisalign	5.55	7.50	24.66	4.38	9.21	24.58	3.16	11.05	23.99	1.35	6.60	16.02	1.17	4.32	18.87
	Traditional	11.02	23.26	30.73	14.77	22.39	32.43	11.26	19.06	38.30	7.04	15.15	25.70	6.19	12.16	26.74
	Prob.		.169			.116			.128			.067			.105	
Last Time Chewed	Invisalign	4.81	8.47	32.87	5.33	8.14	28.85	4.35	6.32	25.50	2.46	6.85	12.79	1.23	7.12	20.36
	Traditional	10.22	24.15	33.91	7.43	23.39	35.59	7.88	20.77	32.15	9.46	17.93	24.66	6.98	13.61	25.98
	Prob.		.259			.141			.141			.095			.202	
Back Teeth	Invisalign	2.88	7.63	29.17	3.02	4.70	29.41	0.33	5.98	22.04	0.26	3.41	11.64	0.00	1.88	16.78
	Traditional	6.90	21.27	34.35	9.51	21.43	36.74	11.20	22.17	32.15	6.39	15.55	22.99	5.17	12.33	23.29
	Prob.		.220			.094			.076			.060			.068	
Front Teeth	Invisalign	3.80	6.47	32.66	5.17	7.90	29.06	4.05	9.64	28.49	2.22	6.82	14.32	1.01	6.24	19.92
	Traditional	13.8	25.96	38.90	12.64	28.99	33.81	9.49	21.76	28.98	8.52	15.57	26.08	8.16	13.83	21.37
	Prob.		.185			.141			.141			.193			.220	

Figure 9. Median pain levels for Invisalign patients at initial bonding, 1 month adjustment and at the 2 month adjustment in response to the question: "Rate how much discomfort you are experiencing when you bite down on your front teeth?"

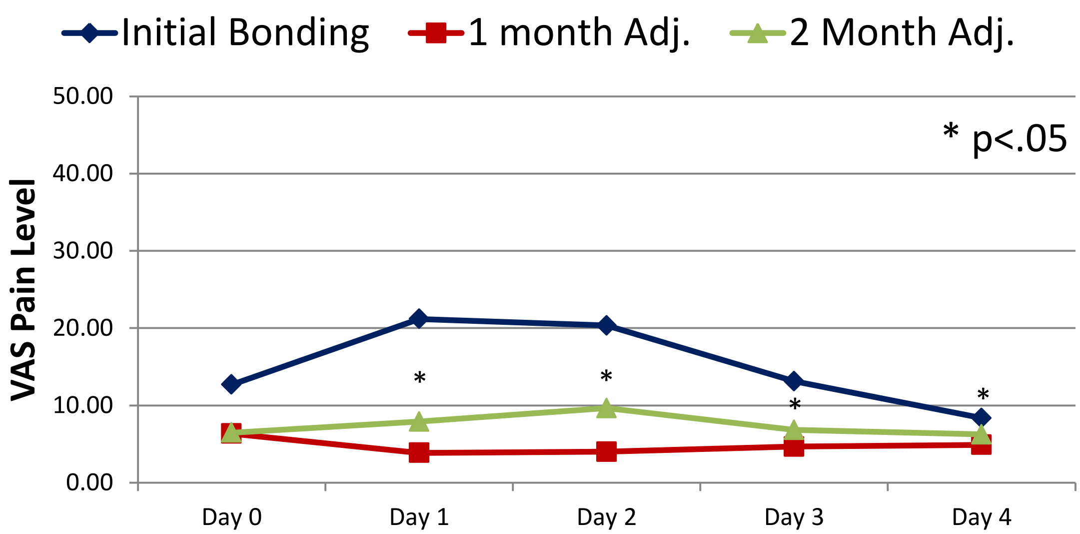


Figure 10. Median pain levels for traditional patients at initial bonding, 1 month adjustment and at the 2 month adjustment in response to the question: "Rate how much discomfort you are experiencing when you bite down on your front teeth?"

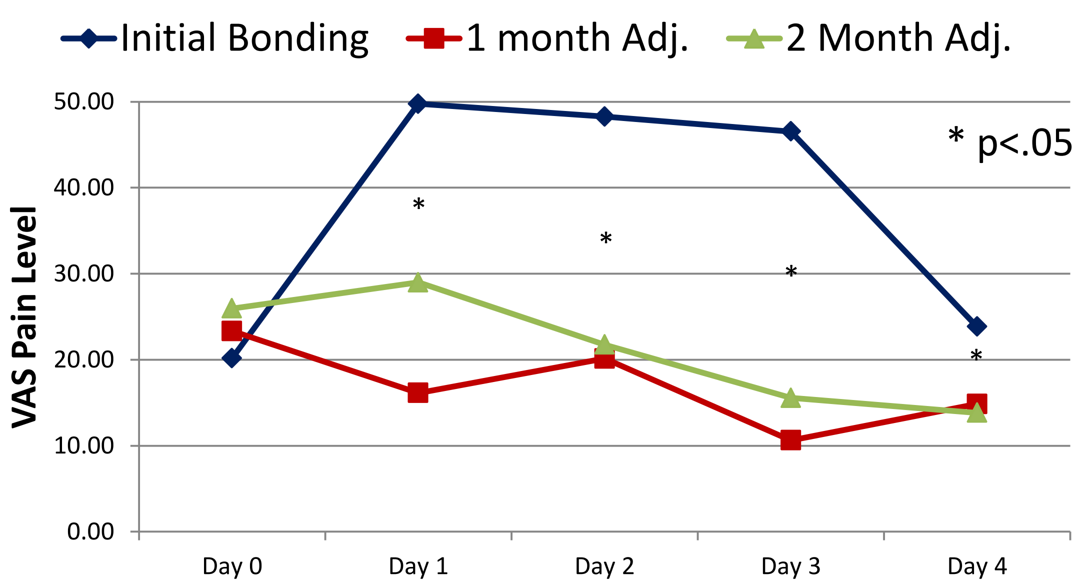


Figure 11. Percentages of patients who took medications for tooth pain during the first week after the initial appliance placement or Invisalign delivery.

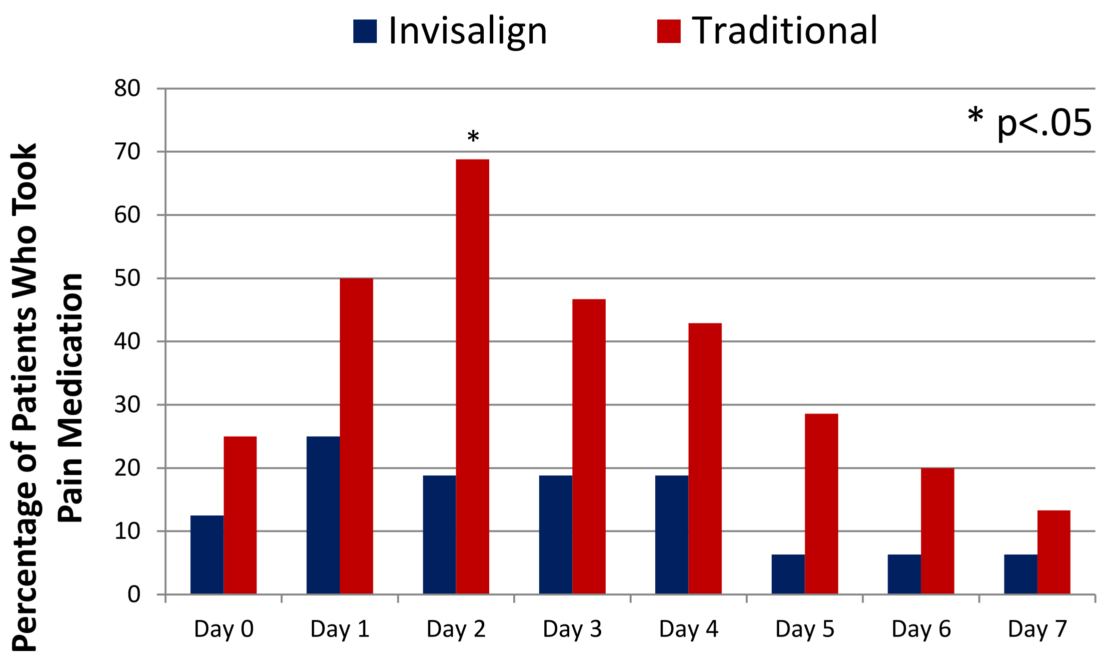


Table 4. Percentages of patients who took medications for tooth pain after the first, second, and sixth month adjustments.

	Day	0	1	2	3	4
Adjustment						
First Adjustment	Invisalign	6.3	12.5	6.3	6.3	12.5
	Traditional	23.1	16.7	0	7.7	9.1
	Prob.	0.191	0.755	0.359	0.879	0.782
Second Adjustment	Invisalign	15.4	15.4	8.3	7.7	8.3
	Traditional	9.1	0.0	0.0	0.0	0.0
	Prob.	0.642	0.174	0.328	0.347	0.328
Sixth Adjustment	Invisalign	30.0	40.0	30.0	20.0	20.0
	Traditional	22.2	22.2	0.0	0.0	0.0
	Prob.	0.701	0.405	0.090	0.180	0.357

Figure 12. Percentages of patients who had sleep disturbance from tooth pain during the first week after the initial appliance placement or Invisalign delivery.

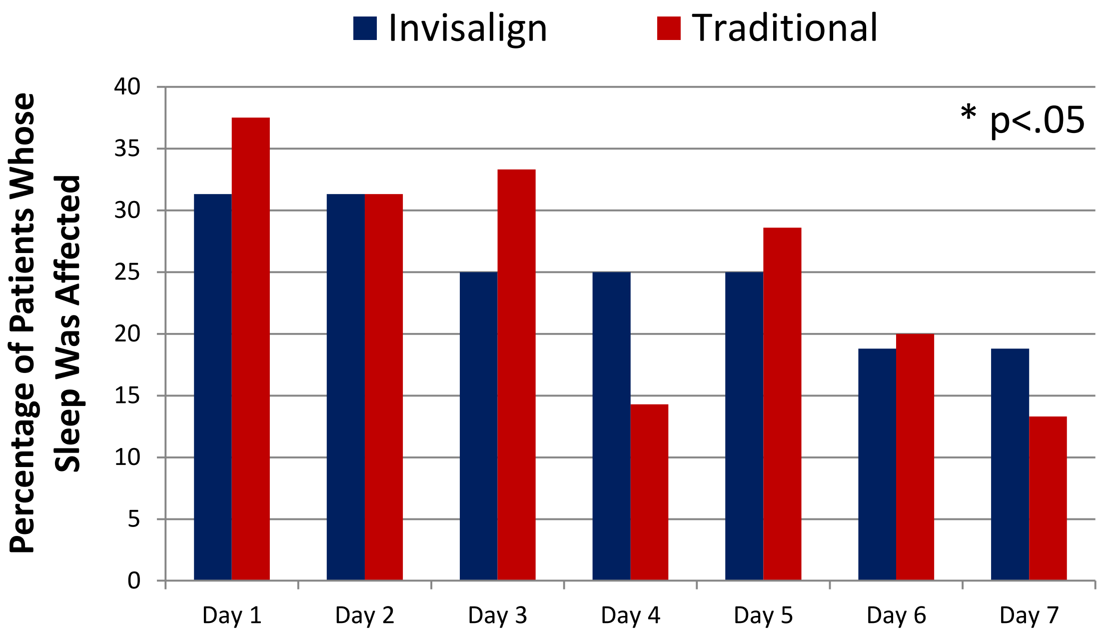


Table 5. Percentages of patients who had sleep disturbance from tooth pain after the first, second, and sixth month adjustments.

	Day	1	2	3	4
Adjustment					
First Adjustment	Invisalign	18.8	18.8	18.8	18.8
	Traditional	16.7	15.4	7.7	14.8
	Prob.	0.887	0.811	0.390	0.488
Second Adjustment	Invisalign	23.1	16.7	7.7	8.3
	Traditional	0.0	0.0	0.0	0.0
	Prob.	0.089	0.156	0.347	0.328
Sixth Adjustment	Invisalign	10.0	10.0	0.0	0.0
	Traditional	22.2	12.5	12.5	12.5
	Prob.	0.466	0.867	0.250	0.250

APPENDIX B

DAILY DISCOMFORT DIARY

TEXAS A&M UNIVERSITY
BAYLOR
COLLEGE OF DENTISTRY
Texas A&M Health Science Center

Initials_______________
Date________________
Time________________

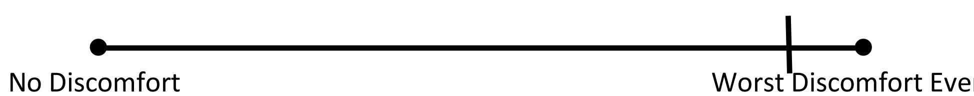
1. Each of the sheets that follow has **8** questions apiece, except for the first sheet.
    a. The first sheet will be filled in before you have received your Invisalign/Braces.
    b. The other sheets will be filled in by you after the braces or Invisalign are on your teeth.
    c. Try to fill out the forms at the same time each day. E.g. If you fill out the first form at 7 P.M., try and fill out the remaining forms at 7 P.M. at each consecutive day.

2. The 8 questions will ask you about discomfort you have previously experienced and are currently experiencing as well as about pain medications that you have taken.
    a. The ***first question*** will ask you to remember the worst discomfort of your life and record the discomfort on the line between the phrases, "*No Discomfort*" and "*Worst Discomfort Ever*"

Example 1:

Please rate the worst physical discomfort that you have ever experienced in your life on the following line.

Let's say that the worst discomfort that I have ever experienced was a broken arm and nothing else that I have ever done has hurt that bad. I would mark this experience near the right end of the line near "Worst Discomfort Ever"



Example 2:

In the past 24 hours how often did you take medication to relieve tooth pain?

Please answer these questions with a 1 for never, 2 for seldom, 3 for often, and 4 for always by ***CIRCLING*** the appropriate response.

E.G. In the past 24 hours how often did you take medication to relieve tooth pain?
1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS

INITIAL BONDING/PLACEMENT OF INVISALIGN	Initials______________ Date______________ Time______________

1. Please rate the worst physical discomfort that you have ever experienced in your life on the following line.

No Discomfort ——————————— Worst Discomfort Ever

2. Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign

No Discomfort ——————————— Worst Discomfort Ever

3. Rate how much discomfort did you experience that last time that you chewed

No Discomfort ——————————— Worst Discomfort Ever

4. Rate how much discomfort you are experiencing when you bite down on your back teeth?

No Discomfort ——————————— Worst Discomfort Ever

5. Rate how much discomfort you are experiencing when you bite down on your front teeth?

No Discomfort ——————————— Worst Discomfort Ever

In the past 24 hours, how often:

6. Did you take medication to relieve tooth pain?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
7. Did you take medication to relieve pain not associated with tooth pain?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS

1 DAY AFTER PLACEMENT OF BRACES OR INVISALIGN

Initials_______________
Date_________________
Time_________________

TEXAS A&M UNIVERSITY
BAYLOR
COLLEGE OF DENTISTRY
Texas A&M Health Science Center

1. Please rate the worst physical discomfort that you have ever experienced in your life on the following line.

No Discomfort — Worst Discomfort Ever

2. Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign

No Discomfort — Worst Discomfort Ever

3. Rate how much discomfort did you experience that last time that you chewed

No Discomfort — Worst Discomfort Ever

4. Rate how much discomfort you are experiencing when you bite down on your back teeth?

No Discomfort — Worst Discomfort Ever

5. Rate how much discomfort you are experiencing when you bite down on your front teeth?

No Discomfort — Worst Discomfort Ever

In the past 24 hours, how often:

6. Did discomfort caused by your orthodontic appliance interfere with your sleep?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
7. Did you take medication to relieve tooth pain?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
8. Did you take medication to relieve pain not associated with tooth pain?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS

2 DAY AFTER PLACEMENT OF BRACES OR INVISALIGN

Initials_______________
Date_________________
Time_________________

TEXAS A&M UNIVERSITY
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COLLEGE OF DENTISTRY
Texas A&M Health Science Center

1. Please rate the worst physical discomfort that you have ever experienced in your life on the following line.

No Discomfort —————————— Worst Discomfort Ever

2. Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign

No Discomfort —————————— Worst Discomfort Ever

3. Rate how much discomfort did you experience that last time that you chewed

No Discomfort —————————— Worst Discomfort Ever

4. Rate how much discomfort you are experiencing when you bite down on your back teeth?

No Discomfort —————————— Worst Discomfort Ever

5. Rate how much discomfort you are experiencing when you bite down on your front teeth?

No Discomfort —————————— Worst Discomfort Ever

In the past 24 hours, how often:

6. Did discomfort caused by your orthodontic appliance interfere with your sleep?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
7. Did you take medication to relieve tooth pain?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
8. Did you take medication to relieve pain not associated with tooth pain?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS

3 DAY AFTER PLACEMENT OF BRACES OR INVISALIGN

Initials_______________
Date_________________
Time_________________

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1. Please rate the worst physical discomfort that you have ever experienced in your life on the following line.

No Discomfort ——————————————— Worst Discomfort Ever

2. Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign

No Discomfort ——————————————— Worst Discomfort Ever

3. Rate how much discomfort did you experience that last time that you chewed

No Discomfort ——————————————— Worst Discomfort Ever

4. Rate how much discomfort you are experiencing when you bite down on your back teeth?

No Discomfort ——————————————— Worst Discomfort Ever

5. Rate how much discomfort you are experiencing when you bite down on your front teeth?

No Discomfort ——————————————— Worst Discomfort Ever

In the past 24 hours, how often:

6. Did discomfort caused by your orthodontic appliance interfere with your sleep?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
7. Did you take medication to relieve tooth pain?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
8. Did you take medication to relieve pain not associated with tooth pain?
   1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS

4 DAY AFTER PLACEMENT OF BRACES OR INVISALIGN

Initials________________
Date__________________
Time__________________

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9. Please rate the worst physical discomfort that you have ever experienced in your life on the following line.

No Discomfort —————————————— Worst Discomfort Ever

10. Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign

No Discomfort —————————————— Worst Discomfort Ever

11. Rate how much discomfort did you experience that last time that you chewed

No Discomfort —————————————— Worst Discomfort Ever

12. Rate how much discomfort you are experiencing when you bite down on your back teeth?

No Discomfort —————————————— Worst Discomfort Ever

13. Rate how much discomfort you are experiencing when you bite down on your front teeth?

No Discomfort —————————————— Worst Discomfort Ever

In the past 24 hours, how often:

14. Did discomfort caused by your orthodontic appliance interfere with your sleep?
    1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
15. Did you take medication to relieve tooth pain?
    1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
16. Did you take medication to relieve pain not associated with tooth pain?
    1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS

5 DAY AFTER PLACEMENT OF BRACES OR INVISALIGN

Initials_______________
Date_______________
Time_______________

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17. Please rate the worst physical discomfort that you have ever experienced in your life on the following line.

No Discomfort — Worst Discomfort Ever

18. Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign

No Discomfort — Worst Discomfort Ever

19. Rate how much discomfort did you experience that last time that you chewed

No Discomfort — Worst Discomfort Ever

20. Rate how much discomfort you are experiencing when you bite down on your back teeth?

No Discomfort — Worst Discomfort Ever

21. Rate how much discomfort you are experiencing when you bite down on your front teeth?

No Discomfort — Worst Discomfort Ever

In the past 24 hours, how often:

22. Did discomfort caused by your orthodontic appliance interfere with your sleep?
    1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
23. Did you take medication to relieve tooth pain?
    1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS
24. Did you take medication to relieve pain not associated with tooth pain?
    1 = NEVER 2 = SELDOM 3 = OFTEN 4 = ALWAYS

6 DAY AFTER PLACEMENT OF BRACES OR INVISALIGN

Initials________________
Date_________________
Time_________________

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25. Please rate the worst physical discomfort that you have ever experienced in your life on the following line.

No Discomfort — Worst Discomfort Ever

26. Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign

No Discomfort — Worst Discomfort Ever

27. Rate how much discomfort did you experience that last time that you chewed

No Discomfort — Worst Discomfort Ever

28. Rate how much discomfort you are experiencing when you bite down on your back teeth?

No Discomfort — Worst Discomfort Ever

29. Rate how much discomfort you are experiencing when you bite down on your front teeth?

No Discomfort — Worst Discomfort Ever

In the past 24 hours, how often:

30. Did discomfort caused by your orthodontic appliance interfere with your sleep?
    1 = NEVER   2 = SELDOM   3 = OFTEN   4 = ALWAYS
31. Did you take medication to relieve tooth pain?
    1 = NEVER   2 = SELDOM   3 = OFTEN   4 = ALWAYS
32. Did you take medication to relieve pain not associated with tooth pain?
    1 = NEVER   2 = SELDOM   3 = OFTEN   4 = ALWAYS

7 DAY AFTER PLACEMENT OF BRACES OR INVISALIGN

Initials________________
Date________________
Time________________

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33. Please rate the worst physical discomfort that you have ever experienced in your life on the following line.

No Discomfort ———————————— Worst Discomfort Ever

34. Rate the amount of discomfort that you are currently experiencing with your braces or Invisalign

No Discomfort ———————————— Worst Discomfort Ever

35. Rate how much discomfort did you experience that last time that you chewed

No Discomfort ———————————— Worst Discomfort Ever

36. Rate how much discomfort you are experiencing when you bite down on your back teeth?

No Discomfort ———————————— Worst Discomfort Ever

37. Rate how much discomfort you are experiencing when you bite down on your front teeth?

No Discomfort ———————————— Worst Discomfort Ever

In the past 24 hours, how often:

38. Did discomfort caused by your orthodontic appliance interfere with your sleep?
    1 = NEVER   2 = SELDOM   3 = OFTEN   4 = ALWAYS
39. Did you take medication to relieve tooth pain?
    1 = NEVER   2 = SELDOM   3 = OFTEN   4 = ALWAYS
40. Did you take medication to relieve pain not associated with tooth pain?
    1 = NEVER   2 = SELDOM   3 = OFTEN   4 = ALWAYS