Saurabh Mannan
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Education

University of Maryland Dental School Endodontic Residency
Summer 2016- Summer 2019
Certificate of Endodontics Completion June 2019 Master of Science Completion June 2019

University of Pennsylvania School of Dentistry
D.M.D. Doctor of Dental Medicine 2011

Indiana University Purdue University Indianapolis
M.P.H. Master in Public Health 2007

SGRD Dental College, Amritsar, India
B.D.S. Bachelor of Dental Surgery 2003

Professional Experience

Teaching Resident–University of Maryland Fall 2016 - Current

- Teach 2nd year dental students the basics of endodontics in a pre-clinical course
- Supervise 3rd and 4th year dental students in their treatment of patients

Dental Director
Texas Department of Aging and Disability, the Health & Human Services Commission – Spring 2015- 2016

Dental Director
Dental Practice – Spring 2012-2015

Associate Dentist
Dental Practice – 2011-2012

Adjunct Assistant Professor
University of Houston – 2008-2009

SGRD Dental College, Amritsar, India
Internship in General Dentistry 2004

Research Experience

Resident, University of Maryland Dental Summer 2016 – Current

- Observational Study Evaluating Pain in Endodontic Patients Diagnosed with Depression. Summer 2016

- Poster presentation at 2018 AAE national conference Mentor
    - Dental Abscess to Septic shock within 24 hours – Case Report
    - Mentor: Dr. Patricia Tordik

- Poster presentation at 2016 AAE national conference
    - What Every Endodontist Should Know About Opioids.
    - Mentor: Dr. Patricia Tordik

University of Pennsylvania School of Dentistry 2009 - 2011

- Blatz, M.B., Mante, F.K., Saleh, N., Atlas, A.M., Mannan, S., & Ozer, F. (2012) "Postoperative tooth sensitivity with a new self-adhesive resin cement – a randomized clinical trial" Published Clinical Oral Investigation.

Indiana University School of Dentistry 2005 - 2007

- Maupome, G., Schrader, S., Mannan, S. Garetto, L., & Eggertsson, H. (2008) "Diagnostic thinking and information used in clinical decision-making: a qualitative study of expert and student dental clinicians". Published BMC Oral Health

- Maupome, G, Geretto, L.P., Eggertsson, H., Schrader, S.M., & Mannan, S. (2007). Content analysis of diagnostic thinking processes and concepts used in clinical decision-making by expert and novice dental clinicians" Journal of Dental Education International American Dental Research's 86th General Session & Exhibition, held at the Metro Toronto Convention Centre in Toronto, ON, Canada from July 2-5.

- Maupome, G, Geretto, L.P., Eggertsson, H., Schrader, S.M., & Mannan, S. (2007). Standardized patients as a research model for clinical decision-making: Expert and novice dental clinician using live patients (poster), presented on September 21 -24, 2007, at 8th Advances in Qualitative Methods Conference in Banff, Alberto, Canada.

Indiana Minority Health Coalition, Inc., Department of Research 2005 - 2007

- Mannan, S, Roberson, Jr., C., & Ohmit, A. (2006). Nutrition (Poster), Indiana Minority Health Coalition, Inc., presented in IN Shape Indiana Health Summit 2006, Indianapolis.

- Mannan, S., Roberson, Jr., C., & Ohmit, A. (2007). A Cross-Sectional Study to Identify Variables Influencing Food Choices (Poster), Indiana Public Health Association Summer Conference 2007, Bloomington.

The Methodist Hospital, Houston, Texas 2008 - 2009

- Patel, S.J., Knight, R.J., Suki, W.N., Abdellatif, A., Duhart, B.T. Jr., Krauss, A.G., Mannan, S., Nezakatgoo N, & Osama, G.A. (2011). "Rabbit antithymocyte induction and dosing in deceased donor renal transplant recipients over 60 yr of age". Published: Clinical Transplantation

- Liebl, M., Nguyen, P.H., Vojticek, B., Mannan, S., & Hamilton, D. (2008). Efficacy and Safety of Transitioning from Continuous Insulin Infusion (CII) to an Insulin Glargine Based Regimen in Cardiovascular Surgery Patients (Poster # 493), presented in Society of Critical Care Medicine 37th Critical Care Congress 2007.

- Assessment of safety regarding rapid rituximab infusion. Published: Community Oncology. Special Accomplishment for Study design and data analysis

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Academic Awards

University of Pennsylvania
Honors in Clinical Restorative Seminar at University of Pennsylvania School of Dental Medicine

Indiana Minority Health Coalition, Inc., Department of Research
Project received highest honor in the state of Indiana in IPHA, summer conference, 2007

SGRD Dental College, Punjab, India
Gold Medal (2002) in Inter State College Soccer

Licensures/Certifications

- Basic Cardiac Life Support 2018
- State of Maryland Dental License 2015- Current
- State of Indiana Dental License 2019- Current

Board Certifications

- North East Regional Boards Clinical Licensure Examination 2011 - Present
- National Dental Board Examinations 2005

Professional Membership Organization & Activities

- Member of American association of Endodontics AAE 2016 - Present

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Community Services

Provided dedicated individualized comprehensive oral screenings and multidisciplinary oral health care to the community in Amritsar, India – 2004 - 2005

Provided dedicated individualized comprehensive oral screenings and multidisciplinary oral health care to the community in Lubbock, Texas – 2014-2015

Teaching Experience

Adjunct Assistant Professor, University of Houston, 2006 - 2009
Teaching Resident–University of Maryland Spring 2017 – Current

ABSTRACT

TITLE: Observational Study Evaluating Pain in Endodontic Patients Diagnosed with Depression – A Pilot Study

Saurabh Mannan, Master of Science 2019

Thesis Directed By: Joel Greenspan, PhD

AIM: To evaluate the role of depression in endodontic post-procedural pain

METHODOLOGY: This prospective observational study enrolled 42 patients that explored the correlation between patient's level of depression and pain perception following non-surgical root canal treatment (NSRCT). The Hospital Anxiety and Depression Scale (HADS) assessed the patient's level of anxiety/depression pre-and postoperatively. The patient used a visual analog scale (VAS) to record their pain intensity and feelings of unpleasantness with their dental experience immediately following their NSRCT. Pain diaries recorded pain intensity post-operatively at the 2nd, 4th, and 7th day. A cohort of endodontic patients who were not diagnosed with depression served as controls.

RESULT: A total of 41 patients were included, 30 non-depressed patients and 11 patients diagnosed with depression by their physicians. Two patients did not return the pain dairy. Therefore, data from 29 non-depressed patients and ten depressed patients were available for analysis. This study showed that the diagnosis of depression was significantly associated with both higher immediate post-operative pain and immediate sensations of unpleasantness. Furthermore, HADS ≥ 8 was found to be a significant predictor of greater post-operative pain at day two.

CONCLUSIONS: Within the limitations of this study, either a diagnosis of depression, or signs of anxiety or depression are a positive predictor of greater post-operative pain.

Observational Study Evaluating Pain in Endodontic Patients Diagnosed with Depression

A Pilot Study

by
Saurabh Mannan

Thesis submitted to the Faculty of the Graduate School of the

University of Maryland, Baltimore in partial fulfillment

of the requirements for the degree of

Master of Science

2019

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vi. I want to acknowledge Dr. Mir Khan, D.D.S., M.S. for giving me the original concept.

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INTRODUCTION

Pain is considered to be a multidimensional experience with sensory, affective-motivational and cognitive components (1). The sensory component includes the perception of location, quality, and intensity of the noxious stimulus and the emotional component processes the affective salience or unpleasantness of the stimulus. Depression is an emotion dominated by sadness and associated with feelings of hopelessness and gloom (2). When pain and depression occur together, both conditions worsen (3). Physical symptoms have been found to increase the duration of a depressed mood. Behavior that includes withdrawal and avoidance of other people and social activities is likely to increase in patients who have other co-morbid anxiety disorders, such as depression (4).

UNDERSTANDING PAIN

Evoked pain has two aspects: a) nociceptive transmission and pain perception and b) pain reaction. Nociceptive transmission and pain perception may be divided into three steps: a) detection, b) processing (CNS modulation), and c) perception (5). Detection occurs in response to trigger/insult to the peripheral nerve endings and surrounding tissues. In odontogenic pain, a noxious stimulus excites a class of A-delta and C fibers (nociceptors), the cell bodies of which lie in the trigeminal ganglion. The central end of these fibers synapse in the subnucleus caudalis of the trigeminal nuclear complex in the medullary dorsal horn. The trigeminal nuclear complex receives craniofacial and intraoral sensory information within four components a) the main sensory nucleus, b) nucleus oralis, c) nucleus intermedius, and d) nucleus caudalis. Information from nociceptors (and thermoceptors) arrives in nucleus caudalis. In the nucleus caudalis, the nerve signals are either attenuated or exaggerated by descending nerve fibers (6). The attenuation is called inhibition whereas exaggerated is called facilitation (7). Descending fibers utilize several neurochemical mechanisms to modify the pain (8). In 2007, Tracy et al discussed the role of the amygdala, hypothalamus, insula, and anterior cingulate cortex in pain modulation (9). The trigeminal nerve fibers up to this point of this first synapse are referred to as first degree projection.

The neurons in the Nucleus caudalis send their fibers across the midline to form the trigeminothalamic tract, terminating in the ventral posterior medial (VPM) nucleus of thalamus. This is the second-degree projection. The neurons in VPM (third order neurons) project their fibers to the cerebral cortex via the thalamocortical tract (10). Nociceptive signaling needs to reach the cerebral cortex in order for perception to occur. The resulting perception of pain is modified by both present and past emotional components (10). In 2000, Price elaborated upon pain's affective dimension (11). Among other things, he noted that the anterior cingulate cortex has an important role in perceiving pain as unpleasant.

UNDERSTANDING DEPRESSION

Depression is a mood disorder which entails physiologic, cognitive, and psychomotor dysfunction (12). The etiopathology of depression is multifactorial; genetic diathesis and stress are major contributory factors in developing depression (13). It is found to be associated with hyperactivity of the hypothalamo-pituitary-adrenal (HPA) axis; which has been related to reductions in hippocampal volumes and prefrontal cortex (PFC) activity (14). The reduction of hippocampal volume and prefrontal cortex activity disrupts homeostasis within the neurocircuit contributing to depression. Depression is also associated with reduction in neurotrophins, the reduced activity of noradrenergic and serotonergic neurotransmission and hyperactivity of the inflammatory response system. All of these changes are associated with both structural deficit and functional abnormalities within the cortico-thalamic-striatal-limbic neurocircuit disrupting the system balance. Hence, the prefrontal cortex (PFC) is not able to regulate overactivity within the cortico/limbic region. This impairment of PFC and resultant consequences manifests clinically as symptoms of depression (15).

RELATIONSHIP BETWEEN DEPRESSION AND POST-OPERTIVE PAIN

In the medical literature, depression has been extensively studied as a predictor of post-operative pain. However, there are conflicting conclusions. A 3-year study was conducted to assess role of anxiety/depression in the postoperative pain experienced by adolescents (16). According to the authors, it was the first large British assessment of adolescent post-operative pain. All patients underwent surgical procedures (gynecology, general surgery, orthopedics, ear nose and throat, oral and plastic surgery). The study used HADS tool to measure anxiety/depression. The study found that the patients with symptoms of depression were more likely to experience moderate to severe pain (χ^2= 44.40, $p < 0.001$).

Other study (17,18) enrolled 85 women receiving surgery, and subsequently, interviewed 37 out of 85 women by telephone four to six weeks following surgery. Most women had abdominal hysterectomies (n=71) and the remaining women had laparotomies (n = 7), colposuspension (n = 5), and myomectomy (n = 2). The study used the HADS tool to measure anxiety/depression. The participants with a HADS score > 7 had higher pain scores, post-operatively.

Gureje et al. (2010) also found a strong relationship between persistent pain and psychological issues (19). Patients who had high levels of depression reported pain in multiple sites in the body, including the jaw. This may have clinical importance in depressed patients who require root canal treatment. The symptoms of a toothache could be exacerbated.

De Cosmo, et al. also found that patients with preoperative anxiety and depression reported higher pain intensities postoperatively and a larger consumption of pain medication, such as tramadol (20). The study used Self-rating anxiety scale (SAS) and self-rating questionnaire for depression (SRQ-D). Similar results, that is, depressed patients reporting more post-operative pain, were observed in a study done by Taenzer et al (21).

In contrast, in 2017, a systematic review done by Dadgostar et al. found no significant relationship between depression and post-operative pain (22). In this meta-analysis, 8 studies (comprising a total of 1314 patients) showed a significant relationship between depression and post-operative pain. However, 10 studies (comprising a total of 1226 patients) failed to show depression as a predictor of post-operative pain.

HEALTH PROBLEM GAP IN THE CURRENT LITERATURE

Depression is one of the most common mental disorders in the United States (23). Psychological factors increase the complexity of the pain experience (19). Previous studies have shown that the severity of depression modifies the pain intensity and vice versa (24). In other words, a patient with a higher severity of depression is more likely to perceive pain of higher intensity. Despite advancements in medical care, depressed patients suffer from moderate to severe postoperative pain that leads to decreased patient satisfaction, delayed postoperative ambulation and the development of chronic postoperative pain (16). There is limited literature exploring the relationship between acute postoperative pain and psychological morbidity. To our knowledge, no exploration has been done to correlate depression and pain experiences in patients receiving a non-surgical root canal treatment (NSRCT). Managing dental pain in depressed patients may present a challenge. The extent of the relationship between dental pain and depression is unknown. Understanding if there is a positive correlation between dental pain and depression can assist the dentist in managing the depressed patient's pain, peri-operatively. This study will explore the correlation between the severity of depression and the pain intensity associated with an initial non-surgical root canal treatment (NSRCT).

DENTAL LITERATURE REVIEW FOR PREDICTORS OF PAIN

Gedney et al. (25) illustrated that a pre-existing affective state (mood) affects post-operative unpleasantness and pain. The study found that a sensory component (pain intensity) predicts only a 1-week memory of pain intensity. In contrast, a patient's pretreatment affective state predicts the memory of pain intensity and unpleasantness up to 18 months. The study emphasized the importance of anxiety management for minimizing the patients' long-term recollection of their aversion toward dental procedures.

In 2007, one study found that orofacial pain can be significantly related to a level of distress (26). The study provided a systematic description of clinical findings and psychosocial factors in patients suffering from atypical odontalgia (AO) and concluded that a majority of the AO patients had higher scores for depression.

In endodontics, the most common strategy for providing immediate post-operative pain relief is making an accurate pre-operative assessment of the patient's symptoms, establishing a correct diagnosis, and postoperative pain management. Eliminating the pathogens, necrotic tissue and toxins through root canal debridement provides adequate pain relief, in most cases.

The predictors of post-operative pain have been well documented in endodontics. According to Nusstein et al., short-term drainage through the tooth in symptomatic, necrotic cases with bone loss did not significantly reduce pain, including percussion pain, swelling, or the number of analgesic medications taken (27). However, relieving the functional tooth contacts provided postoperative pain relief in those patients whose teeth initially exhibited pulp vitality, percussion sensitivity, preoperative pain, and/or the absence of a periradicular radiolucency (28). An endodontic flare-up is defined as an acute exacerbation of a periradicular pathosis after the initiation or continuation of nonsurgical root canal treatment (29). In a meta-analysis, the incidence of flare-up has been reported to be 8.1% (30). Flare-up is multifactorial involving chemical, mechanical, and biological factors (31). Flare-up has been associated with gender, age, tooth location, tooth type, type of endodontic treatment, history of allergies, genetics, pre-operative diagnosis, and pre-operative analgesic use (32–35).

To our knowledge, depression has not been explored as a predictor for post-operative pain in dentistry. There could be a complex interaction of root canal pain and psychological distress amongst patients diagnosed with depression. Studies supporting this theory are lacking and research in this area may assist dentists in developing interventions designed for effective pain management during an NSRCT procedure, improving the patient satisfaction.

HOSPITAL AND DEPRESSION SCALE

Almost 35 years ago, the Hospital and Depression Scale (HADS) was formulated (36). The HADS contains a total of 14 questions: a) 7 questions to assess anxiety and b) 7 questions to assess depression. Each question has a possible score from 0-3. Therefore, on each subscale, the score ranges from 0 – 21. A HADS-Total score (sum of anxiety and depression) ≤ 7 is normal (non-depressed), between 8 – 10 is borderline, and a HADS-Total score ≥ 8 is considered the cases of depression. Both sensitivity and specificity of HADS-subgroup has also been explored. The HADS-Anxiety (HADS-A) subscale, with a cutoff score of 8+, has a sensitivity of 0.9 and a specificity of 0.78. Similarly, the HADS-Depression (HADS-D) subscale, a cutoff score of 8+, has a sensitivity of 0.83 and a specificity of 0.79 (37).

VALIDITY OF HAD SCALE (HADS)

HADS is a well-published measure of anxiety and depression (16). HADS has been validated in different age groups (38,39), in settings including a medical setting and in the general population (37), different languages (40), different countries (41), and in different medical conditions (42). HADS is one of the recommended tools by the National Institute for Health and Care Excellence for diagnosing depression and anxiety (43).

However, in a few scenarios HADS has shown limited validation. In medical conditions affecting cognitive behavior (dementia), HADS was shown to have limited validity (44). These findings were confirmed by Stott et al. (45). HADS in patients undergoing cancer therapy, HADS might also not be a valid tool to assess anxiety and depression (46).

CATEGORIES OF PAIN SCALES

There are two major categories of pain scales: a) multidimensional and b) unidimensional scales (47). Examples of a multidimensional scales are the McGill Pain Questionnaire, and the Wisconsin Brief Pain Questionnaire. Examples of a unidimensional scales are the Visual Analog Scale (VAS), Visual Rating Scale (VRS), Numerical Rating Scale (NRS), Faces Pain Scale (FPS), Wong-Baker Faces Pain Rating Scale (WBS), and Full Cup Test (FCT). The multidimensional pain scales are useful in assessing both acute and chronic pain. They can also evaluate the impact of pain on a patient's mood and functionality. Disadvantages includes the complexity of the multidimensional scales and the time required for the patient to complete the scale (it may take up to 30 minutes).

A unidimensional scale, on the other hand, measures only the sensory aspect of pain (48). The VAS is the most commonly used scale of this type, and is as easy to complete, and less vulnerable to bias than a Likert scale (49).

VALIDITY OF VAS

The validity of VAS has been evaluated both in the medical literature (50) and the dental literature (51). Both the vertically oriented VAS and the horizontally oriented VAS are equally valid for oral surgery (52). The VAS scale with the end phrase on the right hand side "worst pain imaginable" was found in one study to be most suitable in evaluating dental pain (53). In addition, scales with multiple descriptors have been reported to be less valid tools because descriptors create bias in their interpretation among different age groups, therefore, questioning VAS reliability in dental literature (54).

The VAS also has limitations. Although VAS may be used to assess both acute and chronic pain, multidimensional pain scales provide more relevant information when scoring chronic pain as mentioned above (55).

PURPOSE

This prospective observational study explores the association following non-surgical root canal treatment between the level of depression and pain perception.

STUDY AIMS

- To determine if there is a difference in the levels of pain, both pre and post-operatively, experienced by depressed vs. non-depressed patients.
- To determine if there is a difference in the levels of unpleasantness, both pre and post-operatively, experienced by depressed vs. non-depressed patients.

- To determine if there is a correlation at different pre and post-operative time points between the level of depression and pain intensity.

NULL HYPOTHESES

- H_1: Endodontic pain patients with depression do not experience greater pain intensity (as measured on the pain intensity VAS scale) than those who are not depressed. This was measured at multiple time points: pre-operatively, immediately post-operatively, and two, four, and seven days post-operatively.
- H_2: Endodontic pain patients with depression will not experience greater sensory unpleasantness (as measured on the unpleasantness VAS scale) than those who are not depressed. This was measured at two time points: pre-operatively and immediately post-operatively.
- H_3: Higher level of depression (as measured on HADS) will not be correlated with endodontic pain (as measured on the VAS, both preoperatively and postoperatively).

METHODS AND MATERIALS

RESEARCH DESIGN

The proposed design is a prospective cohort study.

PATIENT SELECTION/SUBJECT RECRUITMENT

Subjects were recruited from the Advanced Specialty Education in Endodontics (ASE) clinic. Patients who present to the clinic for emergent or non-emergent endodontic treatment were considered for inclusion in the study. Patients who met the inclusion criteria and who wished to participate were consented for the study by a member of the study team (SM, PT, PC, FM). Endodontic residents, who were part of the research team, did not consent their own patients to be in the study.

INCLUSION CRITERIA

- Patients who received an NSRCT in the ASE Endodontics clinic.
- Patients with a pretreatment diagnosis of symptomatic irreversible pulpitis with or without symptomatic apical periodontitis or pulpal necrosis with symptomatic apical periodontitis.
- The affected tooth had to be a permanent tooth with a mature apex.
- The affected tooth had to have a favorable prognosis at the time of treatment, as determined by the resident.
- Patients had to be 18 years of age or older and able to consent for themselves to be in the study.
- Patients must to be able to read and understand the English language.
- For inclusion in the experimental group, the patient had to have a diagnosis of depression from his physician that is currently managed with at least one antidepressant.

EXCLUSION CRITERIA

- Patients that could not consent for treatment.
- Patients that could not understand the two scales (VAS & HADS).
- Patients who presented as emergencies with a diagnosis of acute apical abscess.

RESEARCH INSTRUMENTS

A VAS was used to measure pain intensity. This scale consists of a horizontal line on a piece of paper. The participant was asked to make a mark at one point along that line that reflects his/her current pain intensity. The scale is anchored by “no pain” (score of 0) at the left end, and “the most intense pain imaginable” (score of 100 on a 100-mm scale) on the right end (Figure 1).

FIGURE 1. Pre-operative pain VAS scale for pain intensity ratings.

Date:____________________ Participant ID:____________________ Time:________ am/pm

Please rate the INTENSITY of your dental pain RIGHT NOW by placing a vertical mark on the line below.

No Pain | **The most intense pain imaginable**

Please rate the LEAST INTENSE dental pain you have experienced OVER THE PRECEDING 24 HOURS by placing a vertical mark on the line below.

No Pain | **The most Intense pain imaginable**

Please rate the MOST INTENSE dental pain you have experienced OVER THE PRECEDING 24 HOURS by placing a vertical mark on the line below.

No Pain | **The most intense pain imaginable**

A VAS scale was also used to measure sensory unpleasantness. The scale also consists of a horizontal line on a piece of paper. The participant was asked to make a mark at one point along that line that reflects his/her current sense of unpleasantness. The scale is anchored by “not at all unpleasant” (score of 0) at the left end, and “the most unpleasant imaginable” (score of 100 on a 100-mm scale) on the right end (Figure 2).

FIG 2. Pre-operative VAS scale for sensory unpleasantness ratings.

Date: Participant ID: Time: am/pm

Please rate the UNPLEASANTNESS of your dental sensation RIGHT NOW by placing a vertical mark on the line below.

Not at all unpleasant	|———————————————————|	**The most unpleasant imaginable**

Please rate the **LEAST** UNPLEASANT dental sensation you have experienced OVER THE PRECEDING 24 HOURS by placing a vertical mark on the line below.

Not at all unpleasant	|———————————————————|	**The most unpleasant imaginable**

Please rate the **MOST** UNPLEASANT dental sensation you have experienced OVER THE PRECEDING 24 HOURS by placing a vertical mark on the line below.

Not at all unpleasant	|———————————————————|	**The most unpleasant imaginable**

The HADS scale (56) was used to determine the levels of anxiety and depression that a patient was experiencing (Figure 3).

FIG 3. Preoperative HADS

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate response is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:
Total score: Depression (D) ___________ Anxiety (A) _____________
0-7 = Normal
8-10 = Borderline abnormal (borderline case)
11-21 = Abnormal (case)

A pain diary was also used for record-keeping. It helped participants to keep detailed records of their pain experience (again using the VAS pain scale) at the time of treatment and in the evenings of days two, four and seven (Figure 4, 5).

FIG 4. Immediate post-operative VAS scale for pain intensity and sensory unpleasantness.

Date: ______________________ Participant ID: ______________________ Time: __________ am/pm

Please rate the **INTENSITY** of your dental pain RIGHT NOW by placing a vertical mark on the line below.

No Pain |————————————————————————————| **The most intense pain imaginable**

Please rate the **UNPLEASANTNESS** of your dental sensation RIGHT NOW by placing a vertical mark on the line below.

Not at all unpleasant |————————————————————————————| **The most unpleasant imaginable**

FIG 5. Post-operative VAS scale for pain intensity.

- Use this diary to record your pain and pain medication usage in the evening of the **2nd, 4th and 7th days** following your 1st visit of the root canal procedure. We are interested in knowing about **any pain in your teeth or face** that you feel is related to your root canal treatment or your recovery. Be sure to record date and time that you fill each one.
- Please fill this pain diary at approximately the same time each evening.
- Please complete this diary as instructed, and mail it to the study center in the pre-addressed, postage-paid envelope provided to you.

Date: ______________________ Participant ID: ______________________ Time: ________ am/pm

Please rate the INTENSITY of your dental pain RIGHT NOW by placing a vertical mark on the line below.

No Pain |————————————————————————| **The most intense pain imaginable**

Please rate the LEAST INTENSE dental pain you have experienced OVER THE PRECEDING 24 HOURS by placing a vertical mark on the line below.

No Pain |————————————————————————| **The most intense pain imaginable**

Please rate the MOST INTENSE dental pain you have experienced **OVER THE PRECEDING 24 HOURS by placing a vertical mark on the line below.**

No Pain |————————————————————————| **The most intense pain imaginable**

PROCEDURES

- A member of the study team consented/enrolled interested and eligible patients into the study. IRB approved consent and HIPAA forms were used for the enrollment process.
- A member of the study team instructed study participants on how to complete the preoperative and postoperative assessments of pain, unpleasantness, and depression.
- A pain diary was given to the study participants after the initial visit of the NSRCT procedure to complete at home on days two, four and seven. A member of the study team instructed study participants on how to complete the diary. Participants returned the completed diary using a pre-addressed, stamped envelope.
- A phone call was made to the subjects by a member of the research team on days two, four, and seven to remind them to complete the diary.
- A flow chart of this procedure can be found in Appendix I.

NSRCT PROCEDURES

- All NSRCT procedures were done by the residents at the ASE program at the University of Maryland.
- Local anesthesia (type and volume) was administered based on the location of tooth.
- Isolation was done by a rubber dam.
- Under a dental operating microscope, an access cavity was made by a diamond round bur, and canal instrumentation was done with either Vortex blue or Protaper gold.
- Irrigation was done with a 30-gauge needle with both 2.5% sodium hypochlorite and 17% ethylenediaminetetraacetic acid (EDTA). The needle was placed one mm short of the working length.

- Canals were dried with paper points.
- When an interim dressing was used, canals were medicated with a calcium hydroxide paste.
- When obturation was done, one of the following techniques was used: a) Continuous wave technique, b) lateral condensation, c) Single cone technique. For sealer, either AH Plus (Dentsply®) or BC sealer (Brassler®) was used.
- The tooth was temporarily restored with a sterile sponge, followed by either Cavit or Fuji Triage.

STATISTICAL METHODOLGY

The sample size of 31 in each group for hypothesis 1 was determined using Power and Precision software (57). No prior research had been done on the hypothesis. Therefore, a power analysis was done on data reported by Carr et al. 2005 (3). The data from the index of pain and depression scores at day four was used to calculate sample size because this timing provides the largest expected effect size. Based on data from that study, the following power analysis was conducted: With an N of 31 in each group, a large effect size (0.40) two experimental groups, a $p \leq 0.05$ and a one- tailed t test, power was equal to 0.80.

Given the skewed distribution and the unequal number of participants (depressed: 11 participants vs. non-depressed: 30 participants), the data were summarized with the median and the interquartile range. For hypotheses one & two, the Mann-Whitney U test was used. For hypothesis three, the association between the data taken from the pain diary and the HADS scale was evaluated using Spearman's Rho. For the secondary analysis, the date was grouped based on the

HADS score (HADS ≤ 8 vs. HADS ≥ 7). The Mann-Whitney U test was used to compare the reported pain and unpleasantness between two groups ((HADS ≤ 8 vs. HADS ≥ 7). Logistic regression was used to compare the predictive value of HADS score and the diagnosis of depression in predicting post-operative pain at day 2.

RESULTS

Primary Analysis:

A total of 41 participants were enrolled in the study; 30 in the non-depressed group and 11 in the depressed group. Two participants did not return the pain dairy; 1 in the non-depressed group and 1 in the depressed group. These participants were excluded; thus data from 29 participants in the non-depressed group and 10 in the depressed group were available for analysis. Baseline characteristics (age, sex, ethnicity, tooth-type, pulpal diagnosis, and periapical diagnosis) were found to be similarly distributed in both groups (Table 1). Figure 6, 7, 8, and 9 reflect the age, sex, ethnicity, and tooth-type distribution of all participants.

Table 1: Baseline characteristics of the participants

Baseline Characteristics	Non-depressed	Depressed	p value
	N=29	N=10	
Age: Mean(StDev)	43.1(14.5)	48.2(14.8)	.33
Sex: Frequency(%)			
Female	16 (55.2%)	7 (70%)	.48
Ethnicity: Frequency (%)			
White	10 (34.5%)	7 (70%)	.46
African-American	9 (31%)	2 (20%)	
Hispanics	4 (13.8%)	1 (10%)	
Southeast Asian	3 (10.3%)	0	
Asian	2 (6.9%)	0	
Others	1 (3.4%)	0	
Tooth type: Frequency (%)			
Molar	22 (75.9%)	7 (70%)	.71
Premolar	6 (20.7%)	3 (30%)	
Anterior	1 (3.4%)	0	
Mandibular Molar	16 (55.2%)	4 (40%)	.77
Pulpal Diagnosis: Frequency (%)			
Symptomatic Irreversible Pulpitis	15 (51.7%)	5 (50%)	.60
Necrotic Pulp	14 (48.3%)	5 (50%)	
Apical Diagnosis: Frequency (%)			
Symptomatic Apical Diagnosis	24 (82.8%)	9 (90%)	.51
Normal Apical Tissue	5 (17.2%)	1 (10%)	

Figure 6: Age distribution of the all participants

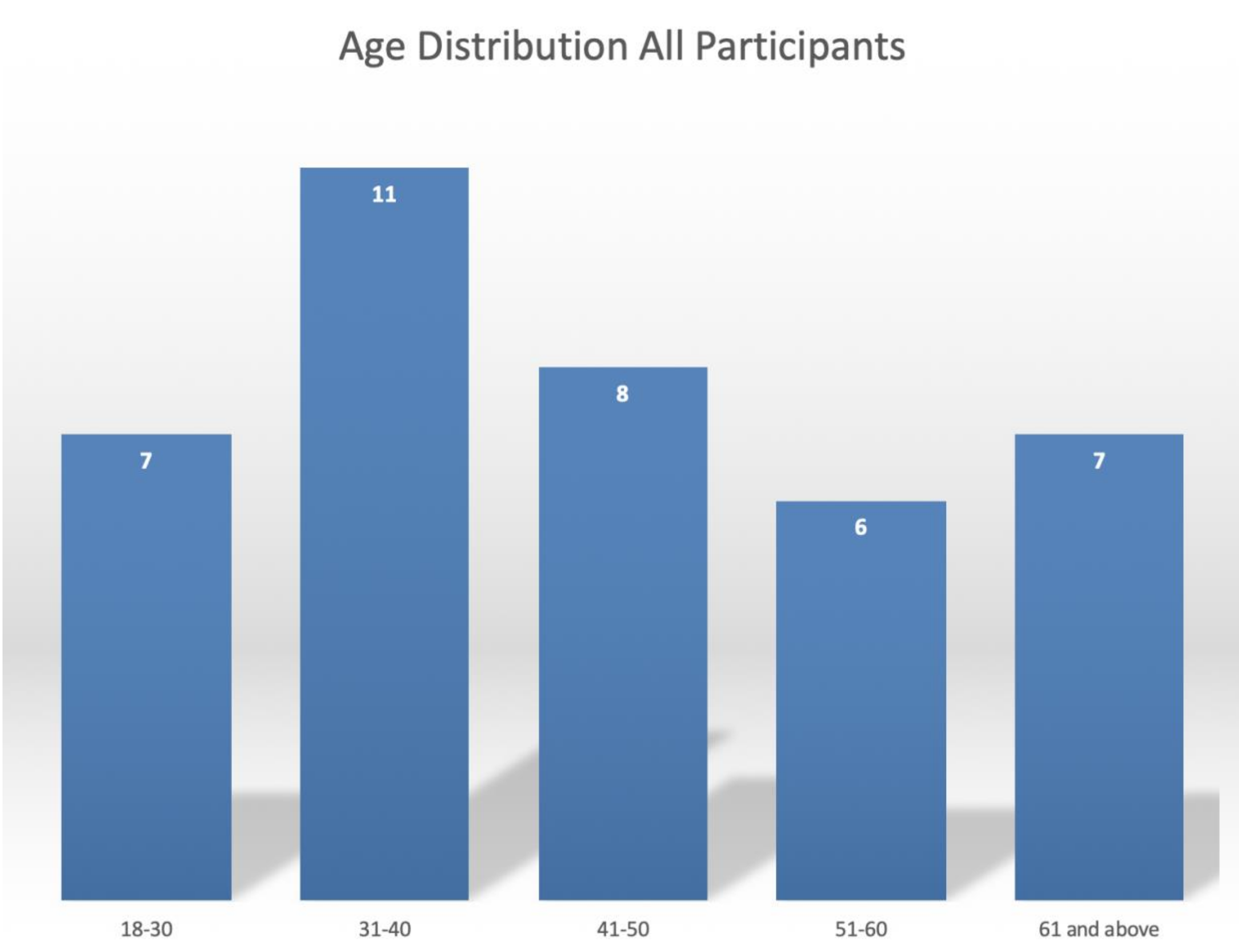


Figure 7: Sex distribution of all participants

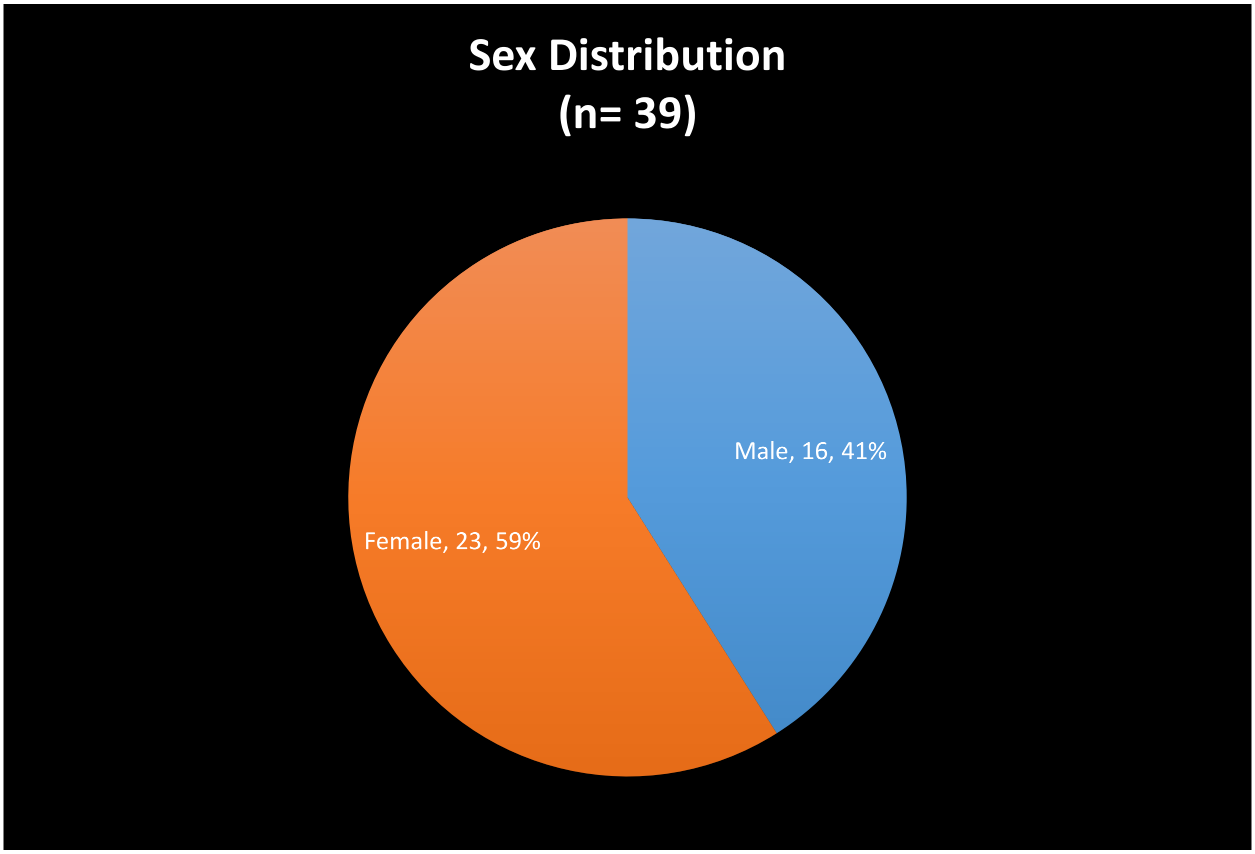


Figure 8: Ethnicity distribution of all participants

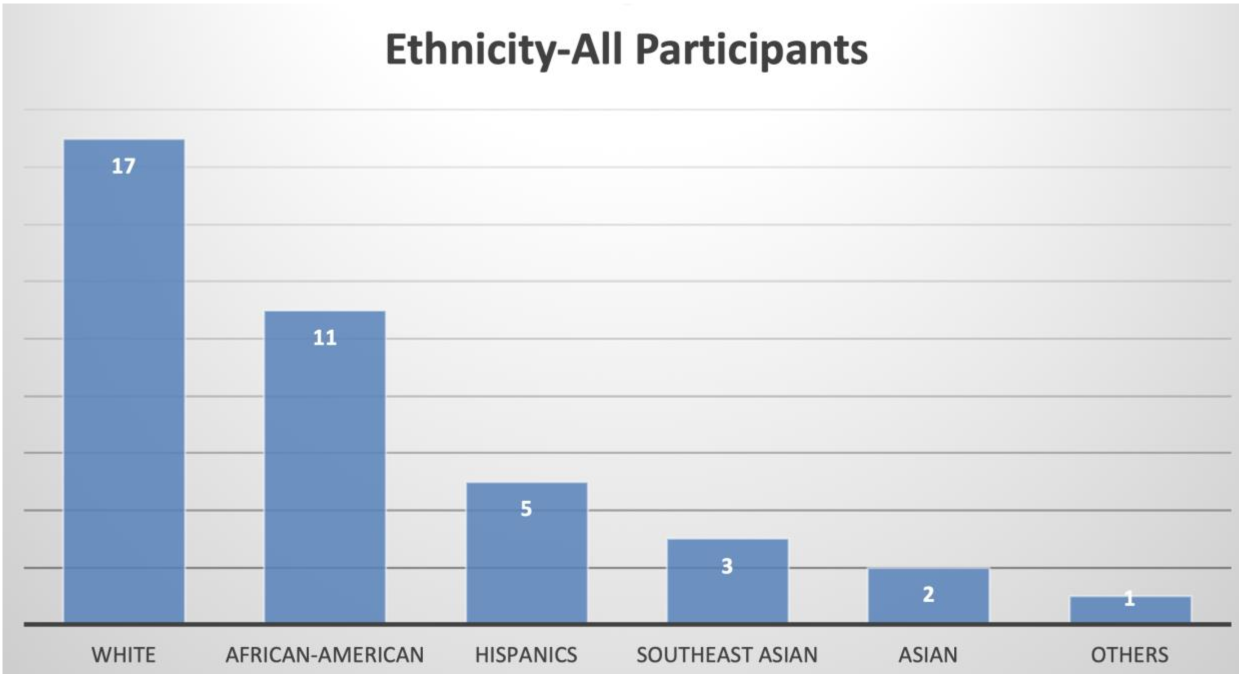
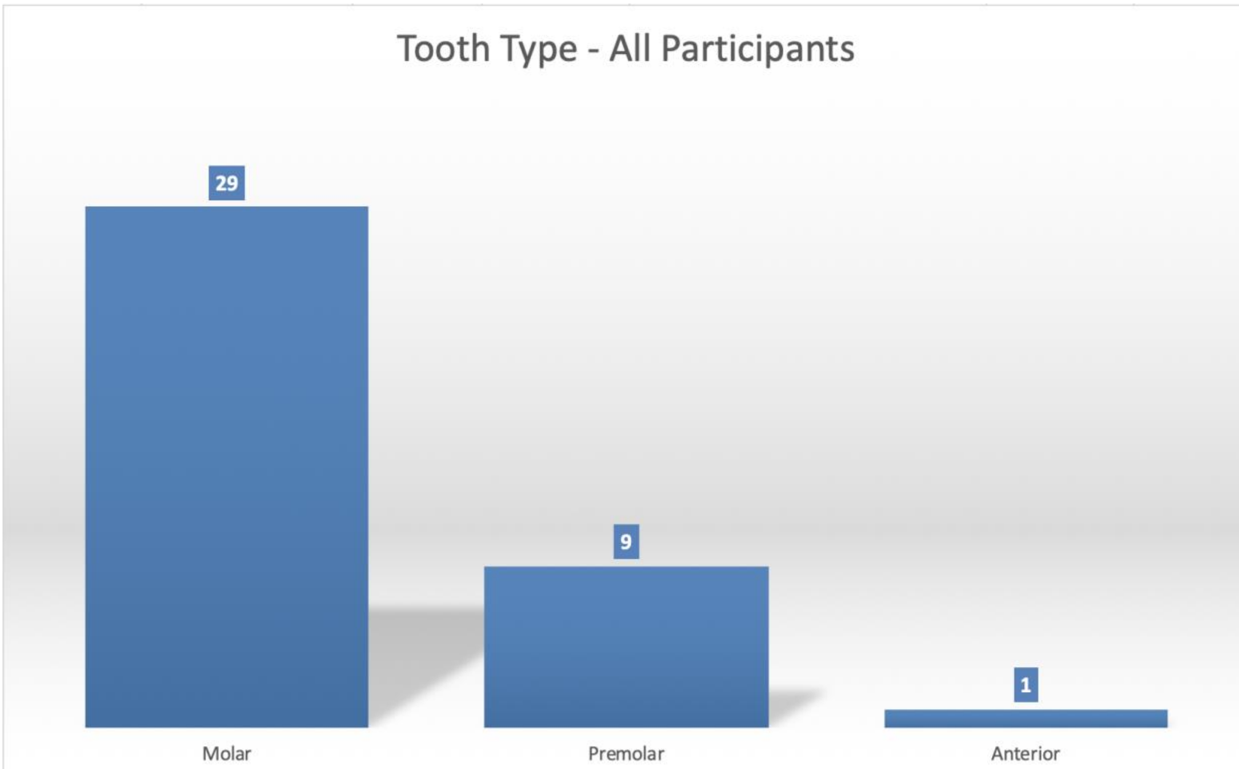


Figure 9: Tooth-type distribution of all participants



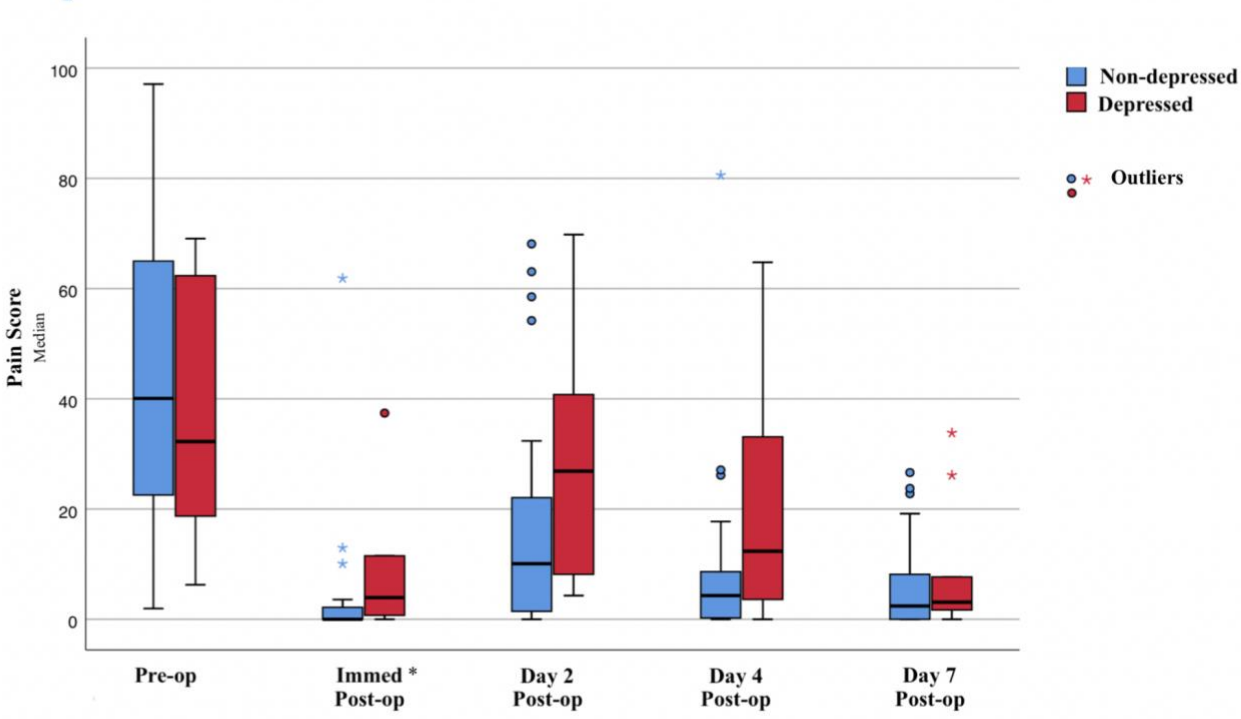
Pain: Hypothesis 1:

The median (IQR) of pre-operative pain in the depressed group was 32 (18-64) vs. that in the non-depressed group was 40 (22-66); this difference was not statistically significant ($p \leq .76$, Table 2; Figure 10). Immediate post-operative pain, however, was found to be greater in the depressed group, median (IQR): 4 (1-12) as compared to that in the non-depressed group, median (IQR): 0 (0-2) and this difference was statistically significant ($p \leq .01$, Table 2). Post-operative pain at day two, four and seven were not statistically different between the two groups (Table 2; Figure 10).

Table 2: Differences in reported pain between the depressed vs. the non-depressed group

Hypothesis	Time Point of Reported Pain	Depressed	Non-depressed	p value
1	Pre-operative Pain: Median 25-75 Percentile Range	**32** 18-64 6-69	**40** 22-66 2-97	.76
	Post-operative Pain: Median 25-75 Percentile Range			
	Immediate	**4** 1-12 0-37	**0** 0-2 0-62	.01*
	At Day 2	**27** 7-44 4-69	**10** 1-23 0-68	$.053^{\Pi}$
	At Day 4	**12** 3-36 0-64	**4** 0-9 0-80	.06
	At Day 7	**3** 1-12 0-33	**2** 0-11 0-26	.47

Figure 10: Comparison of reported pain between the depressed vs. non-depressed group



***Significantly different**

Unpleasantness: Hypothesis 2

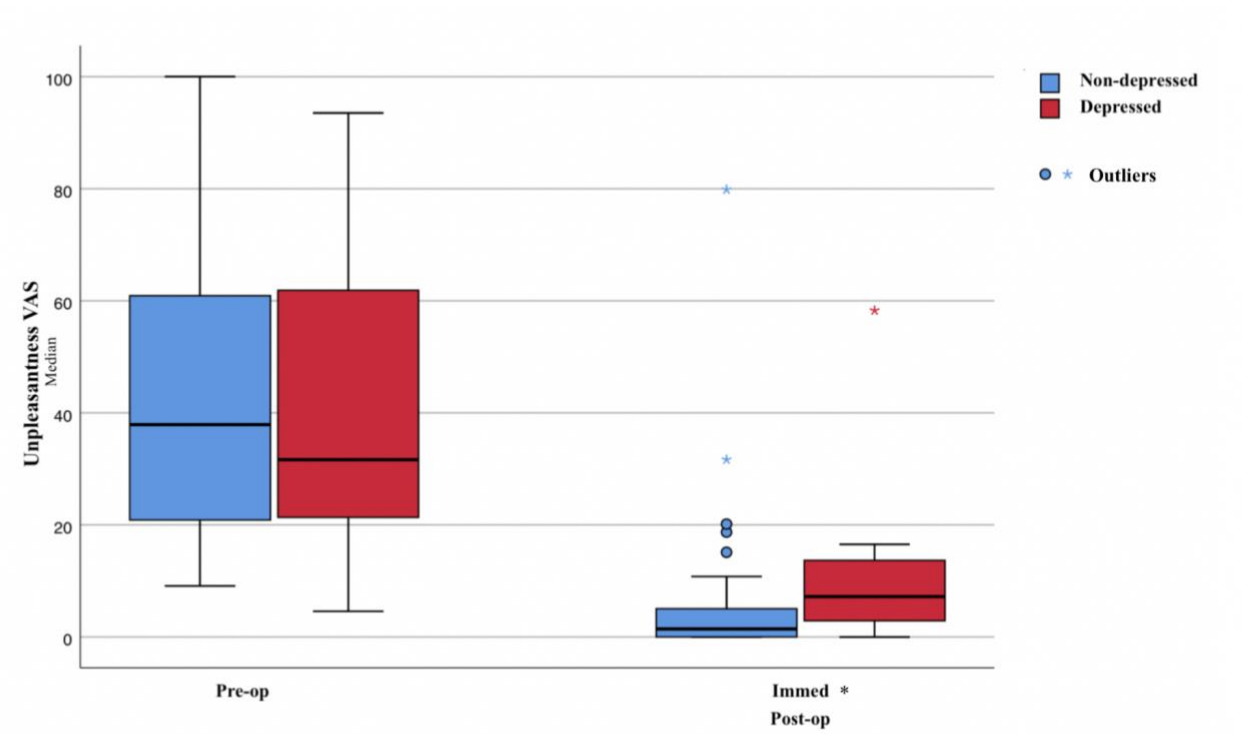
Similarly, the median (IQR) of pre-operative unpleasantness in the depressed group was 32 (21-65) vs. that in the non-depressed group was 40 (18-62). This difference was not statistically significant ($p \leq .91$). Immediate post-operative unpleasantness, however, was found to be significantly greater in the depressed group, median (IQR): 6 (3-14), as compared to that in the non-depressed group, median (IQR): 1 (0-6, $p \leq .04$, Table 3, Figure 11). Unpleasantness was only recorded immediately after the procedure; thus, no additional time point data is available.

Table 3: Differences in reported unpleasantness between the depressed vs. non-depressed group

Hypothesis	Time Points of Reported Unpleasantness	Depressed	Non-depressed	p value
2	Pre-operative Unpleasantness:			0.91
	Median	**32**	**40**	
	25-75 Percentile	21-65	18-62	
	Range	5-94	9-100	
	Post-operative Unpleasantness:			.04*
	Median	**6**	**1**	
	25-75 Percentile	3-14	0-6	
	Range	0-58	0-80	

***Significantly different**

Figure 11: Comparison of unpleasantness between the depressed vs. non-depressed group



Relationship: Hypothesis 3

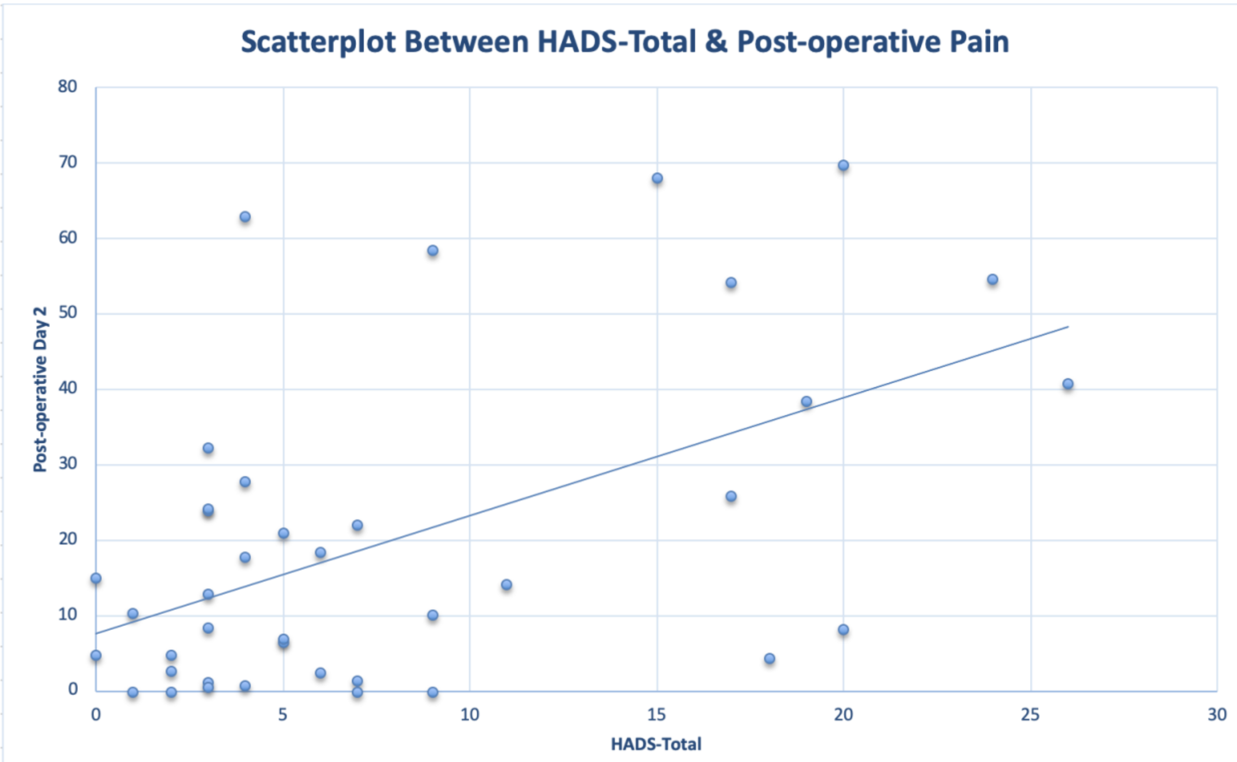
The correlation between the HADS score and post-operative pain was explored (Table 4). Among all participants, a statistically significant positive correlation was found between the HADS score and the post-operative pain at day two (Spearman's Rho: .41, $p \leq .009$; Figure 12). Correlation was not statistically significant at day four and day seven (Table 4).

Table 4: Spearman's rho between HADS-total and reported pain

		Total
Hypothesis 3:	Pre-operative pain	-.142(.39)
	Post-operative pain:	
	Immediate	0.17(.27)
	At Day 2	0.41(.009*)
	At Day 4	0.18(.27)
	At Day 7	0.12(0.45)

***Significantly different**

Figure 12: Scatter plot diagram between HADS score and post-operative pain at day two



Secondary Analysis:

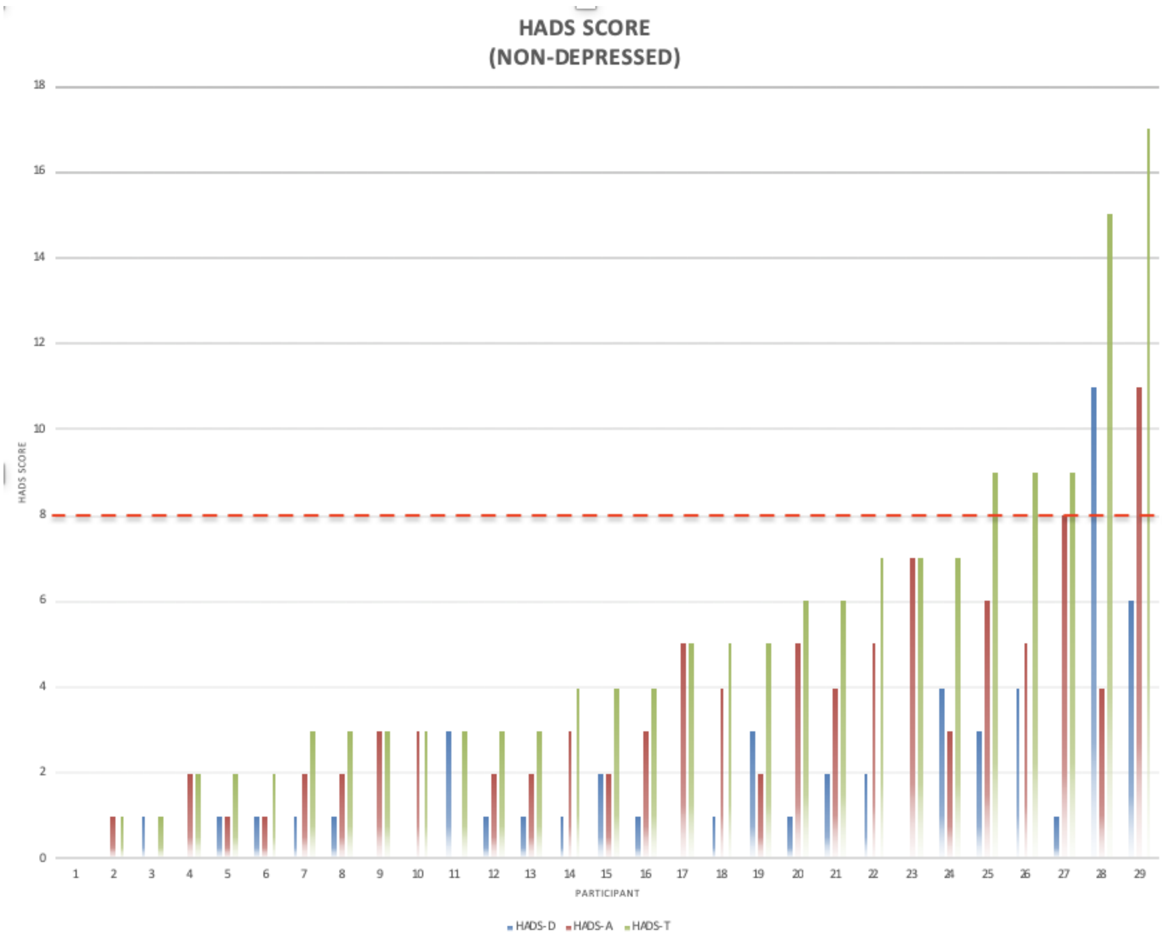
The HADS score between the depressed vs. the non-depressed group was compared (Table 5). As expected, the HADS score (median IQR) was significantly higher ($p \leq .001$) in the depressed (19, 9-21) vs. the non-depressed group (4, 3-7). In the subgroup HADS-depression, a significantly higher score ($p \leq .004$) was also observed in the depressed group (8, 2-9) vs. the non-depressed group (1, 0-3). Similarly, in the subgroup HADS- anxiety, a significantly higher score ($p \leq .001$) was reported in the depressed group (9, 7-16) vs. the non-depressed group (3, 2-5).

Table 5: Comparison of HADS score between depressed vs. non-depressed group

	Depressed	Non-depressed	p value
HADS-Total Score:			
Median	**19**	**4**	.001*
25-75 Percentile	9-21	3-7	
Range	0-26	0-17	
HADS-Depression			
Median	**8**	**1**	.004*
25-75 Percentile	2-9	0-3	
Range	0-11	0-11	
HADS-Anxiety			
Median	**9**	**3**	.001*
25-75 Percentile	7-16	2-5	
Range	0-18	0-11	

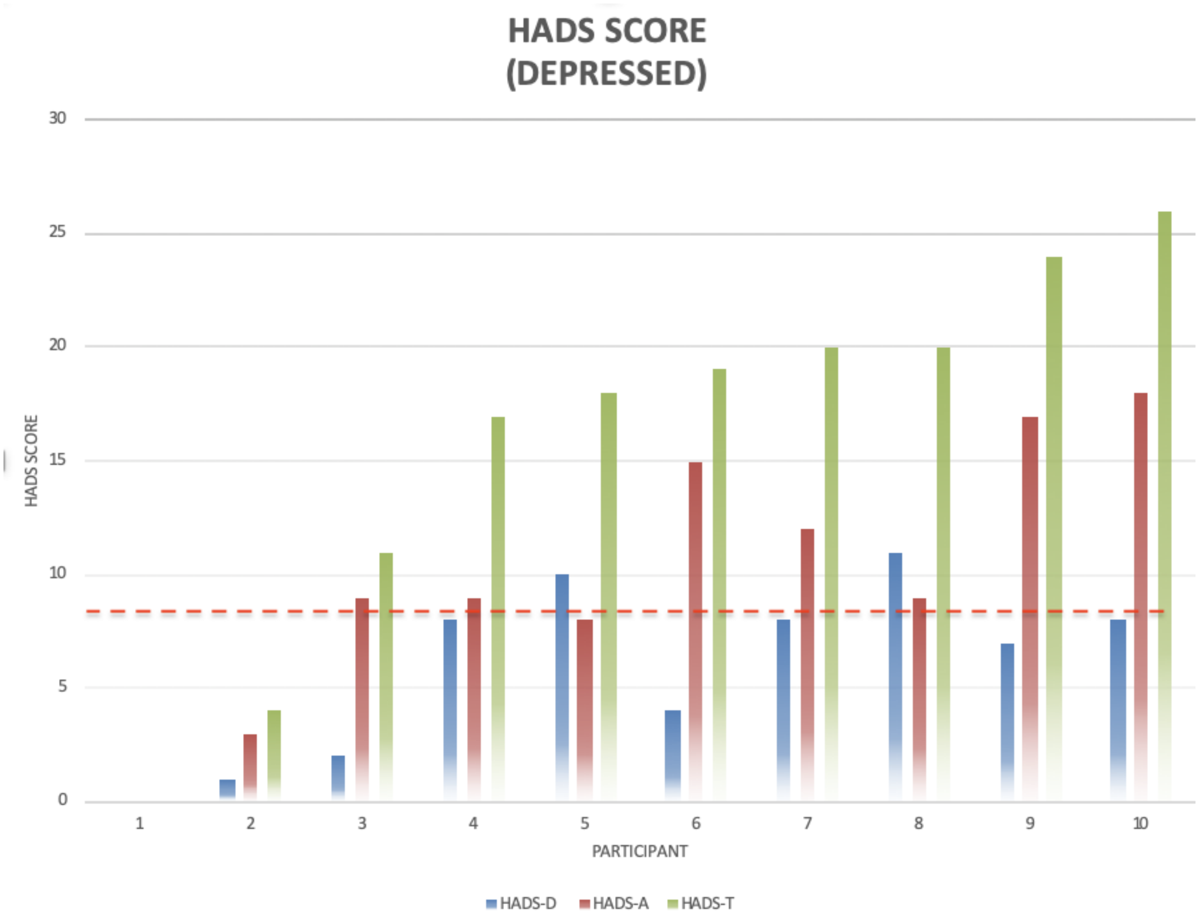
The distribution of the HADS scores was also evaluated for depressed and non-depressed patients separately. The two figures reveal that two depressed participants had a HADS-T score < 7 (Figure 13). In contrast, five non-depressed participants had a HADS-T score > 8 (Figure 14).

Figure 13: HADS score distributions in depressed patients



Dotted line: Cut-off value of 8

Figure 14: HADS score distributions in the non-depressed patients



Dotted line: Cut-off value of 8

Therefore, this data was grouped based on the HADS score: HADS score ≤ 7 vs. HADS Score ≥ 8 (17). After regrouping, there were 26 participants with HADS score ≤ 7 and 13 participants with HADS Score ≥ 8. Baseline characteristics were equally distributed in HADS score ≤ 7 vs. HADS Score ≥ 8 (p ≥ .05, Table 6).

Table 6: Baseline characteristics of participants when grouped based on HADS score (HADS ≥ 8: Depressed vs. HADS ≤ 7: Non-depressed)

Baseline Characteristics	HADS ≥ 8	HADS ≤ 7	p value
	(n=13)	(n=26)	
Age: Mean(std)	41 (12.8)	46.1 (15.38)	.30
Sex: Frequency (%)			
Female	8 (61.5%)	15 (57.7%)	.81
Ethnicity: Frequency(%)			
White	7 (53.8%)	10 (38.5%)	.60
African-American	4 (30.8%)	7 (26.9%)	
Hispanics	2 (15.4%)	3 (11.5%)	
Southeast Asian	0	3 (11.5%)	
Asian	0	2 (7.7%)	
Others	0	1 (3.8%)	
Tooth type: Frequency (%)			.58
Molar	9 (69.2%)	20 (76.9%)	
Premolar	4 (30.8%)	5 (19.2%)	
Anterior	0	1 (3.8%)	
Mandibular Molar	6 (46.2%)	14 (53.8%)	.77
Pulpal Diagnosis: Frequency (%)			.82
Necrotic Pulp	6 (46.2)	13 (50%)	
Symptomatic Irreversible Pulpitis	7 (53.8%)	13 (50%)	
Apical Diagnosis: Frequency (%)			.34
Symptomatic Apical Diagnosis	12 (92.3%)	21 (80.8%)	
Normal Apical Tissue	1 (7.7%)	5 (19.2%)	

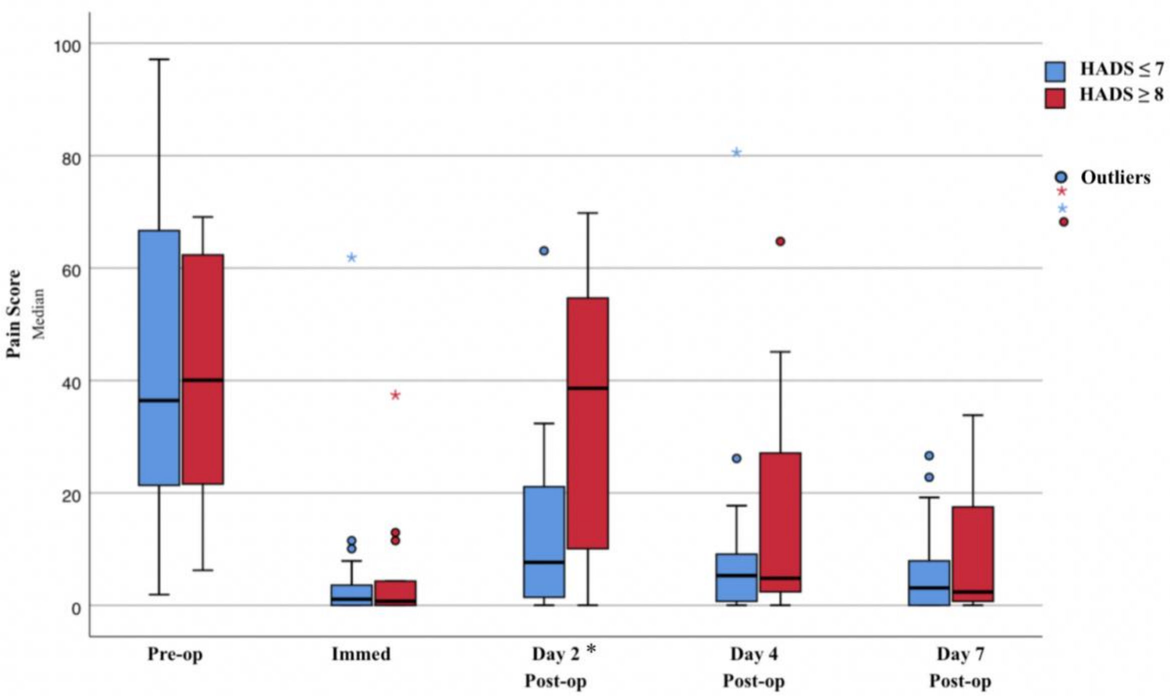
The pre-operative pain between HADS score ≤ 7 vs. HADS score ≥ 8 was similar in both groups ($p \leq .40$). The median (IQR) of pre-operative pain in the HADS Score ≥ 8 was 40 (19-63) vs. in the HADS score ≤ 7 was 36 (21-67). Post-operatively, the participants with a HADS score ≥ 8 experienced significantly greater pain ($p \leq .01$) at day two [median (IQR): 39 (9-57)] as compared to those with a HADS score ≤ 7 [(median (IQR): 8 (1-21), Table 7, Figure 15)].

Table 7: Comparison of pre and post-operative pain between HADS score ≤ 7 vs. HADS score ≥ 8 (HADS ≥ 8: Depressed vs. HADS ≤ 7: Non-depressed)

Time Points of Reported Pain		HADS ≥ 8	HADS ≤ 7	p value
Pre-Operative Pain:	Median 25-75 Percentile Range	**40** 19-63 6-69	**36** 21-67 2-97	.40
Post-Operative Pain:	Median 25-75 Percentile Range			
	Immediate	**1** 0-8 0-37	**1** 0-4 0-62	.40
	At Day 2	**39** 9-57 0-69	**8** 1-21 0-63	.01*
	At Day 4	**5** 1-30 0-64	**5** 1-11 0-80	.35
	At Day 7	**2** 0-21 0-33	**3** 0-8 0-27	.69

***Significantly different**

Figure 15: Comparison of reported pain between HADS ≤ 7 & HADS score ≥ 8



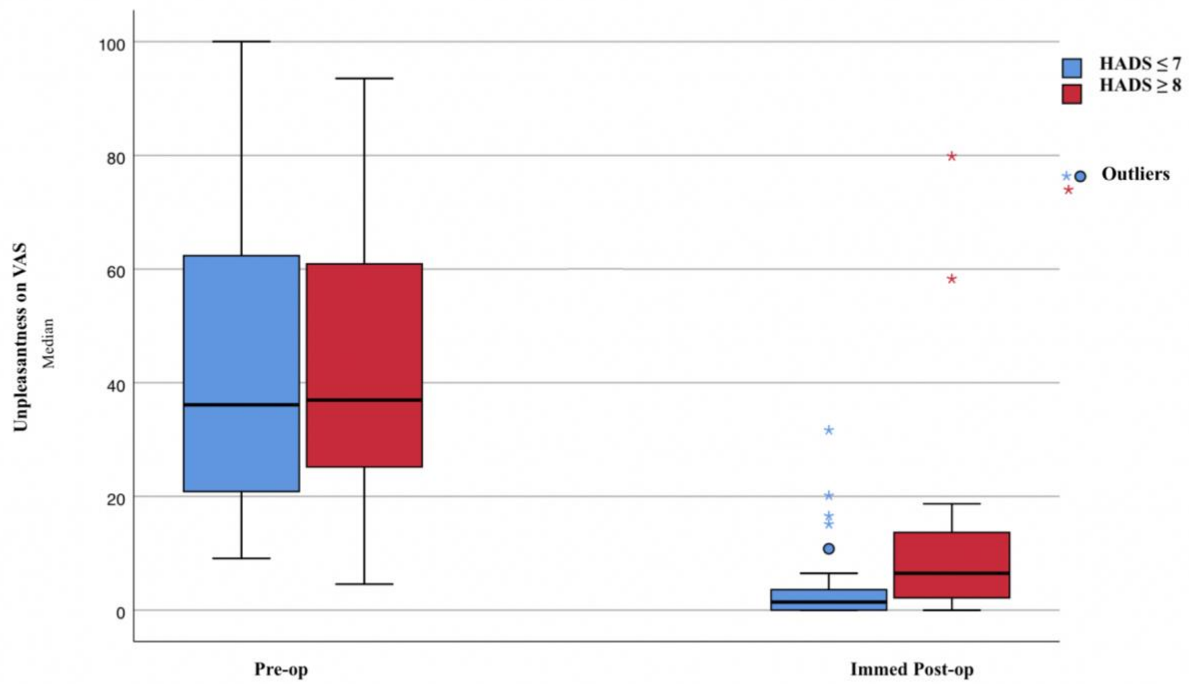
***Significantly different**

The median (IQR) of pre-operative unpleasantness in group with a HADS Score ≥ 8 was 37 (23-61) and that in HADS score ≤ 7 was 36 (20-63, Table 8, Figure 16). This difference was not statistically significant ($p \leq .08$). Post-operatively, the study did not find a statistical difference between the two groups ($p \leq .08$). The median (IQR) of post-operative unpleasantness in a HADS Score of ≥ 8 was 6 (1-16) vs. that in a HADS score of ≤ 7 was 1(0-4); the difference was not statistically significant (Table 8).

Table 8: Comparison of pre and post-operative unpleasantness between HADS score ≤ 7 vs. HADS score ≥ 8

Time Points of Reported unpleasantness	HADS ≥ 8	HADS ≤ 7	p value
Pre-operative Unpleasantness:			
Median	**37**	**36**	.08
25-75 Percentile	23-61	20-63	
Range	5-94	9-100	
Post-Operative Unpleasantness:			
Median	**6**	**1**	.08
25-75 Percentile	1-16	0-4	
Range	0-80	0-32	

Figure 16: Comparison of unpleasantness between HADS ≤ 7 & HADS score ≥ 8



For the next analysis, we wanted to compare the predictive value of the HADS-model (HADS ≤ 7 vs. ≥ 8) vs. the self-reported Depression-model. In this analysis, the pain score was grouped into three categories: mild (VAS 0-30), moderate (VAS 31-60), and severe (61 and above) (58). The logistic regression was performed to compare the predictive value of the HADS-model to the self-reported Depression-model (Table 9). The logistic regression model for the HADS score was statistically significant; χ_2 (1): 10.035, $p \leq .002$. This model explained 39% (Nagelkerke R_2) of the variance in the post-operative pain at day two and correctly classified 82 % of cases (Table 10). We combined moderate and severe pain category because of its clinical relevancy in managing post-operative pain. Additionally, we had only three patients among all participants who experienced severe post-operative pain. In contrast, the logistic regression model for depression was not significant; χ^2 (1): 2.05, $p \leq .15$.

Table 9: Logistic regression models

Independent Variable	β	SE	Wald	df	Sig
HADS Model	2.86	0.94	9.27	1	.002*
Constant	-5.17	1.7	9.25	1	.001
Depression Model	1.16	0.81	2.05	1	.15
Constant	-2.73	1.17	5.39	1	.02
*: Statistically Significant					

Table 10: Positive predictive value of HADS model vs. depression model

Frequency Of Reported Pain		HADS Model	Depression Model
	Day 2	Predicted Pain	
Moderate or Severe	9	7	4
Positive Predictive Value		78%	44%
Mild	30	25	24
Positive Predictive Value		83%	80%
Overall Positive Predictive Value		82%	74%
Reported Pain		Predicted Pain	
		HADS Model	Depression Model
Moderate or Severe	9	7	4
Positive Predictive Value		78%	44%
Mild	30	25	24
Positive Predictive Value		83%	80%
Overall Positive Predictive Value		82%	74%

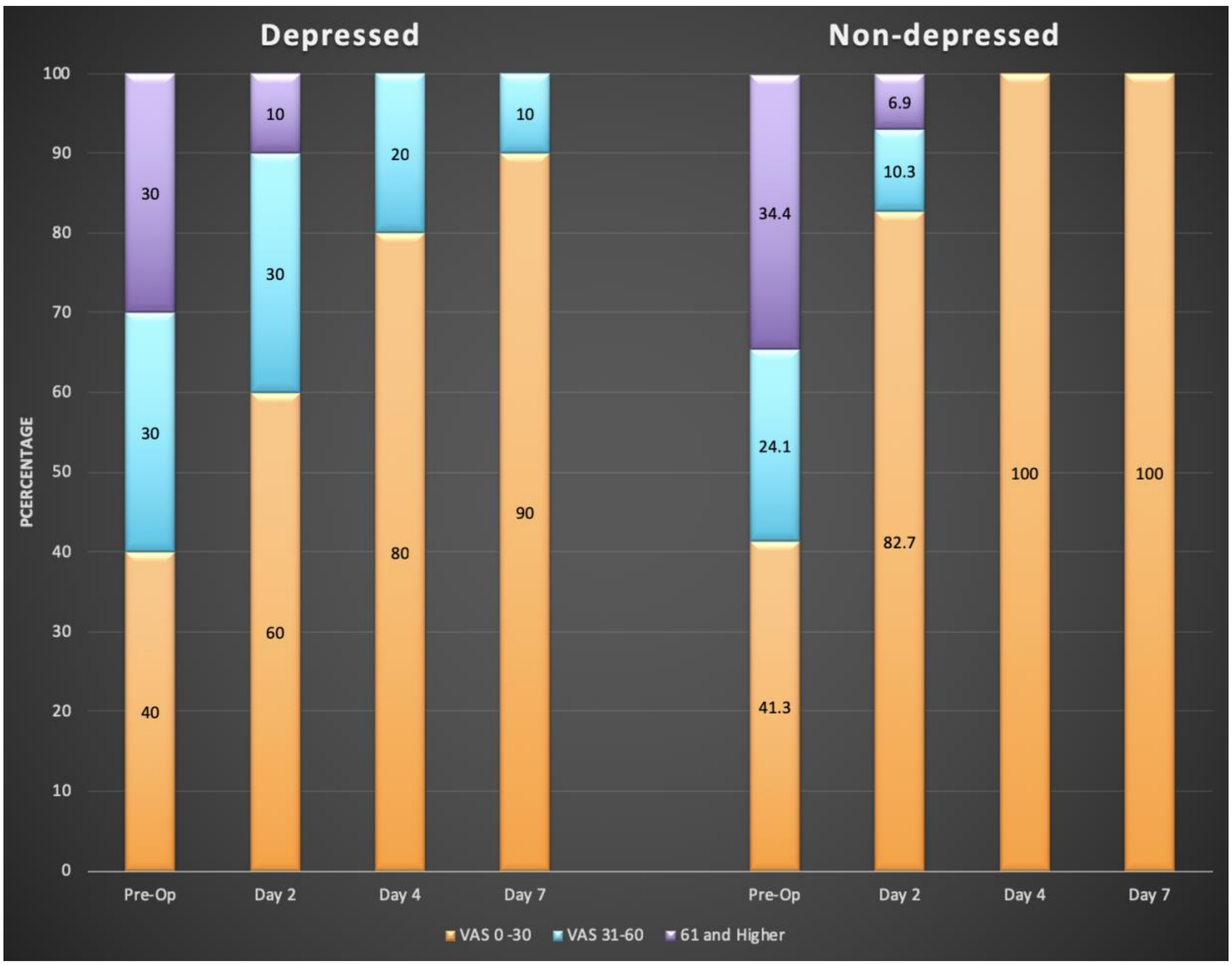
The prevalence of severe pain was calculated. Overall, a total of 7.69% (n = 3) participants experienced severe pain (VAS ≥ 60; Table 11). In the depressed group, the prevalence of severe pain was 10% (n = 1); in contrast, in the non-depressed group, only 6.9% (n= 2) experienced severe pain. In addition, reported severe pain was experienced only at day two (Figure 17). No participant reported severe pain at days four or seven. Statistical analysis was not possible because very few participants experienced severe pain.

Table 11: Prevalence of severe (VAS ≥ 60) pain

Pain Prevalance -Total (n = 39)	
Pain - n (%)	
Post-operative Day 2	3 (7.69%)
Post-operative Day 4	0
Post-operative Day 7	0
Pain Prevalance - Nondepressed (n = 29)	
Post-operative Day 2	2 (6.9%)
Post-operative Day 4	0
Post-operative Day 7	0
Pain Prevalance - Depressed (n = 10)	
Post-operative Day 2	1 (10%)
Post-operative Day 4	0
Post-operative Day 7	0

No flare-up [An acute exacerbation of an asymptomatic pulpal and/or periradicular pathosis after the initiation or continuation of root canal treatment (59)] was reported in the current study. At day 7, approximately 69% of the participants experienced post-treatment pain, although on average this was mild (Median: 3; IQR: 3 – 8, Figure 17).

Figure 17: Distribution of pain among all participants



DISCUSSION

In our study, all three null hypotheses were rejected Both pain and unpleasantness were found to be statistically greater in the depressed group. The study also found a significant positive correlation between the HADS score and the post-operative pain.

In the medical literature, depression is presented as a predictor of post-operative pain severity(20). Gillies et al have suggested that simple administration of HADS tool as a measure of pre-operative evaluation might help in identifying symptoms associated with depression and anxiety (16). Identifying these symptoms might help clinicians manage post-operative pain more effectively, therefore improving patient satisfaction.   Similarly, in the dental literature, depression was found to be related to chronic pain, temporomandibular disorder (TMD), and bruxism. Evaluating patients psychological state is important in improving patient satisfaction (60). In 2007, Slade et al reported that depression was predictive of a two to three fold increase in the risk for TMD (61).

In 2016, Kyle et al evaluated immediate post-operative pain after tooth extraction. That study found no difference in immediate post-operative pain observed in their “high depression” vs. “low depression” group (62). In the Kyle study, the Center for Epidemiological Studies Depression Scale–Revised (CESD-R) was used to assess the psychological status of the patient. CESD-R divided the data into two groups: high depression vs. low depression. Our study used the HADS score to divide the data into two groups: HADS ≤ 7 vs. HADS ≥ 8. We found similar results as Kyle et al for immediate post-operative pain. One might attribute this reduction in immediate post-operative pain to the administration of the local anesthesia.

In 2016, Yang et al published a cross-sectional questionnaire exploring the relationship between depression's effect on quality of life (QOL) and dental pain (63). The authors concluded that participants with depression had both a lower QOL and higher dental pain. Slade et al, in 2007, found that depression, perceived stress, and mood were predictors of pain (61). Our study found similar result although this finding was not significant. At post-operative day two, depressed patients experienced more post-operative pain when compared to the non-depressed group.

Similarly, Su et al showed that higher chronic oral-facial post-operative pain caused a higher level of depression. (64). In endodontics, the post-operative pain is acute. In our study, no clinically important difference was observed between the depressed vs. non-depressed group immediately post-operative nor at day four and day seven. Given that endodontic post-operative pain is acute in nature, pain is not expected to affect the level of depression.

Both symptomatic irreversible pulpitis and symptomatic apical periodontitis have been associated with post-operative pain (65). In the current study, we found a similar distribution of both pulpal and apical diagnoses in both groups. This ruled diagnoses out as a confounding factor in our study.

In 2004, Glennon et al reported that tooth type was related to post-operative pain (58). Molars were more commonly associated with post-operative pain than both anterior and premolar teeth (65). In our study, tooth types were similarly distributed in both groups. In addition, mandibular molars were found to be associated with more post-operative pain. Also, the distribution of mandibular molars was statistically comparable in both groups.

A systematic review published by Pak et al (2011) reported that the prevalence of pre-operative pain intensity was moderate; however, it was dropped to a lower level at post-operative day1 and to minimum at post-operative day 7 (66). Similar findings were reported by Montero et al (67). Our study found equivalent results in the non-depressed group. Pre-operative pain was reported to be 40 on VAS, but dropped significantly at post-operative day two, and to negligible at post-operative day seven. However, in the depressed group, a drop in post-operative pain was not seen at day two. Pre-operative pain was reported to be 32, dropped to 27 at post-operative day two, and to negligible at post-operative day seven. Moreover, when the data was stratified based on HADS ≤ 7 vs. ≥ 8), the results were even more obvious. In HADS ≥ 8, post-operative pain at day two was 39; only 1-point reduction from pre-operative pain (preoperative pain equaled 40). This finding suggests that an administration of HADS as a part of pretreatment evaluation might help the provider to predict post-operative pain. Better communication with the patient regarding the clinician's expectations of post-operative pain along with medicinal pain management might improve patient satisfaction.

The prevalence of post-operative pain has been explored (58,65). The present study categorized VAS scores as 0-30: Mild, 31-60: Moderate, 61 or higher: Severe. The prevalence of severe post-operative pain has been reported to be less than 10% (65). These results are similar to those in our study. In our study, the overall prevalence was 7.69%.

The distribution of the HADS score in our study population revealed that the HADS scores did not match clinical depression diagnosis category in seven cases. A HADS score ≥ 8 is considered to be a sign of depression. However, in our depressed group, 2(20%) had HADS score ≤ 7. Similarly, in the non-depressed group, 5 (17%) had HADS score ≥ 8. The two "discrepant" subjects in the depressed group reported mild pain at day two. In contrast, among the "discrepant" non-depressed patients, three out of the five reported moderate to severe pain. The diagnosis of depression, reflects the patient's past psychological state, while the preoperative HADS score reflects his/her current state. Current psychological status of the depressed patient may be different, particularly considering the effectiveness of anti-depressant medications they might be taking. Similarly, in the control group, some participants might be borderline clinically depressed. In summary, using the HADS instrument pre-operatively might be most beneficial in predicting post-operative pain.

Finally, the predictive value of the HADS score was found to be statistically higher than that of the depression-model in predicting post-operative pain at day two. The positive predictive value of the HADS-model was found to be greater both in predicting mild and moderate to severe pain as compared to that of clinical diagnosis of depression. We chose to compare moderate and severe vs. mild pain because of the clinical relevancy in managing endodontic pain. With the HADS score, the positive predictive value was 82%; in contrast, in depression-model, it was 74%.

LIMITATIONS OF THE STUDY

This study included the participants based on their self-reporting of their diagnosis of depression as made by their physicians. Self-reported has tendency of error. The non-depressed group might have depressed patients that has not yet been diagnosed by their physicians yet.
Second limitation might be the inherent limitations of HADS tool itself. The HADS instrument is completed by the patient. He or she is asked to circle the number representing the severity of the problem. The patient may circle a lower number in an attempt to appear more normal. In addition, at the bottom of the HADS tool, the scoring system explains how to interpret the score. This explanation may cause bias in the patient's response to the individual items. Although previous studies have not reported any bias related to these issues, we believe that it might cause under-representation of the patient's anxiety/depression status.

A third limitation is the standardization of the methodology to perform a root canal procedure. Although all the residents are calibrated in the clinical procedure during their residency training, some factors may influence the degree of post-operative pain that occurs: enlargement of apical foramen (68), extrusion of sodium hypochlorite, and over-instrumentation.

A fourth limitation is that both pre-operative and post-operative medications that might have been consumed by the patient. Pain medications might have influenced both the pre-operative and post-operative pain.

A fifth limitation was the unbalanced number of participants in the groups (29 in the non-depressed group vs. 10 in the depressed group). This is a pilot study and will be continued by a future resident.

FUTURE DIRECTION

Based on the distribution of pain, we believe that future studies measure VAS at multiple time pain at day1 and day 3 as well. In the current study, these time points are missing. It might be valuable to see the reduction of post-operative pain between days two and four. The additional information might enable clinicians to better educate their patients in post-operative expectations of pain reduction. Similarly, long-term data collection at day 30 might be helpful in evaluating whether pain subsides completely post-operatively by that date. Future studies can be designed to minimize the limitations should described above. Finally, to confirm the diagnosis of depression, the patient's physician should be contacted to verify their diagnosis.

CONCLUSION

In our study, diagnosis of depression was found to be a predictor of both post-operative unpleasantness and immediate post-operative pain. In addition, any signs of anxiety/depression shown by the HADS score was found to be a predictor of post-operative pain at day two.

REFERENCES:

1 Casey Kenneth L, Casey Kenneth L. Central Nervous System Generation and Modulation of Pain. *Chas. Pain Search a Neurobiol. Mech.* 2019.

2 Watson David, Clark Lee Anna, Weber Kris, Assenheimer Jana Smith, et al. Testing a tripartite model: II. Exploring the symptom structure of anxiety and depression in student, adult, and patient samples. J Abnorm Psychol 1995;104(1):15–25. Doi: 10.1037/0021-843X.104.1.15.

3 Trivedi Madhukar H. The link between depression and physical symptoms. Prim Care Companion J Clin Psychiatry 2004;6(Suppl 1):12–6.

4 Sherbourne CD, Sullivan G, Craske MG, et al. Functioning and disability levels in primary care out-patients with one or more anxiety disorders. Psychol Med 2010;40(12):2059–68. Doi: 10.1017/S0033291710000176.

5 Keiser Karl, Hargreaves Kenneth M. Building effective strategies for the management of endodontic pain. Endod Top 2004. Doi: 10.1034/j.1601-1546.2002.30109.x.

6 Falace DA, Reid K, Rayens MK. The influence of deep (odontogenic) pain intensity, quality, and duration on the incidence and characteristics of referred orofacial pain. J Orofac Pain 1996.

7 Cognitive Modulation of Pain. *Encycl. Pain*. 2013.

8 Iwata Koichi, Takeda Mamoru, Oh Seog Bae, Shinoda Masamichi. Neurophysiology of Orofacial Pain. *Contemp. Oral Med.* 2019.

9 Tracey Irene, Mantyh Patrick W. The Cerebral Signature for Pain Perception and Its Modulation. Neuron 2007. Doi: 10.1016/j.neuron.2007.07.012.

10 Gedney Jeffrey J, Logan Henrietta, Baron Robert S. Predictors of short-term and long-term memory of sensory and affective dimensions of pain. J Pain 2003;4(2):47–55.

11 Price Donald D. Psychological and neural mechanisms of the affective dimension of pain. Science (80-) 2000. Doi: 10.1126/science.288.5472.1769.

12 Cooper Rachel. Diagnostic and Statistical Manual of Mental Disorders (DSM). Knowl Organ 2018. Doi: 10.5771/0943-7444-2017-8-668.

13 Willner Paul, Scheel-Krüger Jørgen, Belzung Catherine. The neurobiology of depression and antidepressant action. Neurosci Biobehav Rev 2013. Doi: 10.1016/j.neubiorev.2012.12.007.

14 Palazidou Eleni. The neurobiology of depression. Br Med Bull 2012. Doi: 10.1093/bmb/lds004.

15 Nestler Eric J, Barrot Michel, Dileone Ralph J, Eisch Amelia J, Gold Stephen J, Monteggia Lisa M. Neurobiology of Depression Review. 2002 2002.

16 Gillies ML, Smith LN, Parry-Jones WL. Postoperative pain assessment and management in adolescents. Pain 1999;79(2–3):207–15. Doi: 10.1016/S0304-3959(98)00178-X.

17 Carr Eloise CJ, Thomas Veronica Nicky, Wilson-Barnet Jenifer. Patient experiences of anxiety, depression and acute pain after surgery: A longitudinal perspective. Int J Nurs Stud 2005:521–30. Doi: 10.1016/j.ijnurstu.2004.09.014.

18 Carr Eloise CJ. Exploring the effect of postoperative pain on patient outcomes following surgery. Acute Pain 2000;3(4):183–93. Doi: 10.1016/S1366-0071(00)90003-2.

19 Gureje Oye, Simon Gregory E, Von Korff Michael. A cross-national study of the course of persistent pain in primary care. Pain 2001;92(1–2):195–200. Doi: 10.1016/S0304-3959(00)00483-8.

20 De Cosmo Germano, Congedo Elisabetta, Lai Carlo, Primieri Paolo, Dottarelli Alessandra, Aceto Paola. Preoperative Psychologic and Demographic Predictors of Pain Perception and Tramadol Consumption Using Intravenous Patient-controlled Analgesia. Clin J Pain 2008;24(5):399–405. Doi: 10.1097/AJP.0b013e3181671a08.

21 Taenzer P, Melzack R, Jeans ME. Influence of psychological factors on postoperative pain, mood and analgesic requirements. Pain 1986;24(3):331–42. Doi: 10.1016/0304-3959(86)90119-3.

22 Dadgostar Anali, Bigder Mark, Punjani Nahid, Lozo Svjetlana, Chahal Vickramjit, Kavanagh Alexander. Does preoperative depression predict post-operative surgical pain: A systematic review. Int J Surg 2017. Doi: 10.1016/j.ijsu.2017.03.061.

23 The National Institute of Mental Health. NIMH » Major Depression. National Institute of Mental Health. 2017.

24 Kleiber Beverly, Jain Shailesh, Trivedi Madhukar H. Depression and pain: implications for symptomatic presentation and pharmacological treatments. Psychiatry (Edgmont) 2005.

25 Gedney Jeffrey J, Logan Henrietta, Baron Robert S. Predictors of short-term and long-term memory of sensory and affective dimensions of pain. J Pain 2003. Doi: 10.1054/jpai.2003.3.

26 List Thomas, Leijon Göran, Helkimo Martti, Oster Anders, Dworkin Samuel F, Svensson Peter. Clinical findings and psychosocial factors in patients with atypical odontalgia: a case-control study. J Orofac Pain 2007;21(2):89–98.

27 NUSSTEIN J, READER A, BECK M. Effect of Drainage upon Access on Postoperative Endodontic Pain and Swelling in Symptomatic Necrotic Teeth. J Endod 2002;28(8):584–8. Doi: 10.1097/00004770-200208000-00005.

28 Rosenberg Paul A, Babick Peter J, Schertzer Leon, Leung Anthony. The effect of occlusal reduction on pain after endodontic instrumentation. J Endod 1998;24(7):492–6. Doi: 10.1016/S0099-2399(98)80054-X.

29 American Association of Endodontists. J Am Dent Assoc 2015. Doi: 10.14219/jada.archive.1977.0456.

30 Tsesis Igor, Faivishevsky Vadim, Fuss Zvi, Zukerman Ofer. Flare-ups after Endodontic Treatment: A Meta-analysis of Literature. J Endod 2008. Doi: 10.1016/j.joen.2008.07.016.

31 Siqueira José F. Microbial causes of endodontic flare-ups. Int Endod J 2003. Doi: 10.1046/j.1365-2591.2003.00671.x.

32 IMURA N, ZUOLO ML. Factors associated with endodontic flare-ups: a prospective study. Int Endod J 1995. Doi: 10.1111/j.1365-2591.1995.tb00311.x.

33 Torabinejad Mahmoud, Kettering James D, McGraw James C, Cummings Raleigh R, Dwyer Thomas G, Tobias Timothy S. Factors associated with endodontic interappointment emergencies of teeth with necrotic pulps. J Endod 1988. Doi: 10.1016/S0099-2399(88)80181-X.

34 Walton Richard, Fouad Ashraf. Endodontic interappointment flare-Ups: A prospective study of incidence and related factors. J Endod 1992. Doi: 10.1016/S0099-2399(06)81413-5.

35 Applebaum Elizabeth, Nackley Andrea G, Bair Eric, Maixner William, Khan Asma A. Genetic Variants in Cyclooxygenase-2 Contribute to Post-treatment Pain among Endodontic Patients. J Endod 2015. Doi: 10.1016/j.joen.2015.04.021.

36 Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983. Doi: 10.1111/j.1600-0447.1983.tb09716.x.

37 Bjelland Ingvar, Dahl Alv A, Haug Tone Tangen, Neckelmann Dag. The validity of the Hospital Anxiety and Depression Scale: An updated literature review. J Psychosom Res 2002. Doi: 10.1016/S0022-3999(01)00296-3.

38 Djukanovic Ingrid, Carlsson Jörg, Årestedt Kristofer. Is the Hospital Anxiety and Depression Scale (HADS) a valid measure in a general population 65-80 years old? A psychometric evaluation study. Health Qual Life Outcomes 2017. Doi: 10.1186/s12955-017-0759-9.

39 Button Eric J, Loan Philippa, Davies Jo, Sonuga-Barke Edmund JS. Self-esteem, eating problems, and psychological well-being in a cohort of schoolgirls aged 15-16: A questionnaire and interview study. Int J Eat Disord 1997. Doi: 10.1002/(SICI)1098-108X(199701)21:1<39::AID-EAT5>3.0.CO;2-4.

40 Herrero MJ, Blanch J, Peri JM, De Pablo J, Pintor L, Bulbena A. A validation study of the hospital anxiety and depression scale (HADS) in a Spanish population. Gen Hosp Psychiatry 2003. Doi: 10.1016/S0163-8343(03)00043-4.

41 Bocéréan Christine, Dupret Emilie. A validation study of the hospital anxiety and depression scale (HADS) in a large sample of French employees. BMC Psychiatry 2014. Doi: 10.1186/s12888-014-0354-0.

42 Nam Seungree, Tin Diane, Bain Lorna, Thorne J Carter, Ginsburg Liane. Clinical utility of the Hospital Anxiety and Depression Scale (HADS) for an Outpatient Fibromyalgia Education Program. Clin Rheumatol 2014. Doi: 10.1007/s10067-013-2377-1.

43 National Institute for Health and Clinical Excellence. *Common mental health disorders: The NICE guideline on identification and pathways to care*. 2011.

44 Orrell Martin, Scior Katrina, Spector Aimee, Charlesworth Georgina, Sweeney Joanne, Stott Joshua. Limited validity of the Hospital Anxiety and Depression Scale (HADS) in dementia: evidence from a confirmatory factor analysis. Int J Geriatr Psychiatry 2016. Doi: 10.1002/gps.4530.

45 Stott Joshua, Spector Aimee, Orrell Martin, Scior Katrina, Sweeney Joanne, Charlesworth Georgina. Limited validity of the Hospital Anxiety and Depression Scale (HADS) in dementia: evidence from a confirmatory factor analysis. Int J Geriatr Psychiatry 2017. Doi: 10.1002/gps.4530.

46 Mitchell Alex J, Meader Nick, Symonds Paul. Diagnostic validity of the Hospital Anxiety and Depression Scale (HADS) in cancer and palliative settings: A meta-analysis. J Affect Disord 2010. Doi: 10.1016/j.jad.2010.01.067.

47 Sirintawat Nattapong, Sawang Kamonpun, Chaiyasamut Teeranut, Wongsirichat Natthamet. Pain measurement in oral and maxillofacial surgery. J Dent Anesth Pain Med 2018. Doi: 10.17245/jdapm.2017.17.4.253.

48 Briggs Michelle, Closs José S. A descriptive study of the use of visual analogue scales and verbal rating scales for the assessment of postoperative pain in orthopedic patients. J Pain Symptom

Manage 1999. Doi: 10.1016/S0885-3924(99)00092-5.

49 Voutilainen Ari, Pitkäaho Taina, Kvist Tarja, Vehviläinen-Julkunen Katri. How to ask about patient satisfaction? The visual analogue scale is less vulnerable to confounding factors and ceiling effect than a symmetric Likert scale. J Adv Nurs 2016. Doi: 10.1111/jan.12875.

50 Ciprandi G, Schiavetti I, Sorbello V, Ricciardolo FL. Perception of Asthma Symptoms as Assessed on the Visual Analog Scale in Subjects With Asthma: A Real-Life Study. Respir Care 2015. Doi: 10.4187/respcare.04171.

51 Appukuttan Devapriya, Vinayagavel Mythreyi, Tadepalli Anupama. Utility and validity of a single-item visual analog scale for measuring dental anxiety in clinical practice. J Oral Sci 2014.

52 Breivik EK, Skloglund LA. Comparison of present pain intensity assessments on horizontally and vertically oriented visual analogue scales. Methods Find Exp Clin Pharmacol 2005. Doi: 10.1358/mf.1998.20.8.487509.

53 Seymour Robin A, Simpson Judy M, Ed Charlton J, Phillips Michael E. An evaluation of length and end-phrase of visual analogue scales in dental pain. Pain 1985. Doi: 10.1016/0304-3959(85)90287-8.

54 Tammaro Stefano, Berggren Ulf, Bergenholtz Gunnar. Representation of verbal pain descriptors on a visual analogue scale by dental patients and dental students. Eur J Oral Sci 1997. Doi: 10.1111/j.1600-0722.1997.tb00202.x.

55 Breivik Harald. Fifty years on the Visual Analogue Scale (VAS) for pain-intensity is still good for acute pain. But multidimensional assessment is needed for chronic pain. Scand J Pain 2016. Doi: 10.1016/j.sjpain.2016.02.004.

56 Marcolino JA, Suzuki FM, Alli LA, Gozzani JL, Mathias LA. [Measurement of anxiety and depression in preoperative patients. Comparative study.]. Rev Bras Anestesiol 2007;57(2):157–66. Doi: S0034-70942007000200004 [pii].

57 Borenstein Michael. Software for Publication Bias. *Publ. Bias Meta-Analysis Prev. Assess. Adjust.* 2006.

58 Glennon JP, Ng YL, Setchell DJ, Gulabivala K. Prevalence of and factors affecting postpreparation pain in patients undergoing two-visit root canal treatment. Int Endod J 2004.

59 AAE. AAE Glossary of Endodontic Terms 2016. Aae 2016.

60 De Sousa Avinash. Psychological issues in oral and maxillofacial reconstructive surgery. Br J Oral Maxillofac Surg 2008. Doi: 10.1016/j.bjoms.2008.07.192.

61 Slade GD, Diatchenko L, Bhalang K, et al. Influence of psychological factors on risk of temporomandibular disorders. J Dent Res 2007. Doi: 10.1177/154405910708601119.

62 Kyle BN, Mcneil DW, Weaver B, Wilson T. Recall of dental pain and anxiety in a cohort of oral surgery patients. J Dent Res 2016. Doi: 10.1177/0022034516631977.

63 Yang Sung Eun, Park Yong Gyu, Han Kyungdo, Min Jung Ah, Kim Sin Young. Dental pain related to quality of life and mental health in South Korean adults. Psychol Heal Med 2016. Doi: 10.1080/13548506.2015.1098781.

64 Su N, Lobbezoo F, van Wijk A, van der Heijden GJMG, Visscher CM. Associations of pain intensity and pain-related disability with psychological and socio-demographic factors in patients

with temporomandibular disorders: a cross-sectional study at a specialised dental clinic. J Oral Rehabil 2017. Doi: 10.1111/joor.12479.

65 Segura-Egea JJ, Cisneros-Cabello R, Llamas-Carreras JM, Velasco-Ortega E. Pain associated with root canal treatment. Int Endod J 2009. Doi: 10.1111/j.1365-2591.2009.01562.x.

66 Pak Jaclyn G, White Shane N. Pain prevalence and severity before, during, and after root canal treatment: A systematic review. J Endod 2011. Doi: 10.1016/j.joen.2010.12.016.

67 Montero Javier, Lorenzo Beatriz, Barrios Rocío, Albaladejo Alberto, Mirón Canelo José Antonio, López-Valverde Antonio. Patient-centered Outcomes of Root Canal Treatment: A Cohort Follow-up Study. J Endod 2015. Doi: 10.1016/j.joen.2015.06.003.

68 Silva Emmanuel João Nogueira Leal, Menaged Karyne, Ajuz Natasha, Monteiro Maria Rachel Figueiredo Penalva, Coutinho-Filho Tauby De Souza. Postoperative pain after foraminal enlargement in anterior teeth with necrosis and apical periodontitis: A prospective and randomized clinical trial. J Endod 2013. Doi: 10.1016/j.joen.2012.11.013.