

Curriculum Vitae

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**LICENSURE INFORMATION**

- June 1993 Registered Nurse  
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State of Maryland
- Feb 2007 Certified Registered Nurse Anesthetist  
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**EDUCATION**

- June 2017-  
July 2023 University of Maryland Graduate School  
Degree: Doctor of Philosophy  
Major: Nursing
- Aug 2004-  
Dec 2006 University of Maryland  
Degree: Master of Science  
Major: Nurse Anesthesia
- Sept 1997-  
July 1999 John Hopkins University  
Degree: Master of Science in Nursing  
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May 1993 Howard University  
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Title: Resilient Factors and their Relationship to Chronic Orofacial Pain and Patient Expectations of Analgesia

The Aims of this study were to 1) determine how positive and negative psychological constructs, jaw function, and COPCs contribute to pain-related disability in TMD using a structural equation modeling (SEM) approach, 2) describe the coping strategy patterns which patients engage in and compare the differences in these patterns based on pain characteristics, 3) determine the relationship between pain resilience on the magnitude of pain interference and expectations.

October 2021 Proficient in MPLUS and SPSS  
Recipient of Biology and Behavior Across the Lifespan: Grant Award

### Clinical

Dec 2009-  
Present

**Certified Registered Nurse Anesthetist  
Veterans Administration Maryland Health Care System  
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- Provide general and spinal anesthesia care to our Veterans.
- Student Nurse Anesthetist clinical coordinator 2010-2011.
- Participation in Quality Assurance activities for Anesthesia Care Clinical Center (ACCC).
- Responsible for generation of CRNA staff schedule.
- Participation in Hospital Root Cause analysis activity.
- Acting Chief Nurse Anesthetist June 2018.
- Participation in Professional Standards Board for Department Nurse Anesthetists.
- Participation in interview and ranking process for Nurse Anesthetist applicants to ACCC.
- Participation in the interview and ranking process of Nurse Practitioners applicants to Surgical Intensive Care Unit.
- Clinical Student Nurse Anesthetist Preceptor

April 2011 -

**Certified Registered Nurse Anesthetist - Johns Hopkins Medical Institution**

Aug 2012

- Per diem anesthesia services for ENT and general surgery cases.

Feb 2007 -

**Certified Registered Nurse Anesthetist- Union Memorial Hospital.**

Nov 2009

- Provided anesthesia services in Anesthesia Care team model (1:4)

for general surgery, orthopedic, plastic surgery, ENT, and pediatric patients.

Sept 2003-  
Dec 2004

**Acute Care Nurse Practitioner-Cardiac Surgery Progressive Care Unit, Johns Hopkins Hospital**

- Daily collaboration with attending physicians and senior residents to provide post-operative care to cardiac surgical patients.
- Management of patient care after CABG and aortic and mitral valve replacement.
- Management of tubes and lines post-procedure including the removal chest tubes and epicardial pacing wires.

Oct 1999-  
July 2003

**Acute Care Nurse Practitioner- Surgical Intensive Care Unit, Johns Hopkins Hospital**

- Collaborated with intensivists and ICU fellows to provide immediate post-operative care to the following patient groups: otolaryngology head and neck surgery, thoracic surgery, plastic surgery, gastrointestinal surgery, genitourinary surgery, orthopedic surgery and oncology/endocrine surgery.
- Providing critical care to patients with hemodynamic instability and multisystem organ failure.
- Experienced in the placement of central lines, pulmonary artery catheters, and arterial lines.
- Preceptor of nurse practitioner students and trained new nurse practitioners for the Weinberg SICU.
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March 1996 –  
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**Critical care nurse, cardiac surgical intensive care unit, Johns Hopkins Hospital.**

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June 1993-  
Feb 1996

**Registered nurse on Halsted-5 - a telemetry unit, Johns Hopkins Hospital**

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## **CERTIFICATIONS**

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## **MEMBERSHIP IN ACADEMIC ASSOCIATIONS**

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- Recipient of VAMHCS Gold Pin Award.

October 2020

- Dekalb High School of Technology South Health Advisory Board (Dekalb School District-Decatur GA)
  - Presentation to High School students.
  - Introduction of the profession of Nurse Anesthesia to High School students.

April 2018

- Recipient of VAMHCS Gold Pin Award.

March 2018

- Recipient of VAMHCS Gold Pin Award.

March 2017

- Recipient of VAMHCS Employee of the month.

Jan 2006

- Sponsored attendance to the 2006 AANA Assembly of Faculty meeting, Newport Beach, California.

Aug 2005

- Recipient of AANA Foundation scholarship.

March 1996- July 2003

- Assisted in the development of standards of care for the IMC in the Weinberg SICU/IMC at Johns Hopkins Hospital.
- Assisted in the development of medication reconciliation process used in the discharge of patients from the Weinberg SICU.
- Member of the education committee on the CSICU at Johns Hopkins Hospital. Responsible for orienting and training new staff.
- Member of the performance improvement committee on the CSICU where I

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### **WORKSHOPS AND CONFERENCES**

- Invited Presentation: Baltimore Brain series, April 2022; Emotional Regulation in Chronic Pain. Sharon Thomas.
- Poster presentation to the 19<sup>th</sup> World Congress on Pain September 19-23, 2022, Boston, USA.
- Poster presentation to the 17<sup>th</sup> World Congress on Pain September 12-16, 2018, Boston, USA.
- Association of VA Nurse Anesthetists annual conference; 2015.
- Cleveland Clinic Survey of current issues in surgical anesthesia 2012, Naples FL.
- Survey of current issues in Surgical Anesthesia—Cleveland Clinic 2013, Naples FL.
- Wake Forest University Advances in Physiology and Pharmacology, 2010.
- Maryland Association of Nurse Anesthetist Conference 10/2009.
- AANA Annual Meetings Washington DC & Cleveland 2005, 2006.

### **PUBLICATIONS**

Thomas S, Wang Y, Cundiff-O'Sullivan R, Massalee R, Colloca L. How negative and positive constructs and comorbid conditions contribute to disability in chronic orofacial pain. *European Journal of Pain*. 2022 Oct 6.

Colloca L, Thomas S, Yin M, Haycock NR, Wang Y. Pain experience and mood disorders during the lockdown of the COVID-19 pandemic in the United States: an opportunistic study. *Pain Reports*. 2021 Sep;6(3).

Colloca L, Akintola T, Haycock N, R, Blasini M, Thomas S, Phillips J, Corsi N, Schenk L, A, Wang Y: Prior Therapeutic Experiences, Not Expectation Ratings, Predict Placebo Effects: An Experimental Study in Chronic Pain and Healthy Participants. *Psychother Psychosom* 2020; 89:371-378. doi: 10.1159/000507400.

Renn, C.L.; Lin L.; Thomas S.; Dorsey, S.G. (2006). Full-length tropomyosin-related kinase B expression in the brainstem in response to persistent inflammatory pain. *Neuroreport* Jul 31; 17(11):1175-9.

Non-authored publications:

1. Okusogu, Chika; Wang, Yang; Akintola, Titilola; Haycock, Nathaniel R.; Raghuraman, Nandini; Greenspan, Joel D.; Phillips, Jane; Dorsey, Susan G.; Campbell,

Claudia M.; Colloca, Luana: Placebo hypoalgesia: racial differences, PAIN: August 2020 - Volume 161 - Issue 8 - p 1872-1883 doi: 10.1097/j.pain.0000000000001876

## Abstract

**Project Title:** Resilient Factors and Their Relationship to Chronic Orofacial Pain and Patient Expectations of Analgesia

**Applicant's Name:** Sharon L Thomas, Doctor of Philosophy Candidate 2021

**Dissertation Proposal Directed by:** Luana Colloca, MD, Ph.D.,

**Background:** Adults with chronic orofacial pain experience significantly impaired daily functioning and reduced quality of life. Patient expectations are recognized as useful in medical treatment. However, we know little about coping behaviors, beliefs, and attitudes influencing disability or expectations in adults with chronic orofacial pain.

**Purpose:** Positive psychological factors are protective against functional impairment and are implicated in placebo and expectations of analgesia. Examining the relationships between psychological factors, pain-related disability, and patient expectations will help identify correlates of disability, and individual susceptibility to placebo effects, a useful pain management modality.

**Methods:** Three cross-sectional studies explored the correlates of pain-related disability and determined the influence of resilience on pain-related disability and patient expectations in adults with temporomandibular disorder. This study used secondary data from a clinical trial of placebo manipulation to examine the relationships between patient expectations of analgesia and psychological factors (resilience, dispositional optimism) and a correlational observation design to explore the relationship between personal characteristics and psychological factors and pain-related disability in adults with TMD. The Aims were to 1) determine how positive and negative psychological constructs, jaw

function, and chronic overlapping pain conditions contribute to pain-related disability; 2) describe the coping strategy patterns which patients engage in and compare the differences in these patterns based on pain characteristics; and 3) determine the relationship between pain resilience, pain interference, and patient expectations.

### **Results**

Study 1 found that resilience factors, optimism, and positive affect had a positive relationship with pain-related disability. Study 2 demonstrated chronic orofacial pain patients used both wellness and illness coping strategies. High pain interference, pain intensity, and pain catastrophizing were associated with higher frequency use of all coping strategies. Study 3 revealed that pain resilience had an inverse relationship with pain disability and a direct and positive relationship with patient expectations.

**Conclusion:** Psychosocial factors are important targets for clinical management of chronic pain. The effect of pain resilience on pain interference and reinforced expectations of analgesia means that clinicians focus efforts on building pain-resilient mechanisms, which can result in improved pain outcomes, augment its effect on expectations, and directly influence placebo treatment outcomes.

The Relationship of Resilient Factors to Chronic Orofacial and Patient Expectations of  
Analgesia

by  
Sharon L Thomas

Dissertation submitted to the Faculty of the Graduate School of the  
University of Maryland, Baltimore in partial fulfillment  
of the requirements for the degree of  
Doctor of Philosophy  
2023

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## **Dedication**

To my Lord and Savior Jesus Christ who has helped me every step of the way and without whom none of this would have been possible. Isaiah 41:10

## **Acknowledgments**

I want to thank the University of Maryland, Graduate School, and the Biology and Behavior Across the Lifespan grant for their financial support that made this work possible. This work would not have been possible without their investment.

Many people have contributed to the success of my dissertation. I am very thankful to many faculty and staff at the School of Nursing who have contributed through teaching and providing support in a variety of ways. I must particularly thank my Dissertation Chair Dr. Luana Colloca for her generosity and inspiration and drive that has propelled through this journey. I also thank my committee members Dr. Barbara Resnick, Dr. Nicole “Jennifer” Klinedinst, Dr. Shijun Zhu, and Dr. Martin Slodzinski for their suggestions, direction and time provided to while writing this manuscript. I must also thank the fellow PhD students and other members/trainees of the Colloca Lab who have supported me in this endeavor. Thanks to Dr. Yang Wang who answered many questions and provided support to me as I worked through this manuscript. Thanks to my fellow PhD Cohort for looking back and pulling me forward with you. I appreciate you all.

Finally, to my family, my mother, brother, sister-in-law, and niece, you were patient with me and prayed for me and supported me in so many ways, I am thankful this and so much more. To my father who passed away early in this process, I am thankful. I would not be here today without his belief in the value of an education.

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## **List of Abbreviations**

<b>Abbreviation</b>	<b>Terms</b>
AA	African American
AIC	Akaike's Information Criterion
BIC	Bayesian Information Criterion
BLRT	Bootstrapped likelihood ratio test
CFA	Confirmatory factor analysis
CFI	Comparative fit index
CI	Confidence interval
COPC	Chronic overlapping pain conditions
CPCI	Chronic Pain Coping Inventory
DC/TMD	Diagnostic Criteria for Temporomandibular Disorders
DF	Degrees of Freedom
GCPS v2.0	Graded Chronic Pain Scale 2.0 version
JFLS-20	Jaw Function Limitation Scale-20 Item Version
LMRT	Lo Mendell And Rubin Test
LPA	Latent Profile Analysis
LOT-R	Life Orientation Test-Revised
OPPERA	Orofacial Pain Prospective Evaluation and Risk Assessment
OR	Odds Ratio
PANAS	Positive And Negative Affect Schedule
PCS	Pain Catastrophizing Scale
PHQ-15	Patient Health Questionnaire-15 Item Version
RMSEA	Root Mean Square Error Approximation
SD	Standard Deviation
SE	Standard Error
SEM	Structural Equation Modeling
SPSS	Statistical Package for Social Sciences
SRMR	Standard Root Mean Square Residual
TLI	Tucker-Lewis Index
TMDs	Temporomandibular disorders
VAS	Visual analog scale

## Chapter 1: Background and Significance

### **Introduction**

Pain, a common and undesired experience, serves as an internal alarm to protect from potential or actual injury. However, among some individuals, about 37-41% in one study, pain becomes chronic and causes disability and reduced quality of life<sup>1</sup>. Chronic pain is defined as pain lasting more than 3 months and is associated with emotional distress and interference with daily and social activities<sup>2</sup>. Pain diagnoses such as temporomandibular disorder, fibromyalgia, and low back pain represent a cluster of chronic pain disorders without specific identifiable cause for pain persistence<sup>3</sup>.

### **Chronic Pain**

Psychosocial factors have been long recognized as influential in the development of chronic pain. Historically, much attention was devoted to the relationship of negative affect constructs such as pain catastrophizing and depression on poor pain outcomes<sup>4,5</sup>. The revised fear-avoidance model provides a structure for understanding the role of positive and negative psychological factors such as resilience and pain catastrophizing in the development of disability or recovery after painful injury<sup>6-8</sup>. These psychological factors will be used to explain the development of pain-related disability and individual susceptibility to placebo effects via expectations in adults with temporomandibular disorders (TMDs).

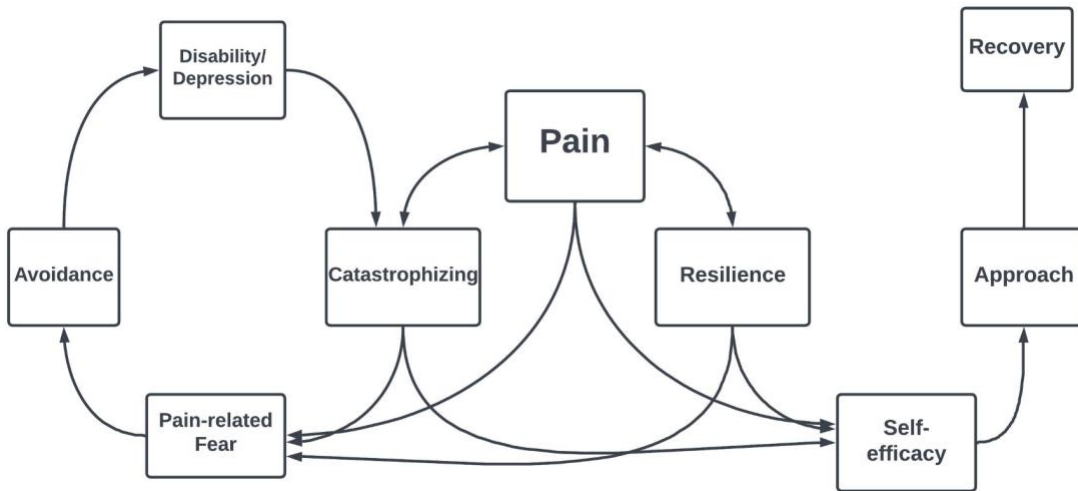


Figure 1.1. Factors influential in pain adaptation based on the proposed Revised Fear Avoidance Model by Slepian et al., 2019.

### Temporomandibular Disorders

Up to 12% of the US population suffer from TMDs, a group of persistent and painful orofacial disorders characterized by alterations in the structure and function of the masticatory system<sup>9,10</sup>. It is the second most common musculoskeletal complaint<sup>11</sup>. Adults suffering from temporomandibular disorders report excruciating pain with everyday activities such as smiling, laughing, kissing, and eating, causing significantly impaired daily functioning and reduced quality of life<sup>11,12</sup>. Temporomandibular disorders are a complex disorder influenced by genetics, sex, gender, environmental, physiological, and psychological factors<sup>10,13,14</sup>. Patients with chronic pain due to temporomandibular disorders seek relief through a variety of treatment options. These include intraoral devices such as mouth guards and oral splints, analgesics, addictive pain medications, and even joint implant surgery<sup>10,13</sup>. The annual cost associated with chronic pain treatment and loss of productivity is approximately \$600 billion and a conservative estimate for

TMDs treatment is roughly \$2 billion<sup>10,15</sup>. The personal and financial burden of overlapping chronic pain conditions such as TMDs and fibromyalgia can be altered by identifying factors associated with worsening pain-related disability. Identifying those associations leading to recovery may lead to the development of innovations chronic pain treatment<sup>16,17</sup>.

### **Pain-Related Disability**

Approximately 100 million adults live with chronic pain in the US, and about 40-50 million experience severe pain-related disability<sup>18-20</sup>. Chronic pain is a source of suffering for broad segments of the population<sup>21</sup>. Disability is the restriction or limitation of activities associated with physical or mental impairment<sup>22</sup>. High-impact chronic pain sufferers report restrictions in employment and recreational activities along with increased cost and health care utilization and reduced quality of life<sup>23</sup>. Pain intensity, pain interference, comorbid pain conditions and chronic health conditions are linked to pain-related disability. Those individuals with high-impact pain disability have four times the odds of having emphysema, liver or kidney disease, arthritis, and diabetes compared to those living with chronic pain without disability<sup>24</sup>.

Psychological influences, such as pain catastrophizing, depression, and anxiety are associated with chronic pain and disability<sup>25-27</sup>. The role of positive psychological factors and coping mechanisms, such as resilience, positive affect, and optimism, has been recently recognized as equally important as they impact pain adaptation and pain outcomes<sup>28-30</sup>. Resilience factors offer protection against the negative aspects of chronic pain including disability<sup>31</sup>.

## **Pain Catastrophizing**

Pain catastrophizing is an exaggerated negative outlook that an individual has toward actual or potential pain, and pain-related fear is the fear of pain and actions connected with pain<sup>32</sup>. Cognition and the perception of painful experiences are recognized as very important in pain adaptation, and pain catastrophizing is a cognitive factor in the development of pain persistence as it contributes to individual sensitivity and response to pain<sup>33</sup>. Clinically pain catastrophizing is linked to suboptimal response to medical treatment and is a strong predictor of pain-related disability, increased pain intensity, and psychological distress<sup>34</sup>. Examining the impact of pain catastrophizing in a model of pain-related disability in adults with temporomandibular disorders, would be beneficial.

## **Resilience**

Resilience, a personality trait, is also believed to be influential in pain adaptation. Resilience is the ability to reach or recover physical or emotional health after injury, adversity, or illness<sup>35,36</sup>. According to Richardson (2002), resilience is a process of handling adversity or change in a manner that results in the “identification, fortification and enrichment of resilient qualities or protective factors”<sup>37</sup>. Richardson's resilience model posits that in stress, individuals can choose consciously or unconsciously the effect of the disruptive event<sup>37</sup>. An individual using internal or external protective factors like self-efficacy and social support, may move along a continuum of resilient responses ranging from resilient reintegration, reintegration back to homeostasis, reintegration with loss, and finally, dysfunctional reintegration<sup>37</sup>. In resilient reintegration, the individual regains full physical and emotional function and even experiences growth<sup>38</sup>. In resilient homeostasis, functional stability is achieved; in reintegration with loss, the

individual does not regain baseline function. In dysfunctional reintegration, the individual cannot cope and relies on substances and negative behaviors to manage. Resilience manifests in different ways, which allows individuals to withstand and thrive under stress.

### Expectations and Placebo

The theoretical concept of expectations or beliefs about a particular treatment efficacy are central to initiation and variation in placebo response<sup>39</sup>. Expectations are formed through prior treatment experiences, observational learning, verbal information from a healthcare provider, and characteristics of a therapeutic encounter<sup>40</sup> and expectations are directly correlated with placebo responsiveness (Figure 1.2)<sup>41</sup>. The placebo response is a reproducible scientific phenomenon, and it is based on positive patient expectations and beliefs about the benefits of a particular treatment.

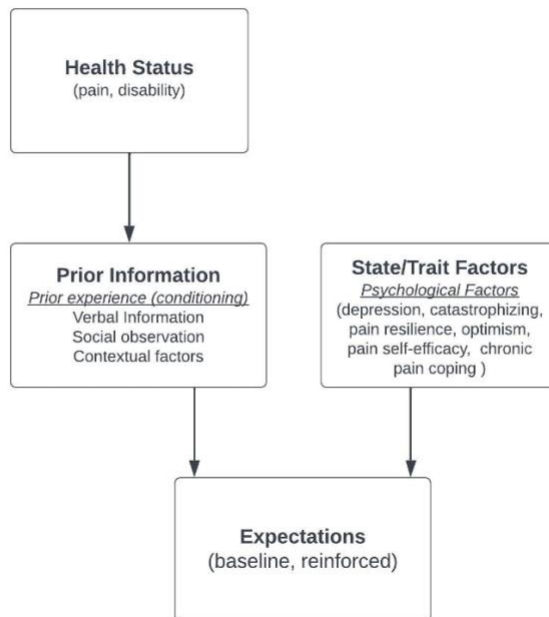


Figure 1.2. Adaptation of Treatment-Expectation Model, Bingel, 2020.

Expectations influence both pain and placebo. Expectation based interventions are linked to improvement of disability outcomes in cardiac surgery <sup>42</sup>. Placebos, (inert substances administered in the guise of an active drug), can augment pain relief, limit the amount of opioid used, and decrease pain and disability <sup>39,43,44</sup>. Placebo effects are caused by a complex interaction of neurobiological and psychological mechanisms that cause the release of endogenous opioids decreasing pain ratings <sup>45,46</sup>. Expectations and placebo response may impact clinical outcomes; however, predicting individual predisposition to this phenomenon remains a challenge.

The psychological mechanisms underlying expectations and placebo response remain a source for investigation suggesting who may benefit from this therapy. Personality traits may explain individual differences and susceptibility to this phenomenon. Individuals with high dispositional optimism and low state anxiety have been found to have reproducible placebo responses <sup>47,48</sup>. Discernment of individual predisposition to the placebo response, vis-a-vis the expectations, may elucidate the clinical therapeutic benefit of the placebo response in adults with temporomandibular disorders. Characterizing which adults with TMDs will benefit from placebo analgesia is imperative for reducing chronic pain and morbidity.

### **Purpose**

Few researchers have addressed the role of protective mechanisms, such as resilience in patients with chronic orofacial pain. This descriptive cross-sectional study adapted portions of the revised fear-avoidance model to examine the contribution of psychological factors to pain outcomes and placebo response. This work examines the relationships between demographics, comorbid medical, and psychological conditions to clinical pain intensity and pain interference components of pain-related disability in adults with temporomandibular disorders; examines the

coping strategies utilized by patients with temporomandibular disorders; and determines the relationship between positive factors (pain resilience, dispositional optimism) on the expectations of analgesia, a crucial link to placebo response. The following are the dissertation specific aims and hypotheses.

### **Aim 1**

Examine the relationships between demographics, comorbid medical, and psychological conditions to clinical pain-related disability in adults with TMDs. H.1. positive psychological constructs will be inversely associated with pain-related disability, H.2. negative psychological constructs will have a direct and positive relationship to pain-related disability, H.3. jaw function limitation will have a direct and positive relationship to pain-related disability, and H.4. chronic overlapping pain conditions will have a direct and positive impact on pain-related disability. This work utilized secondary data from a placebo manipulation trial (HP- 00068315) to examine these relationships.

### **Aim 2**

To identify characteristics of subgroups of patients with chronic orofacial pain based on their coping strategies. H.1. Distinct coping strategy profiles would emerge among the sample of chronic pain patients. H.2. Higher pain intensity, pain interference, pain duration, pain catastrophizing scores, and the presence of chronic overlapping pain conditions<sup>49</sup> such as fibromyalgia, irritable bowel syndrome, migraines, and chronic low back pain, will be associated illness-focused coping styles such as guarding and resting versus wellness-focused strategies such as coping self-statements and exercise.

### **Aim 3**

Determine the relationship between pain resilience on the magnitude of pain interference and expectations. H.1. a negative relationship existed between pain resilience and pain interference while controlling for psychological covariates, and that H.2. pain resilience was positively associated with increased reinforced expectancy of analgesia when accounting for psychological factors (optimism, pain catastrophizing, depression), and other covariates (prior experience, sex, race, education) and H.2.B. pain resilience modified the relationship between conditioning strength and expectation of analgesia.

### **Proposed Study Conceptual Framework**

Negative and positive psychological factors often interact to impact pain affect<sup>30</sup>. Pain catastrophizing has been linked to worsened pain outcomes and positive psychological mechanisms, including resilience, are instrumental in individual variability in acute pain response and chronic adaptation. Positive psychological mechanisms such as positive affect and active coping have been identified as protective in chronic pain and disability and promote greater resilience<sup>50,51</sup>.

The Fear-Avoidance Model<sup>8</sup> provides a framework for understanding individual differences in chronic pain, the influence of psychological factors such as pain related fear and pain catastrophizing on the development of pain chronicity or recovery from a painful injury<sup>8</sup>. The model hypothesizes that individuals who catastrophize develop pain-related fear, leading to activity avoidance, and ultimately these individuals are likely to develop disability and or depression<sup>8</sup>. Whereas those who engage in approach behavior, that is, confronting pain, not as a threat, but as a temporary symptom, move toward recovery after injury<sup>8,52</sup>. When competing life

goals, such as physical fitness, outweigh the focus on pain and the pain-related fear behavior, avoidance behaviors are inhibited. The path to recovery involves beliefs and thought patterns like positive affect and optimism, that are prioritized by the individual and normal activities are gradually resumed after a brief period of inactivity <sup>53</sup>.

A revised Fear-Avoidance Model (Figure 1.1) incorporates the role of resilience as a positive factor integral to adaptation in pain and leading to eventual recovery through approach-oriented behaviors or pleasant moods and emotions <sup>7,54</sup>. This revision posits that resilience has demonstrable effects on coping mechanisms which impact pain adaptation and leads to recovery, from chronic pain. This work explored the relationship between resilience, optimism, and pain disability in patients with TMDs. It is unknown for whom placebo treatment will be most effective. Resilience and optimism are not only implicated in recovery from pain but are associated in placebo effect <sup>55,56</sup>. This work describes the relationships of the biopsychosocial factors which contribute to or may be protective in pain related disability among patients with TMDs. Furthermore, this work also examined the factors which contribute to expectancy a key component of placebo response. (Figure 1.3).

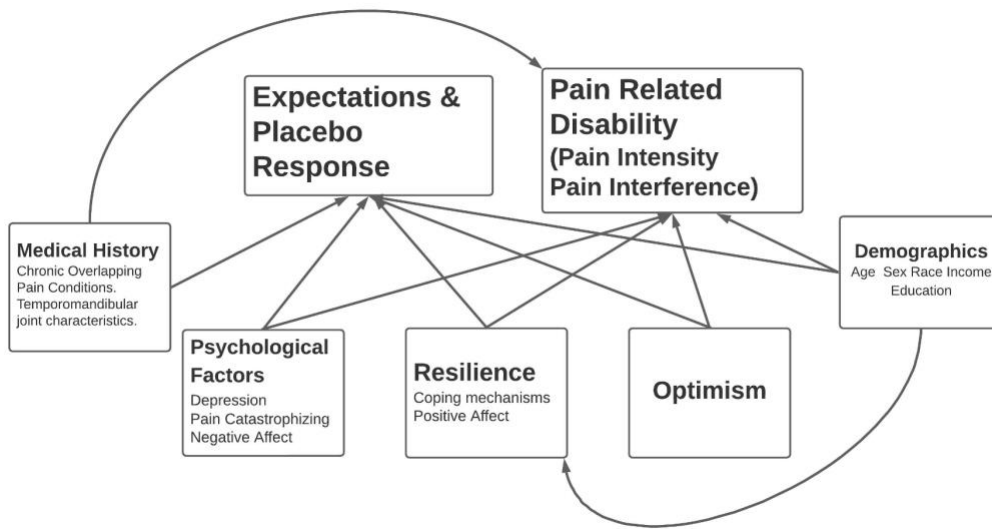


Figure 1.3. Proposed Study Conceptual Framework identifying relationships tested among psychological factors including Resilience and Expectations and Pain Disability.

## Methods

### Sample and Setting

Adults with a confirmed diagnosis of temporomandibular disorder completed a series of surveys. Men and women between the age 18-65 were recruited from the University of Maryland School of Dentistry Facial Pain Clinic. The participants must have had pain for at least 3 months in the jaw, temple, in the ear, or in front of the ear, or on either side face. Each participant understood written and spoken English and had access to a computer or mobile phone for completing survey data. Participants with a history of severe psychiatric diseases, degenerative neuromuscular disease, active cardiovascular disease, current pregnancy and or breastfeeding, color blindness, hearing loss, recent cancer, facial trauma, cervical stenosis, and alcohol or drug dependence were excluded.

## **Study Design**

The following methods were used to address the aims of the study. Aims 1 and 2 of this study were achieved by secondary data analysis obtained from a clinical trial involving placebo manipulation in adults with temporomandibular disorders. For Aim 3, participants in the parent study were recontacted via phone and emails and completed series of online survey instruments. Approval for this study was granted by the University of Maryland Institutional Review Board.

In Aim 1, this work developed a novel structural equation model of pain-related disability based on biopsychosocial contributors identified in this study conceptual model. This study was a cross sectional retrospective design utilizing the medical history and psychosocial questionnaire data from a previous study (Chronic orofacial pain: Genetics, cognitive-emotional factors, and endogenous modulatory systems , HP- 00068315- PI Luana Colloca) on placebo manipulation in adults ( $N=409$ ) with temporomandibular disorders to study the relationships between positive (optimism, positive affect), and negative (somatic symptoms, pain catastrophizing, negative affect) constructs, jaw limitation function and pain related disability while controlling for chronic overlapping pain conditions and demographic variable (sex, race, education). Psychological questionnaire data (Graded Chronic Pain Scale version 2.0<sup>57</sup> Life Orientation Test-Revised Scale<sup>58</sup>, Positive and Negative Affect Schedule<sup>59</sup>, the Pain Catastrophizing Scale<sup>60</sup>, the Patient Health Questionnaire-15<sup>61</sup>, the Jaw Function Limitation scale -20<sup>62</sup>) were used to create the latent variables used in the analysis. Descriptive data were also obtained from the primary study. The required sample size and power estimations for this study were based accepted criteria for structural equation models. The final sample size of 400

met the requirement of 5-10 observations per parameter with 48 freely estimated parameters in the model.

Aim 2 was a cross-sectional retrospective design using secondary data from the study on Chronic orofacial pain: Genetics, cognitive-emotional factors, and endogenous modulatory systems, HP- 00068315. The study focused on coping strategy profiles and the differences in these profiles based on pain interference and pain intensity. The Chronic Pain Coping Inventory (CPCI) <sup>63</sup> provided the data for creation of latent profiles based on the pain intensity and pain interference. Pain Intensity and Pain Interference were measured using the Graded Chronic Pain Scale version 2.0 <sup>57</sup>. Chronic overlapping pain conditions and demographic data were also obtained from the primary study. Sample size and power analysis for latent profile analysis is a developing field of research and is estimated that a sample size between 300-500 and should be the minimum and among 38 studies the median sample size was 377 <sup>64,65</sup>.

Aim 3 was a descriptive cross sectional design using data collected from online survey instruments and secondary data (placebo and expectation data) from the study on Chronic orofacial pain: Genetics, cognitive-emotional factors, and endogenous modulatory systems, HP- 00068315. This work focused on the relationships between pain resilience on pain interference and expectations of analgesia in the presence of psychological factors (depression and pain catastrophizing). This work explored the moderating role of pain resilience on the relationship between conditioning strength and expectations of analgesia. Expectation and conditioning data were obtained from the parent study (HP- 00068315). Participants completed online surveys including the Pain Resilience Scale <sup>50</sup>, Graded Chronic Pain Scale version 2.0 <sup>57</sup> Life Orientation Test-Revised Scale <sup>58</sup>, Pain Catastrophizing Scale <sup>60</sup>, Beck Depression Inventory-II<sup>66</sup>. According

to prior studies on resilience effect on pain-related psychological factors, pain-related beliefs, and resilience interventions, small to medium effect sizes were observed<sup>30,67,68</sup> Based on these data, a power analysis suggested that a total number of 82 participants would be required to achieve a 0.8 statistical power to observe a Cohen's-d small effect of 0.3 at an alpha level of .05.

## **Procedures**

Participants who agreed to be recontacted in the primary study were invited to participate in the current study via phone and email contacts. The participants were screened for inclusion and exclusion criteria to confirm that they were eligible to participate in this study. Study procedures were described to the participants, including the use of prior placebo data and voluntary participation with the option to withdraw.

## **Informed Consent**

Participants reviewed and accepted an informed electronic consent all study procedures. All participant concerns and questions were answered. The electronic consent documented that the participant read, understood, and agreed to participate in the study. A copy of the completed informed consent was be emailed to the participant. Once agreeing to participate, a survey link via REDCap was forwarded to the participant's email. Participants were compensated with a \$25 electronic gift card for the time completing the surveys.

## **Study Organization**

The subsequent chapters of this dissertation include three manuscripts (Chapters 2-4). These chapters address the aims of the study. Chapter 2 (Aim 1) describes the contribution of positive and negative psychological factors to pain related disability in patients with chronic orofacial pain. Chapter 3 (Aim 2) looks further into the coping strategies patterns used by

patients with chronic orofacial pain and how they may be linked to pain intensity and pain interference. This work also looked at whether differences exist in the coping strategy patterns based on pain intensity, pain interference, pain catastrophizing, pain duration, chronic overlapping pain conditions, and sociodemographic variables. Chapter 4 (Aim 3), focused specifically at whether pain resilience maintains an inverse relationship and protective relationship with pain interference. This aim also tested whether higher pain resilience is associated with higher expectations of analgesia in placebo manipulation. The role of resilience as a moderator in the relationship between the conditioning strength and expectation of analgesia in the placebo experiment is investigated.

These studies provide supporting evidence to the role of psychological factors, positive and negative, in pain adaptation outcomes in patient with chronic orofacial pain. I provide new evidence of the importance of pain resilience in augmenting the response to placebo via expectations. These finding provide targets for clinician intervention in the management of chronic orofacial pain and identification of which coping strategies should be supported among patients with chronic pain.

### **Summary**

The purpose of this study was to examine the relationships between demographics, comorbid medical, and psychological conditions to clinical pain intensity and pain interference components of pain-related disability in adults with temporomandibular disorders. This study also examined the coping strategies utilized by patients with temporomandibular disorders and determined the relationship between positive factors (pain resilience, dispositional optimism) on the expectations of analgesia, a crucial link to placebo response.

## Chapter 2: How Negative and Positive Constructs and Comorbid Conditions Contribute to Disability in Chronic Orofacial Pain

### **Introduction**

Temporomandibular disorders (TMDs) are common in the United States, affecting up to 12% of the population with considerable associated costs <sup>9</sup>. TMDs sufferers experience excruciating pain in the temporomandibular joints, significantly impairing daily functioning and reducing the quality of life <sup>69-71</sup>. TMDs symptoms can be acute, self-limiting, or vary over time, and for unclear reasons, 15% of TMD sufferers will have persistent pain 5 years after the complex symptoms appear <sup>72-74</sup>. A greater understanding of the multidimensional nature of TMD pain-related disability will enhance the ability to isolate which patient characteristics exacerbate pain disability, and equally important, which patient characteristics protect against poor pain outcomes.

Previous research suggested the complex relationship between clinical characteristics, psychosocial factors, orofacial function, and underlying pain sensitivity impacts TMDs pain symptoms and outcomes <sup>75,76</sup>. TMDs are often associated with chronic overlapping pain conditions (COPCs) like fibromyalgia, irritable bowel syndrome, headaches, migraines, and chronic low back pain due to an underlying central nervous system hypersensitivity <sup>16,77-80</sup>. Mainly, painful jaw characteristics common to TMDs exist independently in other COPCs, and the presence of greater than three COPCs is associated with greater TMDs symptomology <sup>81</sup>. The contribution of comorbidities to pain outcomes in TMDs warrants further study as poor treatment outcomes may be linked to associated COPCs <sup>82</sup>, and incorporating COPCs into assessment, management and intervention may be beneficial to pain outcomes <sup>83</sup>.

Other factors that can influence disability are depression and pain catastrophizing, a heightened focus on the potential signs and dangers of pain <sup>84-86</sup>. Significant positive associations were found between psychological distress, social stressors, arousal, and pain symptoms in patients with TMDs <sup>87</sup> and between pain disability, psychological difficulties, and jaw function <sup>88</sup>. While the role of psychological distress in chronic pain behavior is well recognized, much less is known about the contribution of positive valence factors <sup>89</sup>, like optimism and positive affect which may counter the adverse effects of psychological distress in chronic pain outcomes. <sup>28</sup>.

This cross-sectional study aims to determine how positive and negative psychological constructs, jaw function, and COPCs contribute to pain-related disability in TMDs using a structural equation modeling (SEM) approach. I hypothesized the following.

1. Positive psychological constructs will be inversely associated with pain-related disability.
2. Negative psychological constructs will have a direct and positive relationship to pain-related disability.
3. Jaw function limitation will have a direct and positive relationship to pain-related disability.
4. COPCs will have a direct and positive impact on pain-related disability.

## **Methods**

This cross-sectional study comprised participants who were suffering from TMDs for at least 3 months between the years 2017 and 2020. The sample was nested in a parent study investigating the genetic predictors of orofacial pain. The University of Maryland Institutional

Review Board approved this study (HP-00068315), and all willing participants signed informed consent before data collection procedures. The risks, benefits, and alternatives were explained before obtaining written consent from all the participants. This study excluded vulnerable groups such as children and prisoners from the study and took every precaution to protect the privacy of all participants. The participants received compensation for their time (\$100).

### **Participants**

I enrolled 409 participants and excluded nine as they did not meet eligibility criteria or withdrew from the study (Figure 2.1). The final sample consisted of 400 participants. Recruitment occurred via advertisements, community events, health fairs, and letters to patients at the Brotman Facial Pain Clinic at the University of Maryland. Demographic data (age, sex, race, and education) were collected, participants completed a series of questionnaires, and a trained examiner confirmed the TMDs diagnosis. A nurse or physician conducted telephone and in-person screenings to verify eligibility to participate in this study.

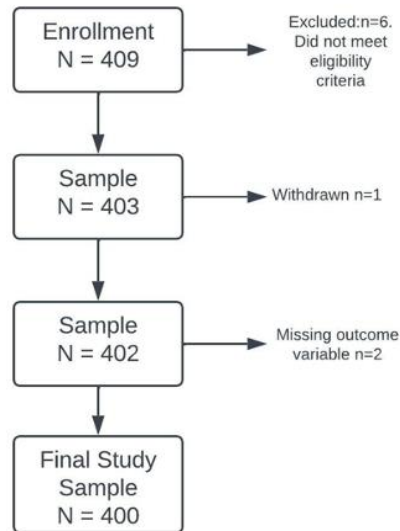


Figure 2.1. Flow diagram. This flow diagram represents sample selection and missing data amongst the TMDs cohort.

### **Diagnostic Criteria for Temporomandibular Disorders**

A trained examiner with expertise in orofacial pain confirmed the presence of TMDs with an in-person clinical exam at the Brotman Facial Pain Clinic at the University of Maryland School of Dentistry. The DC/TMD symptom questionnaire was used to assess the reported pain history and arrive at a research diagnosis based on the presence of myalgia, arthralgia, and myofascial pain with referral <sup>71</sup>. A trained examiner assessed the location of pain across the joint and muscle mass, incisal relationships, and mandibular movements. The exam included evaluating the presence of myalgia, arthralgia, or self-reported headache of any type in the temporal area in the previous 30 days and any headache modified by jaw movement, function, or parafunction. The grading of instruments was per the DC/TMD Scoring Manual for Self-Report Instruments <sup>90</sup>.

## **Inclusion and Exclusion Criteria**

Participants were English speakers between 18 and 65 years of age. Inclusion criteria of the study were facial pain for at least the immediate 3 months prior and symptoms that met the DC/TMD <sup>71</sup>. Facial pain characteristics included pain occurring a minimum of 3 months in the jaw, temple, ear, in front of the ear, or on either side immediately before the examination. The inclusion criteria of the study were facial pain that was always present or intermittent for at least the immediate three months prior. Participants provided their medical history, including current medications, via a checklist of common medical conditions. I excluded participants with a history of severe psychiatric disease, degenerative neuromuscular disease, cardiovascular disease, pulmonary, kidney disease, liver disease, and cancers, all within 3 years. Participants who were pregnant, breastfeeding, color blind, had uncorrected hearing, facial trauma, cervical stenosis, and alcohol or drug dependence were also excluded.

## **Measurements**

*Pain-Related Disability* was measured using the Graded Chronic Pain Scale version 2.0 <sup>57</sup>. The GCPS v2.0 is a reliable and valid tool for measuring the impact of TMDs pain on the patients' ability to function <sup>57,91</sup>. The GCPS consists of eight items, the first inquiring about pain over the last 6 months is not included in the scoring. Three subscale scores, characteristic pain intensity (CPI), pain interference score, and disability days, are derived from the remaining seven items. The pain intensity items are ranked on a scale of 0 (*no pain*) to 10 (*pain as bad as possible*). The pain interference score is derived from Questions 6 through 8 regarding the inability to do daily work or social activities. Interference questions are ranked on a scale of 0 (*no interference*) to 10 (*unable to carry out activities*). Pain intensity and interference scores

were averaged and multiplied by 10. Higher scores indicate higher pain intensity and disability<sup>67</sup>. Pain intensity and pain interference scores were used in this analysis.

*Jaw Limitation* was measured using the jaw function limitation scale (JFLS-20)<sup>62</sup>, a 20-item scale measuring jaw mastication, jaw mobility, and emotional and verbal expression. The scale has excellent reliability for temporomandibular disorder patients.

*Psychological unease*, a latent variable previously created by Miller et al.<sup>88</sup>, was created from subscales: (a) negative affect from the positive and negative affect schedule (PANAS)<sup>59</sup>, (b) the pain catastrophizing scale (PCS)<sup>33,60</sup>, and (c) the patient health questionnaire-15 (PHQ-15)<sup>61</sup> the somatic symptoms scale. Negative affect, the personal feeling of distress, and unpleasant emotions accompanying negative mood states was assessed by the negative affect subscale from the PANAS<sup>59</sup>. Participants ranked on a 5-point Likert scale of 1 (*very slightly*) to 5 (*extremely*), the extent to which 10 negative mood descriptors represented their mood during the past week.

Lower scores ranging from 10-50 mean less negative affect. Pain catastrophizing was measured using the 13-item instrument PCS. Participants rate their feelings and thoughts regarding pain from 0 (*not at all*) to 4 (*all the time*). The total PCS score ranges from 0-to 52.<sup>33</sup> The PHQ-15<sup>61</sup> assessed somatic symptom severity. It includes 15 medically unexplained physical symptoms. Participants rate the level they are bothered by a medical complaint. The total score is 30, with 5, 10, and 15 representing the cutoff for mild, moderate, and severe somatic symptom severity<sup>61</sup>. The TMDs model proposed by the Orofacial Pain prospective Evaluation and Risk Assessment (OPPERA) study demonstrated that somatic symptoms, have a

strong association with psychological distress and are among the psychological variables which predict the risk of new onset TMDs <sup>92-96</sup>.

*Positive Valence Factors* latent variable was adapted from the National Institute of Mental Health Research Domain Criteria framework in which specific psychological traits and characteristics indicate a phenotype. Specifically, positive affect and optimism are part of a broader construct in which motivation and reward seeking influence behavior <sup>89,97,98</sup>. The latent variable was created by using the positive affect score from the (a) PANAS <sup>59</sup> and the (b) the optimism subscale from the life orientation test-revised (LOT-R) scale <sup>58</sup>. Positive Affect is a measure of enthusiasm, attentiveness, and drive and is linked to optimism and task persistence in patients with chronic musculoskeletal pain. <sup>59,99,100</sup>. Positive affect scores are derived from 10 items from the PANAS<sup>59</sup>, ranging from 10-50. Participants ranked on a 5-point Likert scale of 1 (*very slightly*) to 5 (*extremely*), the extent to which ten positive mood descriptors represented their mood during the past week. Higher scores indicate higher levels of positive affect. Optimism, a key personality trait that increases the likelihood of resilient outcomes, was measured using the life orientation test-revised (LOT-R) scale <sup>58</sup>. The 10-item scale consists of 3 optimism subscale questions, three pessimism subscale questions, and four filler items <sup>58</sup>. Each item is scored on a 5-point Likert scale of 0 (*strongly disagree*) to 4 (*strongly agree*). The total score is comprised of direct score optimism items and reverse scored pessimism items. High total scores represent a higher level of dispositional optimism.

The population's demographic and clinical characteristics are presented in Table 2.1, including demographic variables such as sex, race, educational level, and the number of chronic overlapping pain conditions (COPCs). Some researchers have found that TMDs incidence and

prevalence are greater among females and African Americans <sup>101,102</sup>; however, the impact of socioeconomic status is somewhat mixed <sup>101,103</sup>. Likewise, the number of COPCs, namely irritable bowel syndrome, fibromyalgia, migraine headache, and low back pain, were included as they are believed to share common pathophysiology and risk factors that contribute to the onset and continuance of chronic pain conditions <sup>16,49,104</sup>.

### Statistical Analyses

All variables were screened for normality. The proportion of missing data was small (1-6.5%, among the variables), and missing value analysis revealed that the data were missing completely at random (Little's MCAR test: Chi-Square = 49, df = 47, p =.36).

Table 2.1

#### *Observed Variables Comprising Latent Variables*

Latent Variable	Observed Variables	N (%)	Mean (SE)	Min	Max	Missing N (%)	Skew/Kurtosis
Psychological Unease	Pain Catastrophizing Scale	396	13.84(.57)	0	49	4 (1.0%)	.81/-.01
	Negative Affect score	395	19.61(.41)	10	50	5 (1.3%)	1.03/.67
	Somatic Symptoms Scale	399	7.46(.23)	0	24	1 (0.3%)	.78/.39
Positive Valence Factors	<sup>1</sup> LOT-R Optimism Score	396	14.94(.23)	1	24	4 (1.0%)	-.17/-.36
	Positive Affect Score	396	33.03(.42)	10	50	4 (1.0%)	-.05/-.40
Jaw Function	<sup>2</sup> JFLS chewing limitation	400	2.48 (.10)	0	10	0	.86/.47
	JFLS Opening Limitation	400	2.39 (.11)	0	10	0	.85/-.00
	JFLS Expression Limitation	400	1.44 (.10)	0	10	0	1.8/2.9
Pain Disability	<sup>3</sup> GCPS-Characteristic Pain Intensity score	400	47.64 (1.11)	0	100	0	.11/-.31
	GCPS- Pain Interference score	400	27.47 (1.35)	0	100	0	.81/-.34

<sup>1</sup> LOT-R=Revised Life Orientation Scale; <sup>2</sup> JFLS=jaw Function limitation Scale; <sup>3</sup> GCPS=Graded Chronic

#### Pain Scale

I used a structural equation modeling (SEM) approach that allowed us to create latent variables representing our research constructs. The latent variables are created by factor analysis

using the overlapping variance of correlated measured variables. Latent variables are not directly measured but better represent our constructs because they contain less measurement error than the directly measured variables <sup>105</sup>. Using confirmatory factor analysis (CFA), I examined the strength of relationships between the latent variables jaw function, psychological constructs, and pain-related disability while controlling for the presence of chronic overlapping pain conditions (irritable bowel syndrome, fibromyalgia, migraines, and low back pain) and demographic covariates (sex, race, and education). All demographic covariates were made dichotomous in the analysis as follows: sex (M/F) with male coded as 1; race (White/non-White) recoded with white coded as 1; and education (college graduate/non-college graduate) recoded with college graduate coded as 1.

COPCs (fibromyalgia, irritable bowel syndrome, low back pain, and migraines) <sup>3</sup> were captured from self-reported medical history and confirmed by a trained examiner during the in-person medical history review. A continuous variable was created as a count variable (0-4), capturing the number COPCs reported by each participant. Categorical variables may be analyzed as continuous variables if the data approximate a normal distribution and has four or more categories <sup>106,107</sup>; therefore, the number of COPCs was entered as a predictor into the model.

Four latent variables were constructed in the hypothesized measurement model (see Figure 2.2). Two observed variables, pain intensity and pain interference were the factors for the latent variable of pain-related disability. Jaw function limitation latent variable consisted of the JFLS subscales chewing, opening, and expression limitation measurement scores. Negative affect, pain catastrophizing, and somatic symptoms were the factors of the latent variable of

psychological unease. The latent variable positive valence factors comprised positive affect and optimism scores.

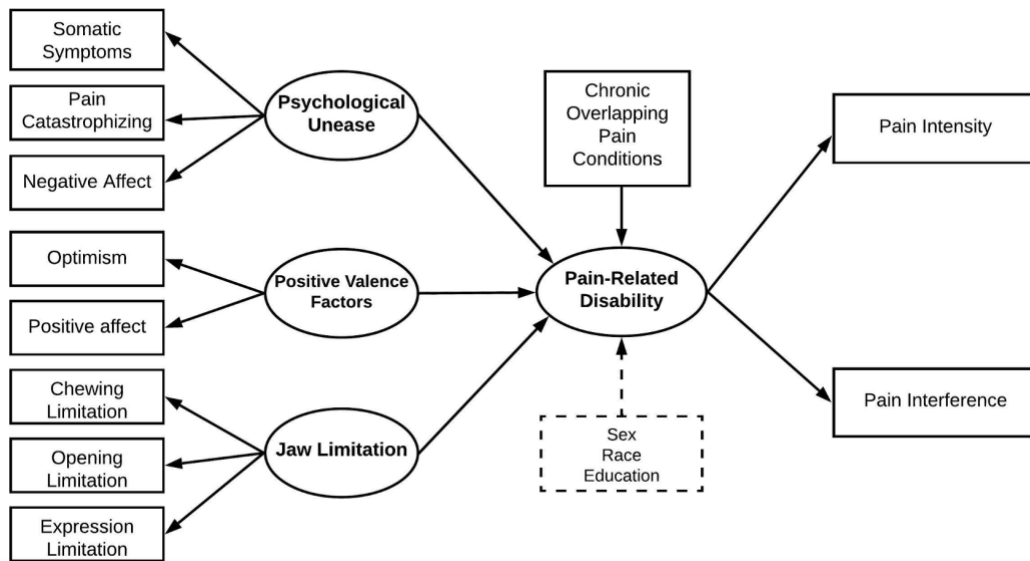


Figure 2.2. Hypothesized model of pain-related disability showing the associations between the latent variables and covariates.

Structural equation modeling evaluated the relationships between observed variables, latent variables, the number of chronic overlapping pain conditions and demographic variables, sex, race, and education. The relationships between latent and observed variables were tested using confirmatory factor analysis and are represented by arrows towards the corresponding observed variables. Circles represent latent variables, and rectangles represent observed variables. Solid arrows between the observed variables, latent variables and covariates represent the relationships tested.

Confirmatory factor analysis (CFA) of the latent variables in the measurement model was performed using maximum likelihood estimator, and goodness of fit indices and factor loadings were evaluated (Table 2.2). The extent to which the observed data fit the proposed model is reflected in the goodness of fit indices. Model fit was assessed using the chi-square test, comparative fit index (CFI), Tucker-Lewis index (TLI), root mean square error approximation (RMSEA), and standard root mean square residual (SRMR). The criteria for a well-fitting model were model, a p-value of chi-square  $> 0.05$ , CFI  $\geq .95$ , TLI  $\geq .95$ , RMSEA  $< .08$ , and SRMR  $< .08$ <sup>108</sup>.

Next, I tested the SEM model, which examined the relationships between the latent variables jaw limitation, psychological unease, positive valence factors, pain-related disability, and the number of COPCs, with the covariates, sex, race, and education, and evaluated global and local model fit and parameter estimates. Maximum likelihood estimator was used to assess the model fit, and global and local model fit were based on previously described indices. Data screening, exploration, and missing data analysis were conducted in SPSS version 27<sup>109</sup>. All CFA and SEM analyses were performed in Mplus<sup>110</sup>. A  $p < 0.05$  was set as the level of significance.

In regards to sample size, a golden criteria is to have approximately 5-10 observations per parameter<sup>106</sup>. For this study, there were 48 freely estimated parameters in the model. Based on these criteria, the sample size of 400 provided sufficient sample size for the SEM analysis.

## Results

### Descriptive Statistics

Four hundred participants were included in the analysis. Seventy-six percent of the sample was female, with African Americans comprising 35% of the sample. The pain intensity and pain interference scores were normally distributed with mean scores of 47.64 (1.11 SE) and 27.47 (1.35 SE) using a scale of 1-100, respectively, with a strong correlation between scores ( $r = .62, p < .001$ ). Within the sample, TMDs pain was characterized by 95% myalgias, 85% arthralgias and 52% TMDs headache. Pain catastrophizing, negative affect, and somatic symptom scores were all normally distributed with medium-sized correlations ( $r = .33$  to  $.43, p < .01$ ) between these variables. Similarly, optimism and positive affect scores were normally distributed with a medium correlation between optimism and positive affect  $r = .45, p < .001$ . Jaw function limitation scores had an acceptable distribution, with jaw expression score having a skew/kurtosis value of 1.8 and 2.9, respectively. These were deemed acceptable as kurtosis was less than 3<sup>111</sup>. The correlations between the jaw function variables were strong ( $r = .67$  to  $.79$ ) as expected, with the largest correlation ( $r = .79, p < .001$ ) occurring between jaw chewing and jaw opening and the smallest occurring between expression limitation and chewing limitation ( $r = .67, p < .001$ ). Correlations among the variables are reported in Tables 2.2 and 2.3 Regarding COPCs, 15% of the sample reported migraines, 5% reported fibromyalgia, and 4% reported irritable bowel syndrome. Mean, minimum, and maximum scores of observed variables are displayed in Table 1.1.

Table 2.2

*Descriptive Statistics 1*

	NEGAFF	CATAS	SOMASY	POSAFF	OPTIMIS	MASTIC	MOBILI
NEGAFF	1						
CATAS	0.429**	1					
SOMASY	0.374**	0.332**	1				
POSAFF	-0.216**	-0.116*	-0.138**	1			
OPTIMIS	-0.368**	-0.270**	-0.218**	0.447**	1		
MASTIC	0.116*	0.258**	0.283**	0.076	-0.019	1	
MOBILI	0.055	0.217**	0.215**	0.102*	-0.002	0.785**	1
COMMU	0.097	0.223**	0.320**	0.025	-0.016	0.670**	0.748**
GCPSCP	0.102*	0.251**	0.343**	0.026	-0.04	0.552**	0.539**
GCPSINT	0.142**	0.254**	0.377**	0.059	-0.001	0.527**	0.489**
CMED	0.100*	0.166**	0.424**	-0.072	-0.125*	0.085	0.004
SEX	0.022	-0.055	-0.088	0.002	-0.084	-0.03	-0.057
RACE	-0.044	-0.106*	-0.158**	-0.088	0.000	-0.206**	-0.139**
EDUC	0.012	-0.047	-0.095	-0.048	0.023	-0.171**	-0.131**

Table 2.3

*Descriptive Statistics 2*

	COMMU	GCPSCP	GCPSINT	CMED	SEX	RACE	EDUC
NEGAFF							
CATAS							
SOMASY							
POSAFF							
OPTIMIS							
MASTIC							
MOBILI							
COMMU	1						
GCPSCP	0.499**	1					
GCPSINT	0.609**	0.617**	1				
CMED	0.083	0.190**	0.213**	1			
SEX	-0.063	-0.157**	-0.038	-0.130**	1		
RACE	-0.145**	-0.113*	-0.170**	0.009	-0.135**	1	
EDUC	-0.109*	-0.169**	-0.147**	-0.026	-0.131**	0.296**	1

\*p&lt;.05

\*\*p&lt;.01

All covariates were made dichotomous in this analysis as follows: sex (M/F) with male coded as 1; race (white/non-white) recoded with white coded as 1; and education (college graduate/non-college graduate) recoded with college graduate coded as 1

## Structural Equation Model

The first step of SEM was the specification of the latent constructs of psychological unease, positive valence factors, jaw limitation, and pain-related disability with observed variables. Confirmatory factor analysis was used to check that the concepts in the latent variables were valid as a single latent variable, and the factor loadings are shown in Table 2.4.

Table 2.4

*Results of Confirmatory Factor Analysis of Measurement Model With Factor Loadings of Psychological Unease, Positive Valence Factors, Jaw Limitation, and Pain-Related Disability Latent Variables*

Variables	Model 1 <sup>a</sup>	Model 2 <sup>b</sup>
<b>Pain disability</b>		
Pain Intensity	0.779	0.747
Pain Interference	0.793	0.827
<b>Jaw function</b>		
Chewing Limitation	0.857	0.874
Opening Limitation	0.902	0.817
Expression Limitation	0.822	0.915
<b>Psychological Unease</b>		
Negative Affect	0.619	0.616
Pain Catastrophizing	0.616	0.613
Somatic Symptoms	0.612	0.617
<b>Positive Valence Factors</b>		
Positive Affect	0.527	0.524
Optimism	0.847	0.853
Model Fit Statistics		
Chi-square (df)	119.8(29)	89.81(26)
P value	<.001	<.001
RMSEA (95% CI)	0.088 (.072-.105)	0.076 (.059-.094)
CFI	0.941	0.960
TLI	0.92	0.933
SRMR	0.054	0.052

<sup>a</sup> All variables in the proposed model.

<sup>b</sup> Added error covariances between chewing limitation and opening limitation & chewing and expression limitation.

Three exogenous latent variables, jaw function, psychological unease, and positive valence factors, and one endogenous latent variable, pain-related disability, were constructed. Results from the final model revealed factor loading values of 0.52 to 0.92, and the overall model fit was enhanced by adding error correlations. The final CFA can be found in Table 2.5

A structural model was constructed to examine the relationships between psychological unease, positive valence factors, and jaw limitation on pain-related disability with the covariates of chronic overlapping pain conditions (irritable bowel syndrome, fibromyalgia, and migraines) and demographic covariates (sex, race, and education). All variables and covariates were entered into the model, with significant relationships observed between the predictors and the outcome variable. Still, a sub-optimal model fit was noted (Model 1 ( $\chi^2(234.16) = 63$ , RMSEA = 0.082 CFI = 0.899)). Overall, model fit was greatly improved by allowing an additional error correlation between the number of COPCs and somatic symptoms. Studies have shown a strong association between somatic symptom burden and the number of COPCs<sup>49</sup>. The final model revealed a good fit of the data with  $\chi^2(160.01) = 62$ , RMSEA of 0.063, and CFI 0.942, indicating that the data were a good fit for the proposed model. The latent variables, jaw limitation, psychological unease, positive valence factors, and the number of COPCs were significant predictors of pain-related disability latent variable. The R-squared for the final model accounted for 68% of the variance in the latent variable pain-related disability (See Figure 3). The final path estimates are reported in Table 2.5 and Table 2.6.

Table 2.5

*Structural Equation Model with Path Coefficients Demonstrating the Relationship Between Latent Variables, Covariates, and the Latent Variable Pain-Related Disability*

<sup>a</sup> Model 1	<sup>b</sup> Model 2
<b>0.272**</b>	<b>0.265**</b>
<b>0.159*</b>	<b>0.158*</b>
<b>0.671***</b>	<b>0.670***</b>
<b>0.153*</b>	<b>0.165***</b>
-0.056	-0.055
-0.019	-0.010
<b>-0.088*</b>	<b>-0.088*</b>
234.16 (63)	160.01 (62)
<.001	<.001
0.082 (0.071-0.094)	0.063 (0.051-0.075)
0.899	0.942
0.864	0.921
0.084	0.067

<sup>a</sup> Full model with latent variables from confirmatory factor analysis, chronic overlapping pain conditions, and demographic variables. We allowed error correlations between the following pairs: chewing limitation with opening limitation, and expression limitation with chewing limitation.

<sup>b</sup> We allowed error correlations between the following pairs: chewing limitation with opening limitation, expression limitation with chewing limitation, and COPCs and Somatic Symptoms.

<sup>c</sup> UNEASE = Psychological Unease, <sup>d</sup> PRD = Pain-related disability, <sup>e</sup> POSVAL= Positive Valence Factors, <sup>f</sup> JAWL = Jaw function limitation, <sup>g</sup> COPC = chronic overlapping pain conditions, <sup>h</sup> female is referent, <sup>i</sup> non-white is referent, <sup>j</sup> educational level - non college graduate is referent.

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$

Table 2.6

*Results of Structural Equation Model with Factor Loadings of Indicator Variables, and the Associations Between Latent Variables Psychological Unease, Positive Valence Factors, Jaw Limitation, and Pain-Related Disability*

Variables	<sup>a</sup> Model 1	Model 2 <sup>b</sup>
<b>Pain disability</b>		
Pain Intensity	0.745	0.748
Pain Interference	0.809	0.810
<b>Jaw function</b>		
Chewing Limitation	0.865	0.862
Opening Limitation	0.824	0.826
Expression Limitation	0.907	0.905
<b>Psychological unease</b>		
Negative Affect	0.634	0.639
Pain Catastrophizing	0.621	0.617
Somatic Symptoms	0.595	0.594
<b>Positive valence Factors</b>		
Positive Affect	0.522	0.521
Optimism	0.856	0.856
<b>Structural Model (<math>\beta</math>)</b>		
<sup>c</sup> UNEASE $\rightarrow$ <sup>d</sup> PRD	<b>0.272**</b>	<b>0.265**</b>
<sup>e</sup> POSVAL $\rightarrow$ PRD	<b>0.159*</b>	<b>0.158**</b>
<sup>f</sup> JAWL $\rightarrow$ PRD	<b>0.671***</b>	<b>0.670***</b>
<sup>g</sup> COPC $\rightarrow$ PRD	<b>0.153*</b>	<b>0.165***</b>
<sup>h</sup> Sex $\rightarrow$ PRD	-0.056	-0.055
<sup>i</sup> Race $\rightarrow$ PRD	-0.019	-0.010
<sup>j</sup> Education $\rightarrow$ PRD	<b>-0.088*</b>	<b>-0.088*</b>
Chi-square (df)	234.16 (63)	160.01 (62)
P value	<.001	<.001
RMSEA	0.082 (0.071- 0.094)	0.063 (0.051- 0.075)
CFI	0.899	0.942
TLI	0.864	0.921
SRMR	0.084	0.067

<sup>a</sup> Full model with latent variables from confirmatory factor analysis, chronic overlapping pain conditions, and demographic variables. We allowed error correlations between the following pairs: chewing limitation with opening limitation, and expression limitation with chewing limitation.

<sup>b</sup> We allowed error correlations between the following pairs: chewing limitation with opening limitation, expression limitation with chewing limitation, and COPCs and Somatic Symptoms.

<sup>c</sup> UNEASE = Psychological unease, <sup>d</sup> PRD = Pain-related disability <sup>e</sup> POSVAL = Positive Valence Factors, <sup>f</sup> JAWL = Jaw function limitation, <sup>g</sup> COPC = chronic overlapping pain conditions, <sup>h</sup> female is referent, <sup>i</sup> non-white is referent, <sup>j</sup> educational level - non college graduate is referent.

\*  $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$ .

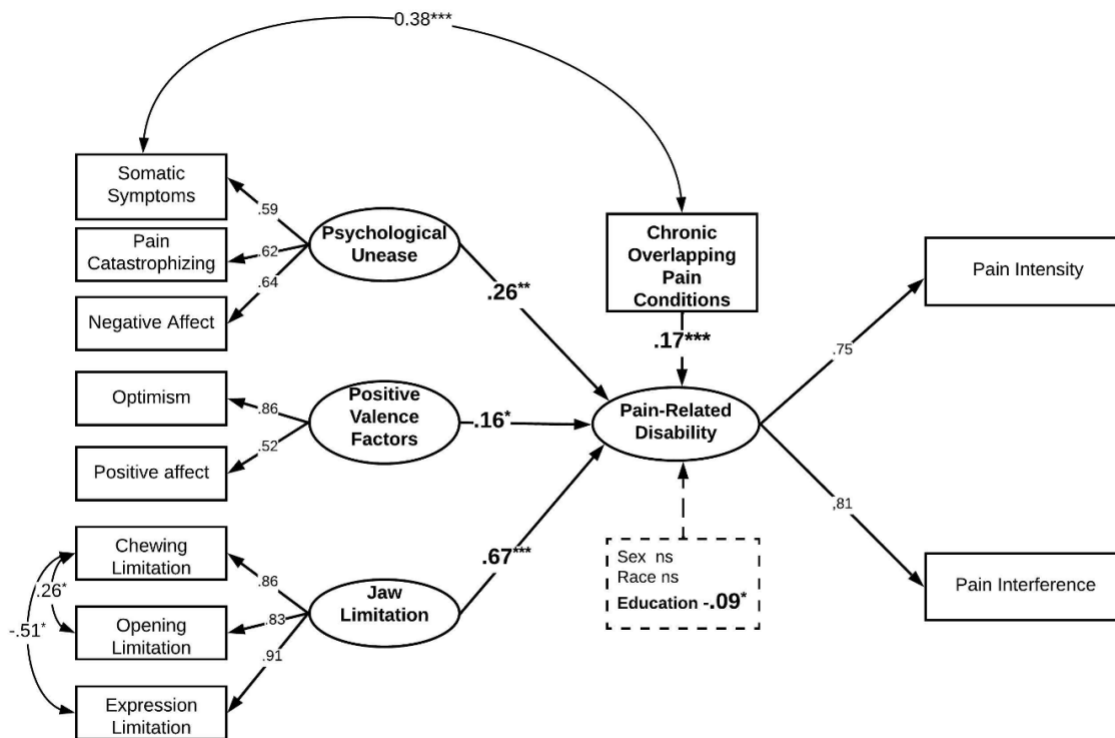


Figure 2.3 Final model with standardized parameter estimates demonstrating the significant relationships between latent variables and pain-related disability. A dashed line with significant parameter estimates bolded represents the relationship between demographic variables and pain-

related disability.  $*p < 0.05$ ,  $**p < 0.01$ ,  $***p < 0.001$ . Curved arrows represent error covariances between observed variables.

While all latent variables had significant relationships with a pain-related disability, the Jaw function limitation latent construct had the most substantial impact ( $\beta = .66$ ,  $p < .001$ ) on the outcome variable when compared with psychological unease ( $\beta = .31$ ,  $p < .01$ ) and positive valence factors ( $\beta = .16$ ,  $p < .05$ ). The number of COPCs also predicted ( $\beta = .16$ ,  $p < .001$ ) with increased pain-related disability. When compared to non-college-educated, being a college graduate predicted less pain-related disability ( $\beta = -.088$ ,  $p = .048$ ). The demographic covariates sex, and race, were non-significant predictors of pain-related disability in this model.

### **Discussion**

The current cross-sectional study evaluated the role of psychological unease (pain catastrophizing, somatic symptoms, and negative affect), positive valence factors (optimism, positive affect), and jaw function limitation (chewing, opening, and expression), the number of COPCs on pain-related disability while controlling for and demographic variables. SEM is a well-organized and parsimonious way of avoiding the repetitive testing of multiple regression equations while controlling for random error and the systematic error characteristic of common method variance<sup>105</sup>. I found significant associations between the positive and negative psychological constructs, COPC, and pain-related disability in chronic TMDs participants. I discovered that jaw function limitation had the most substantial positive impact on pain-related disability, followed by psychological unease and positive valence factors among TMDs patients. I also found that the number of COPC was positively associated with pain-related disability.

## **Jaw Function and Pain-Related Disability**

Jaw limitation had the most substantial effect on pain-related disability among the latent variables of interest. Not surprisingly, higher jaw function limitation was significantly associated with increased pain-related disability. Jaw dysfunction caused by TMDs directly affects activities such as chewing, smiling, and laughing. It can profoundly impact an individual's quality of life and psychosocial functioning <sup>62</sup>. Few researchers have examined jaw dysfunction's impact on TMDs pain-related disability. In this study, the impact of jaw function was stronger than psychological unease on pain-related disability. This effect size is significantly larger than a similar study in which the effect of jaw function limitation associated with pain-related disability was less than that of the negative psychological construct. <sup>88</sup>. This difference may be due to Miller et al.'s (2020) latent variable of pain-related disability, which included the concept of work restriction and a decrease in work efficiency <sup>88</sup>. While an earlier researcher found no significant relationship between oral parafunction and pain intensity and unpleasantness symptoms, pain interference was excluded <sup>87</sup>. The substantial, strong impact of jaw function demonstrated in our study is further confirmed as similar strong correlations were seen in a construct combining TMDs jaw function and GCPS disability points <sup>112</sup>. The strength of the relationship between jaw function and disability indicates that resources should be focused on finding and providing practical strategies such as physical therapy, manual therapy applied to the craniomandibular structures, and exercise which can benefit jaw function <sup>113-115</sup>. Patient education and support in this area might be beneficial <sup>116</sup>.

### **Psychological Unease and Pain-Related Disability**

While Miller et al. demonstrated that the impact of the negative psychological construct is larger than that of jaw function limitation <sup>88</sup>, I found that the positive association between psychological unease (i.e. pain catastrophizing, negative affect, and somatic symptoms) and pain-related disability was less strong than that of jaw dysfunction and pain-related disability. Several factors may have driven this difference including the indicator variables being used to create the psychological unease construct, demographic (i.e., younger participants for the Miller's cohort) and clinical phenotypes (i.e., TMDs duration). In addition, the current model did not include work absenteeism as a component of the pain-related disability variable. Yet, our findings confirm that psychological vulnerability (i.e., pain catastrophizing, negative affect, and somatic symptoms) remains an important contributor to pain disability and that all indicator variables contributed almost equally to the latent construct of psychological unease. Pain catastrophizing increases the risk of pain persistence by 6-fold and is a significant limitation to treatment response in a patient with TMDs <sup>117,118</sup>, while negative affect and somatic symptoms are risk factors for TMDs incidence <sup>93</sup>. While the overall effect is less in this study, it does not negate the need for psychological treatment targets such as cognitive-behavioral therapies to address this issue <sup>118</sup>.

### **Positive Valence Factors and Pain-Related Disability**

While this manuscript did not use the direct resilience measurement tool, this work used the resilience traits of optimism and positive affect which are recognized as resilience traits and are believed to lead to improvement and perhaps protection against poor pain outcomes <sup>119</sup>. I intentionally avoided the term resilience which has been 'overused' across many disciplines

ranging from medicine, psychology, to economics. Its meaning encompasses the view of bouncing back from adversity <sup>36</sup>, thriving in the face of adversity <sup>120</sup> and the process by which trait based resources are used to cope with difficult circumstances such as chronic pain <sup>121</sup>. I identified therefore a higher order construct that represents a phenotype in which motivation (such as escaping pain) and reward seeking (pain relief or pain suppression) produce behavior outcomes such as activity/pain avoidance or approach behaviors <sup>122,123</sup>.

Unexpectedly, there was a positive association between positive valence factors (optimism and positive affect) and pain-related disability. I hypothesized that the positive psychological factors would have an inverse and protective relationship with pain-related disability. One reason for not demonstrating this may be that people with higher levels of pain disability may react with an attitude towards being more positive and optimistic. The duration of TMDs symptoms among our participants may have obscured positive valence factor's effect on disability in this cross-sectional study. However, in sub-analyses, I controlled for the duration of symptoms, and the impact of positive valence factors on the disability construct remained unchanged. The protective effect of this construct on disability may be limited to the acute or subacute phases of pain rather than chronicity <sup>124</sup>. In the sample, the mean pain intensity scores were less than 50% of the maximum possible score and pain interference scores less than 30% of the maximum possible score on the GCPS. The cohort's lower pain intensity and interference scores may mean that that optimism and positive affect have a direct relationship with disability at lower levels of pain intensity and interference on the GCPS in TMDs.

## **Chronic Overlapping Conditions and Pain-Related Disability**

An increasing number of COPCs (migraine headache, fibromyalgia, irritable bowel syndrome, or low back pain) was associated with increased pain disability. COPCs represent a cluster of pain disorders with no identifiable cause for pain persistence, but they share an underlying hypersensitivity of the central nervous system<sup>3</sup>. COPCs and TMDs are reported to have similar and overlapping pain characteristics<sup>16</sup>. For example, patients with fibromyalgia reported widespread body pain in greater percentages than patients with TMDs alone<sup>104</sup>. Psychological variables such as somatic symptoms, negative affect, and pain catastrophizing are strongly linked with COPCs<sup>49</sup>. In addition, TMDs characteristics such as masticatory function and nonspecific jaw symptoms are shared with other COPCs, with the association being most prominent for fibromyalgia<sup>81</sup>. I considered the effect of COPCs independent of the other latent variables on pain disability (pain severity and interference). The finding confirms that independent of latent and demographic variables, the impact of COPCs on pain disability is significant. Control and management of both TMDs and COPCs symptomology remain viable targets for intervention.

## **Sociodemographic Variables and Pain-Related Disability**

Sex and race had a minimal impact on this model. However, higher education trended with lower pain-related disability. Socioeconomic status variables such as race and ethnicity have had varying associations within chronic pain; however, education findings are consistent with other data national data confirming that a higher educational level is associated with lower pain severity ratings and lower odds of high-impact pain<sup>69,125-127</sup>. Higher education is associated with higher income, thus increasing access to health care and medications, health insurance, and

treatment information <sup>128,129</sup>. In addition, higher education and mental stimulation have been linked to a higher cognitive reserve and thus more effective coping resources resulting in less pain disability <sup>130-132</sup>. Lower education increased risk of depressive symptoms in a sample of older adults with physical disability <sup>133</sup>. Education level through improving access to financial and cognitive resources may lessen chronic pain's impact on daily life and protect against poor pain outcomes.

### **Limitations and Strengths**

The cross-sectional design of this study limits the ability to conclude the direction of the relationships between the variables or the effects of the predictor latent variables over time. In addition, all self-report survey tools carry a threat of social-desirability bias <sup>134</sup>. The questionnaire data on constructs such as positive affect and optimism may not reflect actual states but desired states of the participants as they have a certain amount of wishful thinking, which may have influenced their optimism scores <sup>135</sup>. In addition, longitudinal mediational analyses approach would be advantageous in determining whether the relationships between the relationships between latent constructs and the outcome causal and vary over time <sup>35,136,137</sup>. Further research is needed to address other positive valence factors which may modify chronic pain outcomes for TMDs patients.

On the other hand, this study adds several tangible and innovative aspects. First, it quantifies the comparative effects of jaw dysfunction, COPCs, and positive and negative psychological constructs in pain outcomes. It also demonstrates that COPCs have a significant role in pain outcomes and should be evaluated and managed alongside TMDs symptomology.

Finally, positive valence factors such as optimism and positive affect in the pain disability model may be bidirectional and warrant further study.

### **Conclusion**

This study provides helpful insights leading to the development of nonpharmacological chronic pain therapeutics for the prevention and clinical management of pain-related disability. We shed light on which critical factors clinicians should target in orofacial pain management. The use of strategies such as exercise, physical therapy, and psychological therapy, as well as the management of comorbid conditions, should be part of the overall therapeutic plan.

## Chapter 3: Differences in Coping Strategies in Chronic Pain: An Observational Study

### Introduction

Chronic pain afflicts 20% of people in the United States, and about 8% will have disabling pain<sup>125</sup>. Persistent and disabling chronic pain is stressful and carries physical, cognitive, and emotional consequences to patients. Chronic pain patients develop coping strategies which impact physical and emotional health. Pain beliefs, pain catastrophizing, positive self-statements such as “I can deal with this” in response to pain, avoidance of activity in response to pain, and exercising are all examples of coping responses that impact adjustment and functioning to pain<sup>138</sup>.

Chronic pain is not limited to pain transmission from the injury site to the brain but is influenced by psychological and social factors contributing to the development of disability (Fillingim, 2017). Chronic pain produces stress, and many patients cannot work, experience job loss, have a reduced quality of life, and may incur debt due to health care costs and have higher use of health care services<sup>19,139</sup>. Lazarus and Folkman<sup>140</sup> described coping as a process in which an individual under stress exhibits cognitive and behavioral responses to the stressor. This response constantly changes as the individual reappraises the stressor and available resources<sup>141</sup>.

Understanding the context for using specific coping strategies may help personalize coping-based treatment goals and therapies by utilizing, maximizing, or providing alternative coping strategies, which may improve pain outcomes. In the literature, coping strategies are partitioned into dichotomous groupings meant to highlight different ways of responding to pain. Coping strategies such as guarding, resting, asking for assistance are seen as illness-focused coping strategies whereas strategies such as relaxation, task persistence, exercise and coping self-

statements are viewed as wellness-focused strategies<sup>63,142</sup>. Coping can also be described as either active, that is, doing something to control and function despite pain or passive, such as avoiding withdrawing from activity<sup>143</sup>.

Differences in coping strategies impact improved psychological outcomes and better physical function<sup>144,145</sup>. Beliefs regarding pain duration and illness roles, activity limitation, and pain catastrophizing contribute to disability<sup>138,146</sup> while the mindfulness associated with improvements in functional limitations<sup>147</sup> is less influential on disability<sup>146</sup>. Observational studies in chronic pain help us to further our clinical understanding of how patients cope and provide targets for intervention and optimization of treatment plans like cognitive behavioral therapy<sup>148-150</sup>.

I hypothesized the following.

1. Distinct coping strategy profiles would emerge among the sample of chronic pain patients.
2. Higher pain intensity, pain interference, pain duration, pain catastrophizing scores, and the presence of chronic overlapping pain conditions<sup>49</sup> such as fibromyalgia, irritable bowel syndrome, migraines, and chronic low back pain, will be associated illness-focused coping styles such as guarding and resting versus wellness-focused strategies such as coping self-statements and exercise.

## **Methods**

### **Design**

This study was a secondary data analysis using baseline data from a primary study examining placebo response in patients with chronic orofacial pain. The current study focused on

coping strategy profiles and the differences in these profiles based on pain characteristics. This cross-sectional design study aims to identify subgroups of patients with TMD based on wellness-focused or illness-focused coping strategies profiles identified by Jensen et al. (1995). This work aimed to compare pain intensity, pain interference, pain duration and pain catastrophizing ratings as well as demographic variables and the presence of chronic overlapping pain conditions (fibromyalgia, irritable bowel syndrome, migraines, and chronic low back pain) among these subgroups.

### **Sample**

Patients suffering from Temporomandibular disorders (TMDs), a painful condition of the jaw and face, for at least 3 months between 2017 and 2020 were identified from the primary study. All participants spoke English and were between 18 and 65 years of age. The inclusion criteria of the study were facial pain for at least the immediate 3 months in the jaw, temple, and ear prior, according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) <sup>71</sup>. Participants with a history within 3 years of severe psychiatric disease, degenerative neuromuscular disease, cardiovascular disease, pulmonary, kidney disease, liver disease, and cancers were excluded as were those who were pregnant, breastfeeding, color blind, had hearing impairment, facial trauma, cervical stenosis, and alcohol or drug dependence.

Participants supplied their medical history via a checklist of common medical conditions and current medications, and their eligibility was verified via telephone and in-person screenings. Four hundred nine patients with TMDs were enrolled, and nine were excluded as they did not meet eligibility criteria (6), withdrew (1) from the study, or did not contain the outcome variable (2). The final sample consisted of 400 participants from the primary study, the patients were

recruited via advertisements, community events, health fairs, and letters to patients at a Facial Pain Clinic at the University of Maryland. The risks, benefits, and alternatives of participating in the study were explained, and consent was obtained from all the willing participants. Sample demographics are represented in Table 3.1.

Table 3.1

*Descriptive Statistics of Sample and Measures*

Variables	Mean (SE)
Age-years /range	41.3/18-65
Sex-n(%)	
Male	94 (23.5)
Female	306 (76.5)
Education	
High School or less	50 (12.5)
College or more	350 (87.5)
<sup>1</sup> GCPS-Characteristic Pain Intensity score	47.64 (1.11)
<sup>1</sup> GCPS Pain Interference score	27.47 (1.35)
Pain Catastrophizing Scale	13.84 (.57)
Pain Duration- m(range)	140 (3-480)
Chronic Overlapping Pain Conditions (Y/N)	178/222
Migraine- n(%)	58(14.5)
Fibromyalgia- n(%)	20(5.0)
Irritable Bowel syndrome- n(%)	15(3.8)
Low Back Pain- n(%)	136(34)

<sup>1</sup>=GCPS=Graded Chronic Back Pain Scale

**Procedure**

Participants provided demographic data, including age, sex, race, education, and income which were collected during phone screening and in-person screening. A trained examiner with expertise in orofacial pain confirmed the diagnosis of TMDs with an in-person clinical exam at the Facial Pain Clinic at the University of Maryland School of Dentistry. The Diagnostic Criteria for TMDs (DC/TMD) symptom questionnaire <sup>90</sup> was used to establish or confirm TMDs

diagnosis. The DC/TMD was developed from robust NIH-funded studies<sup>151,152</sup> into orofacial pain and comprised a physical diagnosis and psychosocial assessment of the patient. A physical exam establishes the research and clinical diagnosis. The symptoms used for diagnosis include the presence of myalgia, arthralgia, and myofascial pain with referral, pain across the joint and muscle mass or temporal area in the previous 30 days, and any headache modified by jaw movement, function, or<sup>71</sup>. Psychosocial assessment includes various instruments to evaluate jaw function, depression, anxiety, somatic symptoms, physical function, and pain location.<sup>76</sup> After completion of data collection, a secure REDCap link was provided to participants to a series of psychological questionnaires. Participants completed the surveys on a personal computer at home or were given access to a computer on-site for survey completion. After completion of the study, they were compensated \$100 for their time and participation.

## **Measures**

*Descriptive Data*, age, sex, race, and education were collected by a self-report tool. Education level was also assessed with the question, "what is the highest grade or level of schooling?" Participants responded on a Likert scale of 0-5, 0 = *did not complete high school* to 5=*post-graduate level education*. For ease of analysis, this variable was recoded to high school education or less and college education classes or more (See Table 3.1).

*Coping Strategies* were assessed using the Chronic Pain Coping Inventory (CPCI)<sup>63</sup>. The CPCI consists of 65 items asking participants to rate the frequency of use of coping strategies over the previous 7 days. Eight subscales measure the following strategies: guarding, resting, asking for assistance, relaxation, task persistence (continuing activity despite pain)<sup>63,153</sup>, exercising, seeking social support, and coping self-statements. Each subscale contained between

4 to 9 items in which the participant indicated whether a specific coping strategy was used zero to 7 days. Each subscale score was divided by the number of items in the subscale. Subscale scores ranged from 0-7. The CPCI has demonstrated good internal consistency and test-retest reliability<sup>154</sup> and has been used to explain the contributions of different coping strategies to pain severity and pain disability<sup>155</sup>. The CPCI or one of its versions was chosen as it has been used to assess coping in many studies, including chronic pain in older adults, male and female, and diverse and multidisciplinary patient populations<sup>155-157</sup>. The CPCI is well suited for latent profile analysis because it is a comprehensive coping measure containing eight subscales with continuous-level subscale scores. Tan et al. (2001) compared the CPCI with the coping strategies questionnaire<sup>158</sup>, a widely used coping questionnaire. Both questionnaires were comparable in their ability to predict disability. However, the CPCI subscales appeared to have a stronger relationship to disability, and the guarding subscale of the CPCI was the strongest predictor of disability<sup>155</sup>. The CPCI was well-suited to answer the research question.

*Covariates* are used to examine the factors associated with differences in coping strategy profiles among TMDs.

*Pain Intensity and Pain Interference* were measured using the Graded Chronic Pain Scale version (GCPS) 2.0<sup>57</sup>. The GCPS v2.0 is a reliable and valid tool for measuring the impact of TMDs pain on the patient's ability to function<sup>57,91</sup>. The GCPS consists of eight items; the first inquiring about pain over the last 6 months is not included in the scoring. Three subscale scores, characteristic pain intensity, pain interference score, and disability days, are derived from the remaining seven items. The pain intensity items are rated on a scale of 0 (*no pain*) to 10 (*pain as bad as possible*). The pain interference score is derived from Questions 6 through 8 regarding the

inability to do daily work or social activities. Interference questions are rated on a scale of 0 (*no interference*) to 10 (*unable to carry out activities*). The average pain intensity and interference scores were multiplied by 10, with higher scores indicating higher pain intensity and interference<sup>67</sup>. Pain intensity and pain interference scores were used in this analysis.

Pain catastrophizing was measured using the 13-item instrument Pain catastrophizing scale (PCS)<sup>60</sup>. The PCS is a valid and reliable tool for chronic pain research<sup>33</sup>. Participants rate their feelings and thoughts regarding pain from 0 (*not at all*) to 4 (*all the time*). The total PCS score ranges from 0 to 52.

*Chronic Overlapping Pain Conditions* include fibromyalgia, irritable bowel syndrome, migraines, and chronic low back pain<sup>16,77-80</sup>. Patients reported these conditions on the medical history data collection tool. The presence of either pain condition was coded (yes/no with yes coded as 1) to indicate the presence of a coexisting chronic overlapping pain condition.

## **Data Analysis**

In a preliminary analysis, the data were cleaned and checked for normality of the continuous variables and independence of observations. In cases where items were missing, these cases were removed from the analysis ( $n=26$ ). This work used latent profile analysis (LPA) to cluster the participants into mutually exclusive latent classes based on coping strategies. LPA is a type of mixture modeling that identifies sub-groups based on the means of 2 or more continuous indicators<sup>159</sup>. Eight CPCI sub-scales were included in the LPA. Subscale scores ranged from 0-7 and were recoded 1-8 for analysis; subscale means are shown in Table 3.2. Model fit criteria were used to determine the optimal number of profile classes, including Bayesian Information Criterion (BIC), sample adjusted (BIC), and Akaike's Information Criterion (AIC), with smaller

values indicating a better fit; Lo Mendell and Rubin (LMR) likelihood ratio test and Bootstrapped likelihood ratio test to statistically compare the fit of a given model with the fit of a model with one of fewer classes; and entropy was used to measure how well the model separates the data into profiles with lower values, that is, closer to 0, indicating classification uncertainty, and values closer to 1, meaning more certainty in the classification.

Entropy values greater than 0.8 suggest minimal uncertainty in the profiles <sup>64,65</sup>.

Theoretical justification and interpretation of the latent profile classes were based on previous theoretical models in stress and coping, linking coping strategies with adjustment to chronic pain <sup>155,160</sup>. The best-fitting model was identified and exported. Finally, to understand and interpret the differences between profiles, a subsequent analysis was conducted to examine these differences according to pain intensity, pain interference, pain catastrophizing, chronic overlapping pain conditions, and demographic (sex and education) variables among the latent classes. As seen in Figure 3.1., Mplus software version 8.8 <sup>110</sup> was used for running the LPA, and SPSS version 27 <sup>109</sup> was used for data cleaning and descriptive preliminary data analysis.

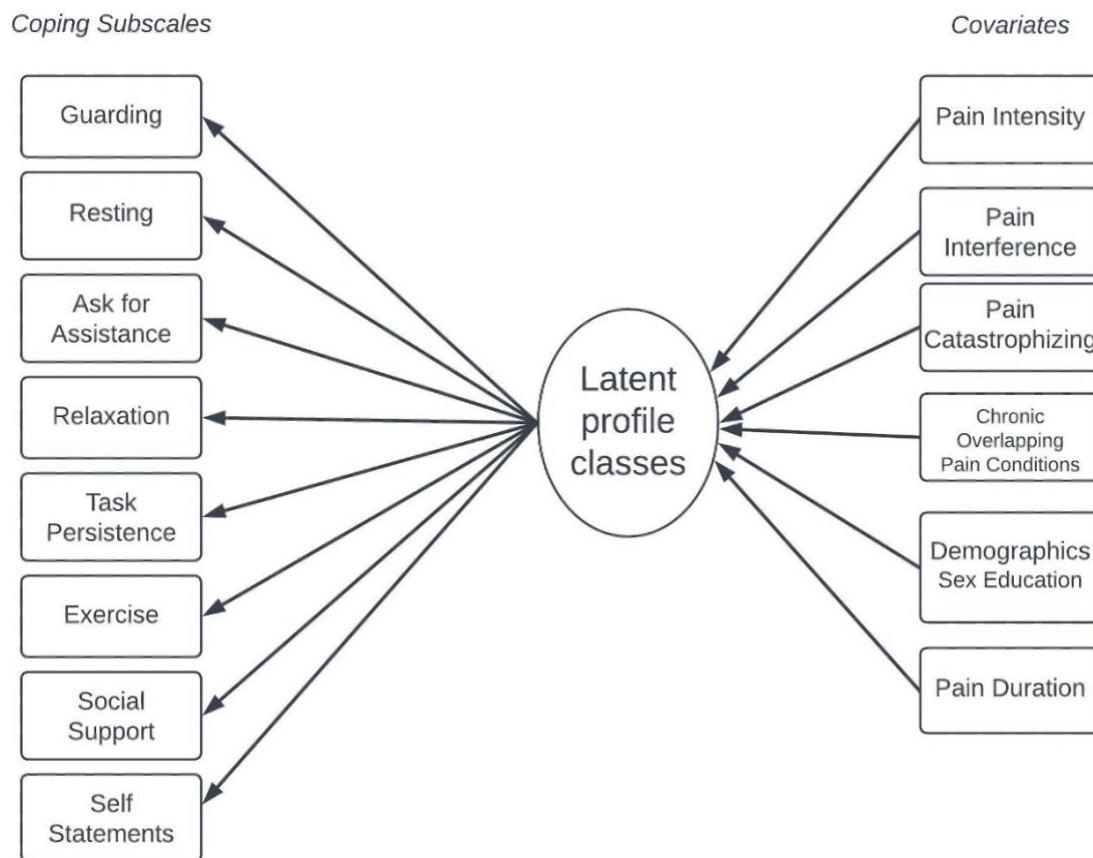


Figure 3.1. Graphical Representation of Latent Profile Analysis with Covariates.

### Results

A sample of 400 participants was included in the analysis. More than three-quarters of the participants were women, and 87% had received a college education or greater. The pain intensity, pain interference, and pain catastrophizing scores were all normally distributed. Mean pain intensity and interference scores were 47.64(1.11 SE) and 27.47(1.35 SE), respectively. The proportion of missing data was small (1-6.5%, among the variables), and missing value analysis revealed that the data were missing completely at random (Little's MCAR test: Chi-Square = 24,  $df = 15$ ,  $p = .063$ ). Overall, the coping strategy used most frequently by patients with chronic TMDs was task persistence ( $M=5.02$  0.1(SE)).

Latent Profile Analysis (LPA) was used to examine the feasibility of 1-, 2-, 3-, or 4- class solutions, and it was determined that the best model fit for the data. Continued improvement in model fit was observed from one to three classes. The LMRT remained significant, and the AIC and BIC values were slightly lower in the 3-class solution indicating that three classes were better than 2-classes. The 4-class solution also had a somewhat lower AIC and BIC; however, the non-significant LMRT meant that the model fit for the 4-class solution was not statistically different from the 3-class solution. In addition, the 4-class solution represented only 6.6% of the sample; therefore, the 3-class solution was judged the best-fitting model. (See Table 3.2 and Figure 3.2). All three models produced high entropy values, indicating model stability <sup>161</sup>.

Table 3.2

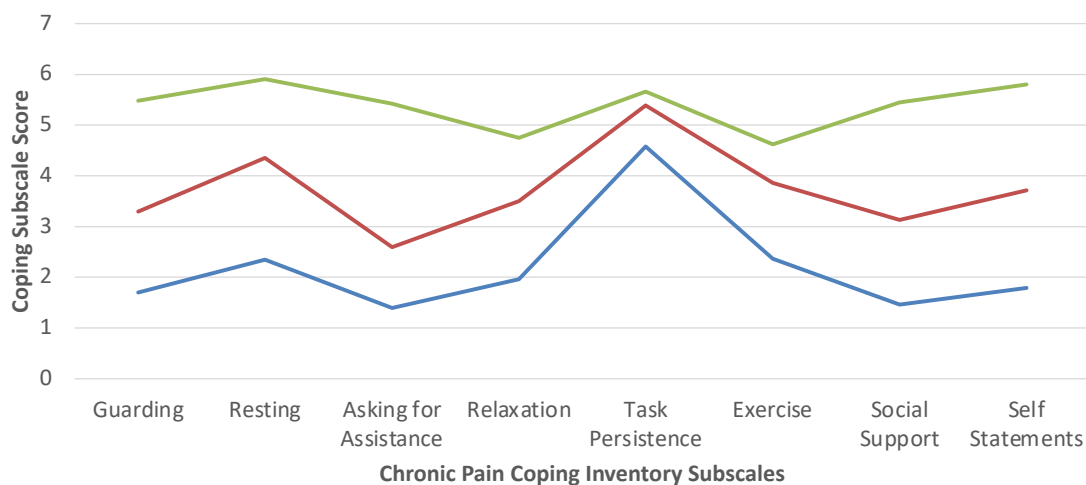
*Fit Indices for Two to Four Class Latent Profile Analyses of Coping*

Model	Final Log Likelihood	AIC	SABIC	Entropy	Smallest class %	LMRT	LMR p-value	BLRT p-value
1 (2 class)	-5408.69	10867.38	10886.165	0.913	30.5	1013.06	0.0018	<.001
2 (3 class)	-5227.18	10522.36	10547.92	0.893	13.9	356.33	0.0103	<.001
3 (4 class)	-5146.4	10378.790	10411.11	0.887	6.6	158.60	0.451	<.001

Note. N=374; AIC= Akaike Information Criterion, BIC= sample size adjusted Bayesian

Information Criterion, LMRT=Lo-Mendell-Rubin test, BLRT= bootstrap likelihood ratio test.

The LMR test and the BLRT compare the current model to k-1 model.



**Class 1: Low Use Copers :n=189**

**Class 2: Moderate Use Copers n= 133**

**Class3: High Use Copers: n= 52**

—Class 1 —Class 2 —Class 3

Figure 3.2. Line graph comparing the latent coping profiles among patients with chronic TMDs.

The models were evaluated, and there were three distinct classes. Class 1, termed low-use copers<sup>162</sup>, contained 51% ( $n= 189$ ) of the participants and was characterized by the lowest use of all coping strategies and included wellness and illness-focused coping strategies. Among low-use copers, task persistence was the most frequently used coping strategy ( $M=4.58$  ( $0.18$  SE)), followed by resting and coping self-statements. Moderate use copers, Class 2, comprised 36% ( $n=133$ ) of the sample and exhibited a similar profile in the use of coping strategies shown by class 1 except with higher frequency. Coping strategies, including exercise, social support and self-statements, and relaxation, had mean scores greater than 3.5. Among moderate-use copers, task persistence was the highest used strategy ( $M=5.39$  ( $0.16$  SE)), followed by resting ( $M=4.35$  ( $0.16$  SE)). Class 3, high-use copers<sup>162</sup>, contained 14% ( $n=52$ ) of the sample. This class exhibited the highest use of all coping styles with mean scores greater than 5, indicating that most chronic orofacial pain participants in Class 3 used six of the eight coping strategies most

days of the week for pain. Among high copers, resting was the highest used coping strategy (M= 5.91 (0.23 SE)), followed by self-statements (M=5.80(0.35 SE)) and task persistence (M=5.66 (0.28 SE)). All latent profile class means are reported in Table 3.3

Table 3.3

*Coping Profiles Subscale Means by Sample and Latent Profile Class*

Coping Subscales	Sample Means(SE)	Class 1 (SE)	Class 2 (SE)	Class 3 (SE)
Guarding	2.79 (0.09)	1.70 (0.07)	3.29 (0.18)	5.48 (0.26)
Resting	3.56 (0.1)	2.35 (0.11)	4.35 (0.16)	5.91 (0.23)
Asking for Assistance	2.38 (0.09)	1.39 (0.06)	2.59 (0.17)	5.42 (0.25)
Relaxation	2.90 (0.08)	1.97 (0.07)	3.50 (0.13)	4.75 (0.28)
Task Persistence	5.02 (0.1)	4.58 (0.18)	5.39 (0.16)	5.66 (0.28)
Exercise	3.21 (0.09)	2.36 (0.12)	3.86 (0.14)	4.62(0.35)
Social Support	2.61 (0.09)	1.46 (0.06)	3.13 (0.16)	5.44 (0.27)
Self-Statements	3.03 (0.10)	1.79 (0.09)	3.71 (0.16)	5.80 (0.35)

### **Differences Across Variables Across Latent Profiles**

*Pain Intensity, Pain Interference, Pain Catastrophizing, Pain Duration.* For each single point increase in pain intensity and pain interference scores, participants were more likely to be high-use copers than low-use copers (OR 1.03, 95% CI[1.01,1.06], OR 1.02, 95% CI[1.00,1.03] respectively). There was also a higher chance of increased pain catastrophizing scores among moderate-use copers compared to low-use copers (OR 1.057, 95% CI[1.03,1.09]) and between high-use copers when compared to low-use copers (OR 1.066, 95% CI[1.03,1.10]). This increase in odds was not maintained when comparing moderate-use copers and high-use copers. When comparing moderate-use copers to high-use copers, no significant differences were observed between pain intensity and interference (see Table 3.4). The mean symptom onset for the sample was 141 months, and no difference in pain duration was observed between the coping profiles.

*Chronic Overlapping Pain Conditions and Sociodemographic Variables.* Those with a chronic overlapping pain condition (fibromyalgia, irritable bowel syndrome, migraines, and chronic low back pain) were more likely to be moderate-use copers (OR 1.78, 95% CI[1.03,3.06]) than low-use copers. There were no differences in the odds of having a coexisting chronic overlapping pain condition between high-use copers and low-use copers or between high-use copers and moderate-use copers.

This work did not find differences between males and females between the three latent profiles. Similarly, there were no differences in college education between the profiles. The results of the covariate analysis are presented in Table 3.4.

Table 3.4

*Multinomial Logistic Regression Predicting Class Membership*

Reference class	High-use Copers		High-use Copers		Moderate-use Copers	
	vs Low-use Copers		vs Moderate-use Copers		vs Low-use Copers	
	Odds Ratio(SE)	95% CI	Odds Ratio	95% CI	Odds Ratio (SE)	95% CI
Pain Intensity	<b>1.03 (0.012)</b>	<b>1.007-1.055</b>	1.02 (0.013)	0.996-1.045	1.01 (0.008)	0.995-1.026
Pain Interference	<b>1.017 (0.008)</b>	<b>1.002-1.032</b>	1.012 (0.008)	0.997-1.028	1.004 (0.007)	0.992-1.017
Pain Catastrophizing	<b>1.066 (0.018)</b>	<b>1.031-1.102</b>	1.009 (0.016)	0.978-1.040	<b>1.057 (0.015)</b>	<b>1.028-1.086</b>
Pain Duration	1.0(.001)	0.997-1.003	1.0(.001)	0.997-1.003	1.0(.001)	0.998-1.003
<sup>1</sup> Sex	0.575 (.301)	0.206-1.606	0.669 (0.359)	0.234-1.917	0.860 (0.277)	0.457-1.618
<sup>2</sup> Education level	0.414 (0.203)	0.158-1.081	0.488 (0.235)	0.190-1.256	0.847 (0.351)	0.376-1.910
<sup>3</sup> COPCs (y/n)	1.046 (0.409)	0.486-2.251	0.588 (0.230)	0.274-1.264	<b>1.778(0.494)</b>	<b>1.032-3.063</b>

<sup>1</sup> female is referent-male is the focus group ; <sup>2</sup>HS=High School graduate is referent CE= College education is the focus group; COPCs= Chronic Overlapping pain conditions none is referent; yes=1 or more

## **Discussion**

The findings from this study supported the identification of three distinct coping profiles characterized by low, moderate, and high use of both wellness-focused and illness-focused coping strategies among patients with chronic orofacial pain. Among low-use and moderate-use copers, task persistence was used most frequently, and among high-use copers, resting was the most frequent coping strategy, followed by self-statements and task persistence. Furthermore, participants in the high-use coping group had increased odds of poor pain characteristics, specifically, increased pain intensity, pain interference, and pain catastrophizing, compared to the low-use coping group. I also found that moderate-use copers had an 80% increase in odds of having a chronic overlapping pain condition and six percent higher odds of having higher pain catastrophizing scores when compared to low-use copers.

### **Coping Profiles**

Data indicated an increasing level of pain intensity, pain interference, and pain catastrophizing accounts for the differences in the type of coping strategy and increased frequency of coping strategy used in our TMDs sample. The contextual nature of coping is described in the literature; the best coping strategies depend on the situation and context <sup>163</sup>. The dichotomy imposed by coping classification systems such as wellness-focused or illness-focused labels and active versus passive is problematic as all strategies offer benefits contextually <sup>164,165</sup>. Perhaps using the coping strategy profile as an indicator of patient status may be more beneficial as it can serve as a marker for worsening symptomology and the need for optimization of treatment and support of the patients.

Patients also engage in task persistence, continuing activity despite the pain, with high frequency among all profiles. Task persistence may be beneficial with uncomplicated pain syndromes, but it has been associated with increased pain and disability, and possible injury in patients with chronic back pain <sup>166</sup>. Encouraging and validating the use of alternate strategies may be beneficial here. Coping skills training, a facet of cognitive behavior therapy, may be of value here. Patients are taught helpful strategies are based on their profile and mechanisms to improve self-efficacy <sup>167</sup>. Clinicians may also promote jaw exercises through physical therapy <sup>168</sup>, which is beneficial and effective in treating TMDs pain. Similarly, the appropriate use of coping self-statements positively impacts mental health outcomes linked to pain outcomes <sup>169</sup> and should be encouraged.

### **Pain Intensity and Pain interference**

The odds of higher Pain Intensity and Pain Interference scores were increased among high-use copers. Distinct differences were observed between high-use copers and low-use copers. This study examined coping strategy profiles among the group to understand this finding. Specifically, high-use copers had the highest simultaneous use of all coping styles, including coping strategies associated with poor psychological and pain outcomes, such as resting, guarding, and asking for assistance. Interestingly, high-use copers also had the highest score of wellness-focused coping styles: relaxation, task persistence, exercise, and self-statement. It may be that persistent high pain intensity and pain interference scores in this chronic pain population cause both high frequency of use of wellness and illness focused strategies, which may be effective in dealing with pain within the context. That is, the short-term resting, an illness-focused strategy may relieve pain in the short term, allowing patients to integrate wellness-

focused strategies such as exercise or coping self-statements at another time point within a 7-day period. However, exploring this theoretical relationship could be better addressed in a longitudinal study.

### **Pain Catastrophizing**

Pain catastrophizing, the exaggerated negative view, magnification, and focus on pain signals and the threat of pain<sup>85</sup> is known to increase the risk of pain persistence<sup>118</sup>.

Catastrophizers are preoccupied with the dangers of pain, so they cannot divert attention away from perceived pain threats. It was found that the odds of higher pain catastrophizing scores were increased in high-use copers and moderate-use copers when compared to low-use copers. While pain catastrophizing is characterized by negative cognitive appraisals, debate exists as to whether it should be considered a personality trait, a cognitive tool, or a coping strategy<sup>163,170</sup>.

Nevertheless, catastrophic thinking profoundly affects pain outcomes, including disability status, and is linked to exaggerated negative mood and depression and understanding how this determined coping mechanism profiles<sup>4</sup>. Among the chronic orofacial pain population, pain catastrophizing has significant associations with pain intensity and pain disability<sup>146</sup>. Coping theory by Lazarus and Folkman (1984) asserted that the ability to cope with stressful situations involves a primary appraisal of a stressor to determine the level of threat involved, followed by a secondary appraisal of the likely success of a particular coping strategy based on transactions with the environment<sup>140</sup>. Catastrophizing is likely linked to secondary appraisal and the individual belief that coping resources would probably be ineffective in dealing with pain.

Sullivan (2012) suggested that catastrophizing as a coping strategy garners emotional and social support this, positively reinforcing pain and pain disability behavior for those with chronic

pain<sup>171</sup>. This view may help to understand why the odds of high pain catastrophizing scores were increased among high-use copers and moderate-use copers with high mean scores of social support and asking for assistance compared with low-use copers. The literature supports this as pain catastrophizing is linked to increased dependency and the need for social support<sup>4</sup>. Additionally, the high mean usage of all coping strategies in a single profile may reflect the helplessness component of pain catastrophizing. High-use copers use all coping strategies with high frequency but remain catastrophic in their thinking regarding efficacy in relieving pain. Using multiple strategies may or may not produce long-term benefits, further feeding the magnification of the painful event.

### **Chronic Overlapping Pain Conditions**

This study found that moderate-use copers had 75% greater odds of having a chronic overlapping pain condition than low-use copers. Examination of the coping strategy profile between moderate-use copers and low-use copers demonstrated that moderate-use copers' scores of resting and asking for assistance were double that of low-use copers. This profile may indicate a heavy reliance on illness focused coping strategies. However, this significance did not persist when comparing high-use with low-use copers. This finding may be due to the difference in sample size between Class 1 ( $n=189$ ) and Class 3 ( $n=52$ ). Fillingim et al. (2020) found that an increasing number of chronic overlapping pain conditions had an inconsistent association with coping strategy use. For example, distraction and distancing (active coping) coping strategies had linear and positive associations with increasing chronic overlapping pain conditions. Other active coping strategies, such as coping self-statements, did not have a similar relationship. In addition, pain catastrophizing, praying, and hoping (passive coping) also had positive linear associations

indicating that both active and passive coping profiles are associated with an increasing number of chronic overlapping pain conditions <sup>49</sup>. The use of active and passive coping strategies is also reflected in our study and warrants further study.

### **Limitations and Strengths**

The principal limitation of this study is its cross-sectional design which prevents from making causal inferences. Coping is a dynamic process hard to capture. The coping strategy profiles were created from a single 7-day report, and one can argue that this may change from week to week. The CPCI asks participants to report pain in the prior week's coping strategies, which may be subject to retrospective bias <sup>163</sup>. In addition, self-reports of coping strategies carry a risk of social desirability bias <sup>172</sup>. Bias should be considered when examining the reporting on task persistence by the patients in our sample. Finally, it should be noted that the generalizability of the findings may be limited to patients with chronic TMDs.

### **Conclusion**

Chronic pain confers stress and adversity, and coping studies provide valuable information on how patients experience and live with pain. Patients use wellness-focused and illness-focused coping strategies to cope with pain with limited efficacy. A greater understanding of how patients adapt and function with chronic pain using a convergence of coping strategies is relevant in isolating targets for treatment in this patient group. The orofacial pain population uses multiple coping strategies, albeit ineffectively, in coping with chronic pain. This may indicate an openness to treatment modalities such as coping skills training to optimize pain outcomes. Clinicians can promote the appropriate use of wellness-focused coping strategies in treatment.

Future improvement should include evaluating coping strategies with a daily momentary assessment of pain and coping, allowing the individual to report pain experience, management, and coping strategy as it changes in time. Healthcare providers can then identify which strategies work for individuals and allow providers to target optimization with coping-based treatments <sup>163</sup>. Finally, examining how coping strategies are used may further elucidate the link between resilient mechanisms and coping responses, which can positively impact pain outcomes <sup>121</sup>.

## Chapter 4: The Role of Pain Resilience in Pain Expectations in People with Chronic Orofacial Pain

### Introduction

Historically, placebo has had a negative connotation among patients and clinicians. Placebos are inert substances administered instead of active drug that produces a therapeutic effect<sup>39</sup>. However, integrating placebos into standard medical therapy, as in dose-extending placebo therapy, has emerged as a viable means of improving clinical outcomes<sup>173</sup>. Experimental studies on pain reveal that placebos augment pain relief, limit the amount of opioids administered, and decrease pain and disability through endogenous opioid release<sup>44,173</sup>. It is also observed that in large randomized clinical trials, the placebo arm of the drug demonstrates improvement, thus revealing the potency of the placebo response<sup>174</sup>. Definitive neurobiological mechanisms have been identified behind the benefits of placebo response in clinical conditions<sup>175,176</sup>. A placebo response occurs within a therapeutic psychosocial context and with patient expectations.

Patient expectations about medical treatment are important prognostic indicators of treatment success and contribute to the individual pain experience. Expectations, beliefs, and predictions about a future pain event impact the ability to generate a placebo response<sup>177</sup>. Individual expectations about placebo treatment are crucial for success as these expectancies not only initiate but can upregulate the placebo response<sup>41</sup>. According to the model adapted from Bingel et al 2020 (see Figure 4.1), expectations are formed through prior treatment experiences, observational learning, verbal information from a healthcare provider, and characteristics of a therapeutic encounter<sup>40</sup> and expectations are directly correlated with placebo responsiveness<sup>41</sup>.

Placebo responsivity also depends on the strength of learning or conditioning associated with the treatment. Classical conditioning happens when a neutral stimulus is paired with a psychologically meaningful event <sup>178</sup>. This pairing eventually evokes responses and emotions that can be harmful or beneficial in medical treatment <sup>176</sup>. When active medications or treatments such as unconditioned stimuli, are repetitively paired with an inert substance or procedure, that is, the Placebo or conditioned stimuli, a beneficial placebo response is produced. Placebo analgesia has also been demonstrated in TMDs patients using prior experiences and classical conditioning techniques <sup>179</sup>. Beyond conditioning and expectations, there is evidence that personality traits may explain individual differences and susceptibility to placebo <sup>55</sup>.

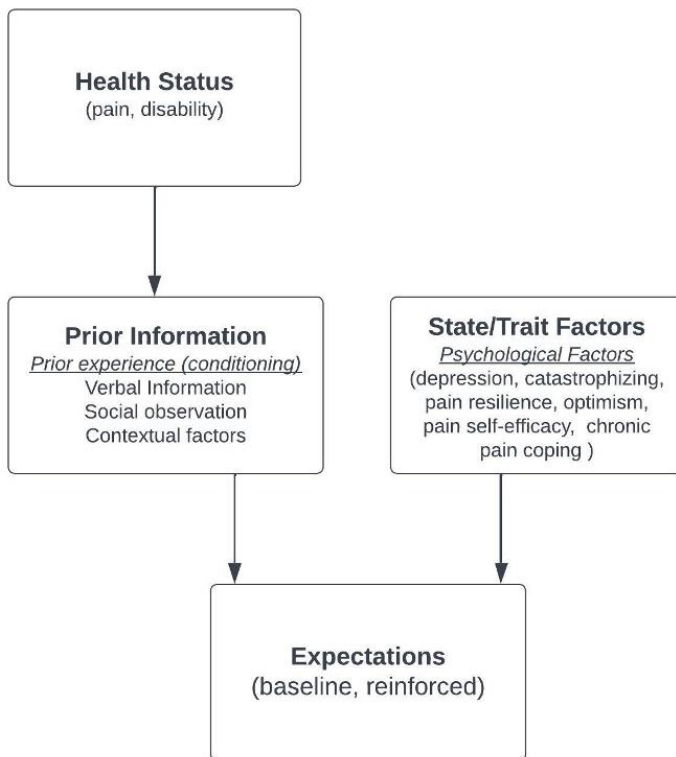


Figure 4.1 Treatment expectation model adapted from Bingel (2020).

Resilience and optimism are not only critical to the recovery from pain but are associated with the placebo effect. Resilience is defined the ability to adapt to stress and adversity <sup>180,181</sup>. Strong resilience was found in a small sample to be a positive predictor of placebo responses <sup>55</sup>. Similarly, high optimism is linked with lower pain intensity in placebo group members <sup>56</sup> and optimism and low anxiety are predictors of placebo response among healthy pain-free participants<sup>48</sup>.

An individual's predisposition to the placebo effect must be understood to advance the clinical therapeutic benefit of the placebo response in patients with chronic pain. It as hypothesized that:

1. Pain resilience was protective against high pain interference as evidenced by a negative relationship between pain resilience and pain interference while controlling for demographic variables and psychological factors (optimism, pain catastrophizing, depression).
2. Pain resilience was positively associated with increased reinforced expectancy of analgesia when accounting for psychological factors (optimism, pain catastrophizing, depression), and other covariates (prior experience, sex, race, education).
- 2b. Pain resilience modified the relationship between conditioning strength and expectation of analgesia.

## **Methods**

### **Design**

This study was a cross-sectional study of participants with a chronic pain diagnosis of temporomandibular disorder for at least 3 months. This study obtained secondary data were obtained from a study examining placebo response in patients with chronic orofacial pain. The current study focuses on the relationship between patient expectations data from the primary study and subsequent pain resilience data collected in this study.

### **Sample**

I recruited 153 patients with a diagnosis of temporomandibular disorder, a chronic orofacial pain condition, to participate in this study. I made phone calls and sent emails to cohort of participants who previously participated in a placebo manipulation study between 2017-2020 and who had agreed to be re-contacted for further study. Recruitment for the current study occurred between the years 2020 and 2022. The participant's eligibility was verified via telephone and in-person screenings. Their medical history was available from data supplied to the parent study via a checklist of common medical conditions. Before enrollment, the study protocol was reviewed and approved by the Institutional Review Board at the University of Maryland Baltimore, and all participants gave written informed consent.

### **Inclusion and Exclusion Criteria**

All participants spoke English and were between 18 and 65 years of age. The inclusion criteria of the study were facial pain for at least the immediate three months in the jaw, temple, and ear prior, according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)<sup>71</sup>. Participants with a history within 3 years of severe psychiatric disease, degenerative

neuromuscular disease, cardiovascular disease, pulmonary, kidney disease, liver disease, and cancers were excluded, as were those who were pregnant, breastfeeding, color blind, had hearing impairment, facial trauma, cervical stenosis, and alcohol or drug dependence excluded.

### **Placebo Procedure**

The placebo manipulation conducted during the former study provided expectation and conditioning data for this study. After participants consented to the procedure, painful heat stimuli were delivered to the inner forearm using the Medoc Pathway system (Medoc Advanced Medical Systems, Ramat Yishai, Israel). Experimental personnel explained that painful stimuli would be delivered to the arm in conjunction with a red computer screen in front of the participant. The participants were also told that the computer screen would become green when the stimulus was less painful. In the calibration phase of the experiment, individual warmth and pain sensitivities were established using an experimental paradigm<sup>182</sup>. After the calibration phase, the conditioning phase followed, in which participants rated repeated and random painful and non-painful stimuli. The ratings allowed the experimenter to calculate an index of conditioning strength. There were two conditioning phases during which the participant rated on a visual analog scale (VAS; 0-100), a series of 12 high and low heat pain stimuli with accompanying red and green screens (see Figure 4.2). Participants were asked to report their expectations for analgesia before and after the conditioning procedure. The testing phase followed, during which a sham electrode was attached proximally to the Medoc thermode. The participants were told that the pain experienced would be reduced when the electrode was activated. Unbeknownst to the participant, during the testing phase, the temperature was secretly

set to a moderate level of heat-pain stimuli with accompanying red and green screen cues. The participant was then asked to rate their pain intensity via the visual analog scale.

## **Measures**

Prior treatment experiences was operationalized with the variable Conditioning Strength<sup>182</sup>. *Conditioning strength* was defined as the mean difference of individual pain ratings on a visual analog scale between painful experimental trials (red screen) and non-painful (green) experimental trials during the conditioning phase of the experiment (see Figure 4.2). The larger the difference, the greater the conditioning attained during the experiment.

Expectations were the participant's self-report of the procedure's effectiveness in reducing pain. The participant was asked before the start of (baseline) and at the end of the procedure (reinforced): How much do you think this procedure will reduce your pain? The expectation rating was done on a visual analog scale of 0-100.

*Placebo response* was defined using the paradigm defined by Colloca et al. (2020)<sup>182</sup> (see Figure 4.2). During the testing phase, the temperature was set to a moderate level of heat-pain stimuli. The participant was asked to rate pain stimuli during the testing phase. The mean difference in participant ratings of the red and green screens during the testing phase was defined as the placebo response.

*Resilience* was measured using the Pain Resilience Scale<sup>50</sup>, a 14-item tool specific to individuals experiencing pain. The scale focuses on intrapersonal contributions to resilience such as optimism and positive affect but does not include aspects such social support. This scale items were then adapted and modified from the Connor-Davidson<sup>120</sup>, the Brief Resilience Scale<sup>36</sup> and the Resilience Scale for Adults<sup>183</sup>. The Pain Resilience scale<sup>50</sup> contains 14 statements which

describe a possible response to intense or prolonged pain. These include *I get back out there*, *I still find joy in life*, and *I avoid negative thoughts*. Respondents must rate their agreement with each statement as 0 (not at all) to 4 (all the time). Two subscales are derived; cognitive/affective positivity focuses on the ability to regulate emotions during pain, and behavioral perseverance which focuses on tenacity and motivation despite intense or prolonged pain. The total score ranges from 0 to 56 with higher scores indicate higher levels of resilience.

*Optimism* was measured using the life orientation test-revised (LOT-R) scale<sup>58</sup>. The LOT-R contains ten items measuring dispositional optimism and consists of three optimism subscale questions, three pessimism subscale questions, and four filler items. Each item is scored on a 5-point Likert scale of 0 (*strongly disagree*) to 4 (*strongly agree*). Three pessimism items were reverse coded before scoring, the filler items were not scored, and the six remaining items were used to obtain a total score. High total scores represent a higher level of dispositional optimism.

*Pain Intensity and Pain Interference* were measured using the Graded Chronic Pain Scale version (GCPS) 2.0<sup>57</sup>. The GCPS v2.0 is a reliable and valid tool for measuring the impact of TMDs pain on the patient's ability to function<sup>57,91</sup>. The GCPS consists of eight items; the first inquiring about pain over the last 6 months is not included in the scoring. Three subscale scores, characteristic pain intensity, pain interference score, and disability days, are derived from the remaining seven items. The pain intensity items are rated on a scale of 0 (*no pain*) to 10 (*pain as bad as possible*). The pain interference score is derived from Questions 6 through 8 regarding the inability to do daily work or social activities. Interference questions are rated on a scale of 0 (*no interference*) to 10 (*unable to carry out activities*). The average pain intensity and Interference

scores were multiplied by 10, with higher scores indicating higher pain intensity and Interference<sup>67</sup>. Pain intensity and pain interference scores were used in this analysis.

*Pain catastrophizing* was measured using the 13-item instrument Pain catastrophizing scale (PCS)<sup>60</sup>. The PCS is a valid and reliable tool for chronic pain research<sup>33</sup>. Participants rate their feelings and thoughts regarding pain from 0 (*not at all*) to 4 (*all the time*). The total PCS score ranges from 0 to 52. Higher scores indicate higher catastrophic thinking.

Depression was measured using the Beck Depression Inventory-II<sup>184</sup>, a 21-item instrument that measures the severity of symptoms of depression in adults and children. Items are ranked 0-4, and scores range from 0-63. Higher scores indicate more depressive symptoms.

Chronic Overlapping Pain Conditions include fibromyalgia, irritable bowel syndrome, migraines, and chronic low back pain<sup>16,77-80</sup>. Patients reported these conditions on the medical history data collection tool. The presence of either pain condition was coded (yes/no with yes coded as 1) to indicate the presence of a coexisting chronic overlapping pain condition.

*Descriptive Data* on age, sex, race, education, and duration of TMDs symptoms were collected by a self-report tool. (See Table 4.1).

### **Statistical Analysis**

The IBM Statistical Package for Social Sciences version 27 was used for data screening, cleaning, exploration, and analysis. All variables were examined to ensure appropriate coding and levels of measurement. This work assessed normality of the quantitative independent and dependent variables (age, pain resilience, optimism, pain catastrophizing, depression conditioning strength, pain interference and reinforced expectation) by examining skewness,

kurtosis, boxplots, stem leaf plots during data exploration. Extreme outliers were identified on stem-leaf plot analysis.

Extreme outliers in the dependent variables pain interference and reinforced expectations were identified, and after reviewing residual and influence statistics, one influential case in pain interference model was identified and eliminated that case as the results of the analysis were altered with that case (See table 4.3B). One influential case was also identified in the linear regression model examining reinforced expectations. That independent variable was winsorized and that case kept as the results of the analysis were not changed.

Missing value analysis revealed that that that up to 2.6% of the data collected were missing. There 1 to 4 missing values per scale item. Little's MCAR test revealed that the data was probably missing completely at random (Chi Square= 1836.01, DF=1889,  $p=.805$ ). The data were replaced by using the mean of nearby points in IBM SPSS missing value function. One participant with multiple missing data points including the resilience variable, and pain interference measures and was excluded from the analysis. Race was recoded into African American (coded 1) and non-African American. Education was recoded into college graduate (coded 1) and non-college graduate. The multicollinearity assumption was checked by the variance inflation factor and tolerance values.

Descriptive statistics were calculated to summarize the demographic variables of age, sex, race, and education, the presence of chronic overlapping pain conditions, psychological variables of pain resilience, optimism, pain catastrophizing, and depression, and the experimental variables of conditioning strength, baseline and reinforced expectations, and placebo response are listed in Table 4.1. Correlational analyses were conducted to examine the relationships

between pain resilience and demographic variables, reinforced expectations of analgesia, and other psychological predictor variables.

Statistical Analysis for Aim 1: Bivariate linear regression was also done assess the relationship of age, sex, race, psychological covariates (optimism, Pain catastrophizing depression and pain resilience) to pain interference. Multiple linear regression was used to determine the independent contribution pain resilience to the outcome variable pain interference while controlling for demographic variables and psychological covariates (optimism, pain catastrophizing and depression).

Statistical Analysis for Aim 2: Bivariate linear regression was also done assess the independent contribution of age, sex, race, psychological covariates (optimism, pain catastrophizing depression and pain resilience), conditioning strength, on the dependent variables of reinforced expectations of analgesia (See Table 4.3). Multiple linear regression was used to determine the contribution of pain resilience to the outcome variable reinforced expectations while controlling for demographic variables and covariates (conditioning strength, optimism, pain catastrophizing and depression. A significance value of  $p \leq 0.20$  was the cutoff for inclusion into both multiple linear regression models.

Statistical Analysis for Aim 2B: In addition, because this work hypothesized that pain resilience would interact with conditioning strength, an interaction variable was created between resilience and conditioning strength and conducted a moderation analysis on the dependent variable reinforced expectations. MPLUS software Version 8.8 to conduct the analysis (see Table 4.2). This study met the criteria for at least 10 subjects per variable and included an adequate sample size with  $> 15$  subjects per predictor<sup>185</sup>.

## Results

### Descriptive Statistics

Descriptive statistics of all variables are found in Table 4.1. The final number of participants in the study was 152 participants with an average age of 42 years. Females outnumbered males at 80%, and African Americans accounted for 30% of the sample. The mean TMDs pain symptom onset was 157 months with modest pain intensity ( $\bar{X} = 36$ ,  $SD=24$ ) and pain interference ( $\bar{X} = 17.6$ ,  $SD=24.8$ ) ratings. Pain resilience total and subscale scores are reflected in Table 1. Pain resilience total score was positively correlated with age ( $r = .30$ ,  $p < .001$ ). Higher total resilience scores were also noted among males ( $t = -2.31$ ,  $p = .02$ ) and African Americans ( $t = 2.08$ ,  $p = .04$ ). However, no differences were observed based on the presence of a chronic overlapping pain condition or college education.

Table 4.1

*Descriptive Statistics of the Sample (n=152)*

Variables	Mean (SD)/(range)
Age (years)	41.8 (19-65)
Sex (n/%)	
Male	30 (19.6)
Female	122 (80.4)
Race (n/%)	
Non-African American	106 (69.9)
African American	46 (30.1)
Education (n/%)	
Completed College (No)	49 (32)
Completed College (Yes)	103 (68)
Conditioning Strength	58.0 (17.43)
Expectation Baseline (0-100)	50.0 (24.2)
Expectation Reinforced (0-100)	79.7 (22.0)
Placebo Response	17.60 (17.0)
Pain Interference (0-100)	17.6 (24.8)
Pain Intensity (0-100)	36.5 (24)
Pain Resilience Scale (0-56)	34.1 (9.3)
Behavioral Subscale (0-20)	13.1(4.0)
Cognitive Subscale (0-36)	20.9 (6.8)
Optimism	15.2 (4.7)
Pain Catastrophizing Scale (0-52)	12.3 (9.9)
Beck Depression Inventory II (0-63)	10.9 (8.9)
Duration of TMDs pain in months	157 (138.9)
Chronic Overlapping Pain Conditions (n/%)	65(42.7)

Differences in pain resilience behavioral perseverance subscale scores between males and females, did not extend to age, race, education, or chronic overlapping pain conditions. Males had higher behavioral pain resilience scores ( $t=-1.98$ ,  $p=.05$ ). Older adults had higher cognitive/affective positivity subscale scores ( $t=4.588$ ,  $p<.001$ ), males trended toward higher cognitive scores ( $t= -1.945$ ,  $p=.054$ ), and African Americans had significantly higher cognitive scores ( $t= -2.854$ ,  $p=.005$ ). No difference was observed in cognitive scores based on chronic overlapping pain conditions.

## Experimental Conditioning and Expectations

Experimental conditioning scores ranged from 17 to 88, with 75% of the sample achieving conditioning scores (i.e., the mean difference between red and green trials) of greater than 50. No significant associations were observed between the conditioning score and resilience variables. Reinforced expectation scores were 30 points higher and significantly different than baseline expectations scores ( $t = -12.685, p < .001$ ). As expected, patients conditioning scores were not correlated ( $r = .045, p = .581$ ) with baseline expectation scores, while conditioning scores were positively and moderately correlated ( $r = .31, p < .001$ ) with reinforced expectation ratings. In addition, we noted that reinforced expectations correlated with the pain resilience behavioral subscale score ( $r = .20, p = .15$ ; see Figure 4.5) but not with pain resilience total score ( $r = .06, p = .45$ ), or with pain resilience cognitive subscale scores ( $r = -.025, p = .76$ ).

Aim 1: There will be a negative relationship between Pain Resilience and Pain Interference.

Participants' pain interference scores were not associated with total pain resilience (See Table 4.2). However, the pain resilience behavioral subscale was significantly and negatively associated with pain interference ( $b = -1.42, t = -2.9, p = .004$ ).

Table 4.2

*Univariate Linear Regression Modeling Factors that Pain Interference in TMDs Participants**(n=152)*

Univariate Predictor	B (unstandardized)	Standard Error (B)	$\beta$ (standardized)	t value	p value
Age	-.022	.147	-0.012	-.149	.882
Sex (male)	-4.248	5.063	-0.068	-.839	.403
Race (AA)	7.968	4.349	.148	1.832	.069
Education (college)	-3.696	4.311	-0.070	-.857	.393
Depression	1.078	.211	.385	5.107	<.001
Pain Catastrophizing	1.138	.183	.453	6.230	<.001
Optimism (LOT-R)	-.377	.432	-.071	-.876	.382
Pain Resilience Total	-.230	.218	-.086	-1.052	.295
Pain Resilience Behavioral Subscale	-1.420	.490	-.230	-2.900	.004
Pain Resilience Cognitive Subscale	.073	.297	.020	.245	.806

Based on the demonstrated univariate relationships and meeting our established model criteria ( $p < .20$ ), Race-African American, depression, pain catastrophizing and pain resilience behavioral subscale were entered directly into a multiple regression model. This study could not establish a relationship between the demographic covariates (age, sex, education) and optimism and the dependent variable pain interference. Race (African American), depression, pain catastrophizing, and pain resilience (behavioral subscale) were entered into a multiple regression model. The analysis revealed that when controlling for covariates, lower pain resilience behavioral subscale score was independently associated with higher pain interference scores ( $b = .93$ ,  $t = -2.107$ ,  $p = .037$ ). This indicated that a negative relationship exists between pain resilience

pain interference (See Table 4.3). As expected, pain catastrophizing and depression were positively associated with pain interference (See Table 4.3).

Aim 2 Pain Resilience is positively associated with increased reinforced expectancy of analgesia when accounting for prior experience (conditioning) and other covariates. Reinforced expectation of analgesia was higher among females ( $\bar{X}$ =81.7, SD= 21.2) than males ( $\bar{X}$  =71., SD = 23.4) ( $t = 2.146, p =.038$ ) and among non-African Americans ( $\bar{X}$ =83, SD = 20.5) compared with African Americans ( $\bar{X} = 72.1, SD = 23.6$ ) ( $t = 2.865, p =.005$ ) . When examining the relationship with reinforced expectations, it was found that the pain resilience behavioral subscale positively associated with reinforced expectations ( $b = 1.09, t = 2.50, p =.014$ ). Still, a similar relationship could not be established with the total score or the cognitive subscale scores. These results indicate that participants with higher pain resilience behavioral subscale scores had higher reinforced expectations of analgesia. In addition, larger conditioning strength was positively associated with higher reinforced expectations of analgesia ( $b = .353, t = 3.567, p <.001$ ; see Table 4.4).

Table 4.3

*Multiple Linear Regression Modeling Factors That Predict Pain Interference\_in TMDs*

*Participants (n=151)*

Univariate Predictor	B (unstandardized)	Standard Error (B)	$\beta$ (standardized)	t value	p value
Race (AA)	3.891	3.701	.074	1.049	.296
Pain Catastrophizing	.656	.203	.270	3.228	.002
Depression	.657	.221	.244	2.974	.003
Pain Resilience-behavioral subscale	-.930	.441	-.155	-2.107	.037

AA=African American; a= 1influential case removed; Model R square =.273

Table 4.3B

*Multiple Linear Regression Modeling Factors That Predict Pain Interference in TMDs**Participants (n=152)*

Univariate Predictor	B (unstandardized)	Standard Error (B)	$\beta$ (standardized)	t value	p value
Race (AA)	5.394	3.851	.100	1.401	.163
Pain Catastrophizing	.791	.209	.315	3.786	<b>&lt;.001</b>
Depression	.565	.229	.202	2.464	<b>.015</b>
Pain Resilience- <b>behavioral subscale</b>	-.662	.455	-.107	-1.456	.147

AA-African Americans; Model R Square=.26

The univariate relationships of the independent variables that entered the multiple linear regression model predicting reinforced expectations are seen in Table 4.4. In this table, we note that sex (male), race (African American), conditioning strength, and pain resilience (behavioral subscale) achieved our established statistical significance relationship criteria ( $p < .20$ ) with the dependent variable reinforced expectations, while age, optimism, pain self-efficacy, pain catastrophizing, anxiety, depression did not have relationships with reinforced expectations of analgesia.

Table 4.4

*Univariate Linear Regression Modeling Factors That Predict Expectation-Reinforced in TMDs**Participants (n=152)*

Univariate Predictor	B (unstandardized)	Standard Error (B)	$\beta$ (standardized)	<i>t</i> value	<i>p</i> value
Age	0.135	0.129	0.085	1.041	0.300
Sex (male)	-10.063	4.415	-0.183	-2.279	<b>0.024</b>
Race (AA)	-10.854	3.789	-0.228	-2.865	<b>0.005</b>
Education (college)	0.043	3.824	0.001	0.011	0.991
Depression	0.211	0.202	0.085	1.047	0.297
Pain Catastrophizing	-0.120	0.181	-0.054	-0.662	0.509
Optimism ( LOT-R)	0.029	0.381	0.006	0.076	0.940
Pain Resilience Total	0.159	0.193	0.067	0.821	0.413
Pain Resilience Behavioral Subscale	1.090	0.436	0.200	2.500	<b>0.014</b>
Conditioning Strength	0.353	0.099	0.280	3.567	<b>&lt;0.001</b>
Interaction conditioning strength by pain resilience behavioral	0.021	0.021	0.247	0.999	0.344

LOTR-Revised Life Orientation Test; AA -African American

In building the multiple regression model, we found that when controlling for covariates, higher pain resilience behavioral subscale score was independently associated with higher expectations of reinforced analgesia ( $b = 1.176$ ,  $t = 2.949$ ,  $p = .004$ ). The model was statistically significant,  $F(4, 147) = 8.743$ ,  $p < .001$  and accounted for 19% of the variance in reinforced expectations of analgesia ( $R^2 = .192$ , adjusted  $R^2 = .170$ ). This indicated that a positive relationship exists between pain resilience and reinforced expectations of analgesia, and that sex (male) and race (African American) did not modify the relationship between pain resilience behavioral subscale and reinforced expectations (see Table 4.5). In this model, being male and African American were associated with reduction reinforced expectations of analgesia scores (see Table 4.5).

Table 4.5

*Multiple Linear Regression Modeling Factors that Predict Expectations-Reinforced in TMDs**Participants (n=152)*

Univariate Predictor	B (unstandardized)	Standard Error (B)	$\beta$ (standardized)	<i>t</i> value	<i>p</i> value
Sex (male)	-11.486	4.052	-.215	-2.835	.005
Race (AA)	-8.266	3.642	-.178	-2.270	.025
Conditioning Strength	.270	.097	.220	2.789	.006
Pain Resilience-behavioral subscale	1.176	.399	.222	2.949	.004

Aim 2B: Pain resilience modified the relationship between conditioning strength and expectation of analgesia. An examination of whether pain resilience behavioral traits modified the relationship between conditioning strength and reinforced expectation did not support this hypothesis. The interaction variable did not have a significant relationship with reinforced expectations of analgesia (See Table 4.4).

### **Discussion**

This study validated the role of pain resilience in relation to other psychological variables (optimism, pain catastrophizing, depression), its association with pain interference, and reinforced expectations of analgesia, a predictor of placebo response. Pain resilience maintained a positive and perhaps protective relationship with pain interference in the presence of other pain-vulnerable factors of depression and pain catastrophizing. The literature corroborates this relationship as pain catastrophizing and depression are viewed as vulnerability factors in chronic pain<sup>186</sup> and are correlated inversely with pain resilience, a positive construct<sup>121</sup>.

Resilience has multiple definitions, but generally, it is defined as the ability to maintain psychological and physical functioning despite a significant disruptive event <sup>187</sup>. Much interest remains in identifying the beneficial effect of resilience among conditions like chronic pain. Evidence suggests that positive psychological constructs such as resilience offer an additive benefit of increased physical and emotional functioning above disease avoidance <sup>188</sup>. Resilience-building interventions and training programs have been shown to foster and improve resilience in mental health using cognitive behavioral therapy and mindfulness programs <sup>189</sup>. Specific to chronic pain, one exploratory study has demonstrated improvement in chronic pain through resilient-building techniques incorporating dance <sup>190</sup>

In this study, the pain resilience behavioral subscale component, and not optimism, was associated with pain interference and reinforced expectations of analgesia. Although optimism is an important resilient resource that bestows protection in adverse life events <sup>191</sup> and shares characteristics with other measures of positive psychological functioning <sup>186</sup>, it remains a distinct construct from resilience.

The pain resilience behavioral subscale items consisted of items related to continuing activity despite intense or prolonged pain linking the pain resilience behavioral subscale to task persistence and continuing activity despite pain <sup>153</sup>. Although not reported, task persistence correlated with pain resilience total and subscale behavioral score in supplementary analyses. The persistence of task performance despite pain is an integral characteristic of pain resilience <sup>192</sup>. It is reasonable that the relationship between behavior perseverance adequately reflects an aspect of pain resilience and thus accounts for the negative association with pain interference.

The pain resilience behavioral subscale also predicted reinforced expectations of analgesia among our patients with chronic orofacial pain. Exploring predictors of expectations is essential because expectations are critical to forming and maintaining placebo responsivity<sup>41</sup> a potential adjunct in treating chronic pain<sup>193</sup>. The effect of placebo in chronic pain conditions has been demonstrated in idiopathic pain<sup>194</sup>, irritable bowel syndrome<sup>195</sup>, fibromyalgia<sup>196</sup> and migraine populations<sup>197</sup>. Placebo response and thus expectations have a role to play in influencing the outcome of chronic pain conditions, and the personality traits like pain resilience can help us predict which individuals with chronic can benefit from the applications of placebo therapy such as medication reduction and elimination of medication side effects<sup>198</sup>.

According to placebo theory, a placebo response occurs because the patient expects it to happen<sup>39</sup>. Indeed, patient expectations are regarded as the strongest predictor of the outcome of any medical treatment<sup>177</sup>. For example, having a positive expectation about the potency of a synthetic opioid, remifentanyl, doubled the drug's analgesic effect, while negative expectations of the potency of the drug almost extinguished its effect<sup>199</sup>. Expectations are determined by prior information as may occur during experimental conditioning procedures, individual psychological factors, e.g., anxiety or stress, and neurobiological characteristics, for example brain connectivity<sup>40</sup>. This study demonstrated a positive relationship between pain resilience behavioral scale and reinforced expectation of analgesia. Perhaps those with high pain resilience behavioral scores were more likely to respond to the repetitive nature of the conditioning experience through the mechanism of task persistence and thus have higher reinforced expectations of analgesia. This hypothesis would need to be proven in a future study.

Similarly, Pecina et al. (2013) demonstrated that personality traits, including high ego-resiliency, were predictive of placebo analgesia<sup>55</sup>. The mechanism for placebo and expectation link to resilience is not clear. One theory is that resiliency is tied to positive emotions<sup>200</sup> and changes in the reward and emotional processing circuitry in the brain<sup>201</sup>. In addition, enhanced activity in an area of the brain responsible for the expectation of reward was noted in resilient soldiers<sup>202</sup>. Synaptic dopamine has been associated with an increased capacity to activate endogenous mu-opioid receptor transmission, which is one mechanism for the link between pain resilience and placebo response<sup>203</sup>.

In this study, pain resilience scores were higher among men compared with women. Literature suggests that women tend to score lower on resilience measures than men<sup>204</sup> because the measures do not capture the differences in adaptation due to gender<sup>205</sup>. Women are likely to report more stressful lives than men and use more emotion-based coping than men, who use active coping mechanisms to deal with stress. Resilience measures that do not capture domains such as family and social support may not reflect gender differences in resilience<sup>205</sup>.

Depending on available resources or vulnerability, resilience may increase or decrease with age<sup>206,207</sup>. Reduced resources, such as finances, and increased vulnerability, such as bereavement, associated with age may account for this variability. The increased resilience associated with age in the current study may be because the mean age of participants in our study was 41, and resilient resources such as social support and a sense of purpose and meaning were readily available to this age group<sup>208</sup>. The ability to adapt through the development of positive interpersonal relationships and high optimism are resilient resources that can be learned as you age, allowing individuals successfully function with pain<sup>209</sup>.

## **Conclusion**

Understanding and promoting resilience is crucial as it offers an opportunity to counteract risk factors, depression, and pain catastrophizing, for poor pain outcomes. This work linked pain resilience to decreased pain interference, and this link suggests that fostering resilience through resilience-enhancing interventions offers promise in reducing the impact of chronic pain.

This study also provides insight into the role of pain resilience in predicting reinforced expectations, an important factor in initiating and maintaining placebo responsiveness. The data supports that among chronic orofacial pain populations, women and non-African Americans, prior experience through conditioning and increased pain resilience behavioral attributes are positively associated with reinforced expectations of analgesia. These characteristics may help identify those who will benefit from placebo therapy in chronic pain. Placebo response and fostering expectations remain underutilized medical therapies, and the evidence is increasing for their clinical usefulness<sup>41,198</sup>. These findings provide insight into the factors which can contribute to the success of these underutilized and unrecognized clinical adjuncts.

## Chapter 5: Summary and Implications of Research

### **Introduction**

Chronic pain has a prevalence of up to 40% <sup>210,211</sup> and leads to significant disability. Discovering new and innovative ways to deal with chronic pain will offset the burden of those who live with the effects of this illness. Temporomandibular disorders do not exist in a vacuum and are often affiliated with other co-occurring pain conditions with similar attributes. This research supports the promising role of resilient mechanisms in promoting improved function and recovery in chronic pain. Resilient mechanisms may also provide a tool for predicting who may benefit from placebo therapy using expectation-based placebo treatment. There is evidence that placebo and expectations have utility in weaning opioid doses weaning<sup>173</sup>, and also in improving outcomes after cardiac surgery<sup>42</sup>. Fostering the expectations using resilient building mechanisms is therefore beneficial.

### **Overview of Major Findings**

Aim 1: Examine the relationships between demographics, comorbid medical, and psychological conditions to clinical pain-related disability in adults with TMDs. H.1. Positive psychological constructs will be inversely associated with pain-related disability, H.2. Negative psychological constructs will have a direct and positive relationship to pain-related disability, H.3. Jaw function limitation will have a direct and positive relationship to pain-related disability, and H.4. Chronic overlapping pain conditions will have a direct and positive impact on pain-related disability.

The results of the analysis did not support hypothesis H.1. The positive psychological construct positive valence factors, consisting of positive affect and optimism, was not inversely

associated with pain-related disability. Instead, there was a positive relationship ( $\beta=.16, p<.05$ ) between positive valence factors (optimism and positive affect) and pain-related disability. The results did support hypotheses H.2, H.3, and H.4. Negative psychological constructs (somatic symptoms, pain catastrophizing, and negative affect) had a direct and positive relationship ( $\beta = .31, p <.01$ ) with pain-related disability. Jaw function limitation had a positive and direct relationship ( $\beta = .66, p <.001$ ), and the number of chronic overlapping pain conditions also had a positive ( $\beta = .16, p <.001$ ) relationship with pain-related disability.

Increases in temporomandibular jaw limitation and negative psychological factors contribute to increases in pain-related disability. These findings are supported in the literature<sup>88</sup> and confirm the need to direct resources such as physical therapy and other exercises to optimize jaw function<sup>113,115</sup>. The positive association between positive psychological factors and pain-related disability has not been supported in the literature. This work attributes this finding to the overall lower pain intensity and interference scores seen among the participants in the sample. In addition, some researchers have reported that the protective effect of resilient type resources may be limited to the acute and subacute phases of pain chronicity<sup>124</sup>, meaning that as the duration of symptoms progresses, the inverse relationship between resilience and pain disability may be obliterated by time.

Aim 2: To identify characteristics of subgroups of patients with chronic orofacial pain based on their coping strategies. H.1. Distinct coping strategy profiles would emerge among the sample of chronic pain patients, H.2. Higher pain intensity, pain interference, pain duration, pain catastrophizing scores, and the presence of chronic overlapping pain conditions such as fibromyalgia, irritable bowel syndrome, migraines, and chronic low back pain, will be associated

illness-focused coping styles such as guarding and resting versus wellness-focused strategies such as coping self-statements and exercise.

The results of the analyses hypothesis H.1. Three distinct coping profiles emerged, low, moderate, and high-use copers of both wellness and illness-focused strategies. The results of the analyses did not support H.2 in that high use of both wellness-focused and illness-focused coping strategies was present in patients with the highest pain intensity, interference, and pain catastrophizing scores. Participants in the high-use group had increased pain intensity (OR 1.03, 95% CI[1.01,1.06]), increased pain interference (OR 1.02, 95% CI[1.00,1.03]), and increased pain catastrophizing(OR 1.066, 95% CI[1.03,1.10] compared to the low-use group. In addition, the presence of illness-focused coping strategies was not restricted to those patients with chronic overlapping pain conditions. Moderate users of both wellness-focused (coping self-statements and exercise) and illness-focused coping strategies (guarding and resting) had higher odds (OR 1.78, 95% CI[1.03,3.06]) of having a chronic overlapping pain condition (fibromyalgia, irritable bowel syndrome, migraines, and chronic low back pain).

This study demonstrated patterns of coping strategy use among chronic orofacial pain patients. However, the usage pattern is not based on a dichotomous system of illness or wellness-based criteria but is a convergence of multiple coping strategies. All coping strategies were present in the three profiles within the participants, and what varied was the frequency of usage. Additionally, all coping groups used the task persistence coping strategy with high frequency. Some argue that coping strategy classification systems' importance in predicting outcomes may be overemphasized <sup>164</sup>. Relatively, it may depend on the context, that is, goal achievement or goal modification, the demands of pain dictate which coping strategy is employed. The

modification of goals based on pain has been linked to optimism and greater task persistence<sup>100</sup>. Although this study did not demonstrate a preference for wellness-based coping by those with less pain intensity and interference, it may be that resilient patients may indeed choose coping strategies depending on the goals and likelihood of achieving them based on pain context. Understanding the motivation for using specific coping strategies and whether participants achieve their goals would be a valuable determinant of resilience.

Aim 3: Determine the relationship between pain resilience on the magnitude of pain interference and expectations. H.1. A negative relationship exists between pain resilience and pain interference while controlling for psychological covariates, and H.2. Pain resilience was positively associated with increased reinforced expectancy of analgesia when accounting for psychological factors (optimism, pain catastrophizing, depression) and other covariates (prior experience, sex, race, education) and H.2.B. pain resilience modified the relationship between conditioning strength and expectation of analgesia.

The results of the analyses supported hypothesis H.1, and pain resilience was negatively associated with pain interference ( $b = -.930$ ,  $t = -2.107$ ,  $p = .037$ ) while controlling for race, depression, and pain catastrophizing. The analyses also supported hypotheses H.2. Pain resilience was positively associated with reinforced expectations of analgesia ( $b = 1.176$ ,  $t = 2.949$ ,  $p = .004$ ) while controlling for sex, race, and conditioning strength. Hypothesis H.2.B was not supported, and pain resilience did not have a significant relationship between conditioning strength and reinforced expectations of analgesia.

This study demonstrated that independent of race and pain catastrophizing, increases in pain resilience were associated with decreased pain interference. This finding is supported by the

revised fear-avoidance model in which resilience is seen as a critical construct on the road to recovery but also impacts disability <sup>7</sup>. This study joins the scant literature on the relationship between resilience and disability in orofacial pain and validates the protective role of resilience in chronic orofacial pain. In addition, increased pain resilience, independent of demographics and experimental conditioning, was directly associated with an increased reinforced expectation of analgesia in a placebo manipulation study. Psychological factors such as mood are believed to cause changes in metabolic activity or electrical activity in the anterior cingulate cortex, amygdala, ventral striatum, and orbitofrontal cortex<sup>174</sup>. Psychological factors, high optimism<sup>56</sup>, and low anxiety<sup>48</sup> are known to have a role in placebo response. Resilience is believed to be linked to placebo response via positive emotions<sup>200</sup> and changes in the reward and emotional processing circuitry, which may interact with the endogenous opioid system<sup>201,212</sup>.

### **Strengths**

Much of the literature regarding the Fear Avoidance Model and positive psychological constructs exists within the area of chronic low back pain. This dissertation expands these concepts to orofacial pain. The strength of this dissertation exists in addressing the contribution of positive psychological factors in both pain-related disability and expectations in patients with chronic orofacial pain.

One strength of the study is the statistical methodology used in Aim 1. The relationship between negative and positive psychological constructs and jaw limitation function on pain-related disability was explored using structural equation modeling. Structural equation modeling is helpful when measuring broad multilayered constructs <sup>213</sup>. It was well suited for psychological

variables in the study model where the concepts are similar, allowing for constructing latent variables and combining different measures representing the broad construct<sup>88</sup>.

These results demonstrate a role for somatic symptoms as an equal contributor to the negative psychologic construct's influence on pain-related disability. The temporomandibular disorders model proposed by the OPPERA study demonstrated that somatic symptoms have a strong association with psychological distress and have been framed among the psychological variables that predict the risk of new-onset temporomandibular disorders<sup>92,93,214</sup>. Statistically, the confirmatory factor analysis demonstrated similar loading strengths (0.6) for all the indicator variables onto the latent construct showing that negative affect, pain catastrophizing, and somatic symptoms contributed equally to the underlying construct of psychological unease. This study further confirms that somatic symptoms, patient complaints that are not medically explained, are linked to psychological distress<sup>61</sup>.

To my knowledge, this is the first study linking resilience to expectations of analgesia in chronic orofacial pain patients. This finding supports other work identifying resilience as predictive in placebo analgesia<sup>55</sup>. The contributors to pain disability, jaw function, and positive and negative psychological interventions remain targets for reducing pain-related disability.

## **Limitations**

### **Study Design**

This study did not have a control group for Aims 1, 2, and 3; therefore, the internal validity of this study is limited and introduces a risk of bias. A control group was not possible in this study as the study was retrospective, and the variables of interest were unavailable for healthy participants. Aims 1, 2, and 3 were based on a cross-sectional design so that the causal

nature of the relationships between the variables cannot be concluded. To determine a causal relationship, a prospective cohort study of adults with temporomandibular disorders must establish the causal nature of the relationships between the predictors and outcome variables in this study.

### **Sample**

The study sample for Aim 3 was a convenience sample with emails sent and phone calls made to prior study participants. Selection bias is possible as the participants who agreed to participate in the study may have shared similar characteristics. Temporomandibular patients who agreed to participate in Aim 3 may have been more resilient than those who did not, thus biasing the results. Using the available population of participants for Aim 1,2,3 limits the generalizability of the results.

Another potential limitation is that the study relied on previously conducted placebo and expectation of analgesia data. The effect of time separating between the experimental data and the collection of resilience measures is unknown. The questionnaire data, including the resilience measure for Aim 3, was collected during the COVID-19 pandemic. The effect of the adversity experienced by participants related to the pandemic may have induced changes in participant perception of pain and their self-reported resilience on the resilience measure. Adding resilience measures to future placebo and expectation experiments will corroborate these findings. Despite this limitation, it is essential to note that the results are supported by other work examining resilience and pain outcomes in other pain populations <sup>30</sup>.

## **Study Model**

Resilience is a dynamic construct, and the relationship established with pain outcomes, such as pain interference, may change over time. A longitudinal study design could address whether the relationships between resilience, pain interference, or expectations of analgesia vary with time. Multiple resilience measure data points linking resilience to pain outcomes and placebo and expectations would answer whether increases in resilience cause decreases in pain interference.

Ultimately the goal of Aim 3 was to characterize patients with higher expectations of analgesia in a placebo model. Resilience was associated with the expectation of analgesia. Future studies would prospectively compare placebo responsivity among highly resilient and low resilient individuals.

## **Implications For Conceptual Framework**

The findings from the aims of this study support the proposed revision of the Fear Avoidance Model<sup>7</sup>. The original Fear Avoidance model<sup>8</sup> has its foundations in psychopathology and focuses exclusively on the psychological factors contributing to how patients interpret pain. The model describes a cyclical process for developing chronic disability or, alternatively, recovery<sup>215</sup>. The proposed revised Fear-avoidance model incorporates resilience alongside pain catastrophizing to understand the dynamics between vulnerability factors and resilience in pain adaptation<sup>7</sup>.

For Aim 1, the model provided a framework for understanding the results of negative psychological constructs which directly and positively relate to pain-related disability. Less clear was the positive relationship between positive psychological construct, which contained positive

affect and optimism, and pain-related disability. While Aim 1 did not use the direct resilience measurement tool, I used the resilience characteristics of optimism and positive affect, which are believed to lead to improvement and perhaps protection against poor pain outcomes <sup>119</sup>. The model does not explain the positive association between this positive valence latent construct and pain-related disability. Vulnerability and resilience factors are not opposite ends of a spectrum <sup>28</sup> but should be viewed as separate constructs impacting an individual's recovery. Resilience factors such as optimism and positive affect can exist in a complex relationship with other negative emotions lending greater emotional complexity in patients with chronic pain <sup>121</sup>. The coexistence of positive affect and optimism in the presence of a pain-related disability may represent an aspect of pain acceptance, experiencing pain without attempts to avoid, reduce or control the pain <sup>216</sup>, while coping with the negative consequences of pain, for example, pain disability.

In Aim 2, the work elucidates the coping strategy patterns which patients engage in and compare the differences in these patterns based on pain characteristics. The Fear-Avoidance Model does not incorporate coping mechanisms into its structure to explain disability or recovery outcomes <sup>217</sup>. The model is silent on how patients function or cope despite experiencing chronic pain. Effective coping is an integral part of resilience mechanisms<sup>121</sup>, and the strategies employed leading to recovery remain an element for development for future research and revision of the Fear-Avoidance Model.

In Aim 3, the Fear-Avoidance Model explains the inverse and protective relationship between pain resilience to pain interference. Increased resilience was also positively associated with increased reinforced expectations of analgesia while controlling for demographic variables

and experimental conditioning. The Treatment Expectation Model<sup>40</sup> described by Bingel (2020) describes the role of psychological factors in impacting expectations.

### **Implications For Research and Clinical Practice**

#### **Research**

The belief that resilience mechanisms contribute positively to chronic pain outcomes is well supported in the literature 28,29. This study is valued because the psychological constructs of resilience and coping are complex, and their impact on chronic pain is now better understood. In the first study, there was a positive association between resilience factors, optimism, and positive affect and pain disability, whereas in the final study, the expected finding was resulted. Future research is needed on how chronic pain patients cope while experiencing pain. Specifically, how does the role of resilience operationalize in patients with ongoing chronic pain? How do patients with functional limitations demonstrate resilient behaviors in the face of pain? Does the presence of functional deficits related to pain indicate an absence of resilient factors? The results from Aim 1 suggest that a patient may indeed be optimistic and have a positive effect in the presence of pain-related disability. One study into resilience and pain acceptance suggested that resilient people may use pain acceptance to cope with chronic pain <sup>218</sup>. Further exploration into the intersection of resilience and pain acceptance may shed light on this topic in the chronic orofacial pain population.

This study also demonstrated that resilient people had higher expectations of analgesia in a placebo manipulation experiment, which is consistent with other findings that other resilient characteristics, such as optimism, were positive and reproducible predictors of placebo response <sup>56</sup>. This study indicates that the behavioral perseverance subscale of pain resilience is associated

with expectations of analgesia. Newer research suggests that the mechanisms of placebo analgesia are mediated through cognitive evaluative and emotional appraisal of pain mechanisms in the brain<sup>40</sup>. Individual mood and coping approaches are areas of research that should be explored as predictors of susceptibility to placebo analgesia.

Optimizing resilience through structured psychological interventions is an active area of new research. One pilot study ( $N=29$ ) in patients demonstrated that a resilience intervention successfully reduced pain catastrophizing and lowered pain sensitivity among patients with temporomandibular disorders<sup>219</sup>. Another study ( $N=22$ ) demonstrated utilizing dance therapy improved resilience and decreased pain intensity in patients with chronic pain<sup>220</sup>. These encouraging studies suggest clinicians can use the link between resilience and expectations to impact pain outcomes.

### **Clinical Practice**

Resilience has utility in the treatment of patients with chronic pain. When patients present to a health care provider for care, identifying those individuals who lack resilient characteristics may be beneficial because patients' beliefs, expectations, and coping mechanisms impact the clinical outcomes. Predicting those more likely to develop chronic pain after injuries or routine surgeries can be considered preventative. In addition, clinicians can prescribe or recommend therapies such as cognitive-behavioral therapy to build resilience among those identified as having low resilience resources<sup>221</sup>. This strategy may be beneficial among patients with chronic pain with accompanying depression and disability and low resilience resources.

Psychological factors such as resilience modulate or predict an individual's expectation of health outcomes<sup>40</sup>. Approaching patient conversations in a way that fosters positive

expectations<sup>198</sup> within the patient can be instrumental in influencing outcomes, benefiting those who exhibit resilient characteristics most. Harnessing the power of positive expectations can be utilized to make their treatment plans more customized.

Finally, the evidence support the efficacy of psychological interventions for resilience enhancement<sup>189</sup>. These interventions vary and target differing resilience resources. Techniques such as cognitive behavioral therapy<sup>149</sup>, which targets thought patterns to deal with maladaptive behavior and moods, and acceptance and commitment therapy<sup>222</sup>, focused on acceptance of negative and positive experiences while focusing on important life goals, have successfully managed chronic pain. Understanding who will benefit from these programs remains challenging as consistent definitions of resilience vary in intervention studies and effect sizes remain small<sup>149,223,224</sup>.

## **Conclusions**

Pain is a necessary protective mechanism but an undesired portion of our experience. Pain that becomes chronic and disabling carries significant personal and societal consequences. Discovering ways to alleviate that suffering and improve the quality of its victims is possible by identifying the characteristics that are positively associated with pain-related disability and those that contribute to the recovery. This study demonstrated that while negative psychological factors impact disability, resilience mechanisms also contribute to pain interference and disability outcomes. A link between resilience and expectations of analgesia has been elucidated, indicating a pathway to identifying who may most benefit from placebo therapy. This study is essential as it has implications for managing patients with chronic pain and disability. Future

research should focus on the best strategies for developing resilience among chronic pain patients.

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