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Response Shift and Functional Outcomes in Individuals with Chronic Ankle Instability

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RESPONSE SHIFT AND FUNCTIONAL OUTCOMES IN INDIVIDUALS WITH CHRONIC ANKLE INSTABILITY

by

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ABSTRACT

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Ankle sprains are one of the most common injuries sustained by those who are physically active. One in three individuals will develop a condition known as chronic ankle instability (CAI) after suffering a single ankle sprain. These individuals suffer from recurrent bouts of ankle instability, residual symptoms, and a myriad of other mechanical and functional impairments as well as health-related quality of life (HRQL) deficits. Due to the abundance of health consequences associated with this condition it is imperative to establish evidence based interventions that are focused on restoring function and HRQL to pre-injury statuses.

The overarching purpose of this dissertation was to add to the available treatment paradigms for those with CAI. To achieve this overarching goal multiple sub-purposes were employed. The first purpose of this dissertation was to perform a systematic review of the available literature to examine the efficacy of current CAI interventions to enhance HRQL (Project IA). The second purpose was to systematically review the literature to evaluate response shift in patients with various orthopedic conditions following rehabilitation (Project IB). The third purpose was to investigate the effects of a 4-week comprehensive evidence-based intervention on disease-oriented measures in those with CAI. Lastly, the final purpose was to evaluate the effect of a 4-week comprehensive evidence-based intervention on patient-oriented outcomes in those with CAI and to determine if those with CAI who undergo this intervention experience response shift.

The systematic reviews (Project IA, IB) determined that the available evidence-based interventions are effective at enhancing HRQL in those with CAI and that those who undergo care for orthopedic conditions may experience a response shift that can confound assessment of HRQL changes. Project II found that robust improvements in disease-oriented measures were obtained immediately following a 4-week intervention and were maintained for 2-weeks after its completion. In Project III, evidence of response shift was not identified in those with CAI following a 4-week intervention. This finding indicates that traditional pre-to-post methods for assessing HRQL changes are accurate in these patients. Furthermore, significant improvements in ankle- and dimension-specific self-reported function as well as global well-being were identified following a 4-week comprehensive intervention for those with CAI. The results of these investigations demonstrate the clinical efficacy of the investigated 4-week comprehensive intervention to enhance a diverse array of detriments associated with CAI.

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CHAPTER I

INTRODUCTION

Background

Ankle sprains are one of the most common orthopedic injuries sustained by the general population.[1-3] Furthermore, ankle sprain incidence can be up to twenty-seven times greater within the athletic and military setting.[1,3] It is estimated that 600,000 ankle sprains occur each year within the United States resulting in over $4 billion in annual aggregated healthcare costs.[1] Nearly half of all ankle sprains occur during athletic activity[1] as they account for nearly 17% of all high school athletic injuries[4] and 30% of all collegiate injuries.[5] These estimates may be highly underestimated as up to 55% of individuals do not seek medical treatment for an ankle sprain.[6] Failure to report these injuries may be due to the fact ankle sprains are considered minor injuries, even though 40% of individuals will be absent from sports participation for 1-3 weeks[4] and nearly 65% of individuals will modify their normal activities for years after injury.[7] With the rise in high school athletic participation[8] and the recommendations to increase physically activity[9] there is great concern regarding the potential for ankle sprain incidence and subsequent consequences.

While initial ankle sprains may result in acute disability, they can also be associated with several long-term consequences. Between 32 and 74% of individuals with a history of ankle sprain will experience repetitive sprains, residual symptoms, and recurrent instability.[10,11] The presence of these characteristics after an ankle sprain has been termed chronic ankle instability (CAI). CAI is a common condition in athletics as 30% of high school and 18% of collegiate athletes suffer from either bilateral or unilateral CAI.[12] Individuals with CAI suffer from a multitude of mechanical, functional and psychosocial impairments that contribute to the repetitive bouts of trauma and instability.[13] Additionally, CAI has been associated with an increased risk of ankle osteoarthritis,[14] decreased physical activity levels,[15] and deficits in health-related quality of life (HRQL).[16] Therefore, there are various short- and long-term consequences associated with CAI that highlights the need for effective evidence-based interventions to manage this condition.

The first step in the development of evidence-based interventions is to thoroughly evaluate the impairments caused by the condition.[17] Once these specific impairments are identified, targeted interventions can be formulated and implemented to combat those impairments. However, when assessing impairments, one must ensure that a comprehensive picture of the health condition is evaluated. Disablement models, such as the World Health Organization's International Classification of Functioning, Disability, and Health model,[18] highlight the importance of classifying impairment and HRQL from not only a disease-oriented perspective but also a patient-oriented perspective. The utilization of these models allows clinicians to look beyond the cause and identify the impact of conditions on overall health across the domains of function. Specific to the ICF model, disease-oriented measures are able to quantify the physical impairments caused by the health condition at the body function/structure level and their impact on function. Patient-oriented measures capture the patient's perspective of their function and HRQL in the presence of a health condition. These measures can be used to quantify the activity limitations and participation restrictions caused by the health condition at the personal and societal levels of function. The incorporation of both measures allows for a holistic evaluation of HRQL and impairment. Within the CAI literature a myriad of disease- and patient-oriented outcomes have been utilized to understand the impact of the health condition on the domains of function.

Chronic Ankle Instability: Disease-Oriented Perspective

Traditionally CAI has been investigated from a disease-oriented perspective that involves the assessment of the physical manifestation of the condition.[13] People with CAI experience mechanical impairments such as pathological laxity, degenerative changes, and or osteokinemaitc/arthrokinematic changes resulting from multiple ankle sprains.[13] Specifically, arthrokinematic changes at the ankle, such as talar and fibular positional faults have been identified.[19-22] These positional faults are malalignments of the boney structures that are thought to impede proper osteokinematics of the ankle complex. The primary osteokinematic impairments are restriction in dorsiflexion range of motion (DFROM) as an estimated 74% of individuals with CAI suffer from a DFROM deficit.[23] DFROM deficits have been identified during static weight-bearing measurement using the weight-bearing lunge test[24] as well as during functional tasks such as walking and jogging.[25,26] Additionally, DFROM deficits have been linked to dynamic balance impairments[27,28] which may indicate that this mechanical deficit may influence functional activity.

Beyond mechanical impairments, individuals with CAI suffer from an array of functional impairments. It is thought that adverse changes in the sensorimotor system develop following lateral ankle sprain and contribute to the repetitive trauma experienced by individuals with CAI.[13] These changes result in impaired postural control,[29-31] strength,[32-34] and plantar cutaneous sensation.[35,36] Impairments in postural control have been identified using measures of static and dynamic balance. Additionally, these postural control impairments have been identified using instrumented techniques as well as clinical assessments.[31,37-39] From an ankle strength perspective the evidence of impairments is contradictory within the CAI literature.[13] However, concentric eversion ankle strength may be an area of consistent deficits as a recent meta-analysis reported deficits measured using isokinetic strength testing.[32] More importantly, strength training interventions have demonstrated the ability to increase strength[40,41] indicating that this may be a modifiable element of CAI. Overall, there are a multitude of disease-oriented impairments that contribute to continued bouts of instability and ankle sprains suffered by those with CAI. Furthermore, a vast array of laboratory and clinician based outcome measures have been used to assess these impairments in individuals with CAI.

Chronic Ankle Instability: Patient-Oriented Perspective

HRQL is an integral part of health surveillance as it incorporates a multidimensional approach to patient health.[42] As such there has been increasing attention placed on the HRQL deficits associated with CAI. A recent meta-analysis[43] found, with a high level of evidence, that those with CAI report decreased HRQL using region-specific patient-reported outcomes (PRO) when compared to healthy controls. The Foot and Ankle Ability Measure (FAAM), the Foot and Ankle Disability Index (FADI), and the Ankle Joint Functional Assessment Tool (AJFAT) are PROs that have all demonstrated the ability to identify decreased region-specific HRQL in those with CAI compared to healthy individuals. It is evident from these findings that individuals with CAI have self-perceived activity limitations due to their ankle health.

Beyond the scope of region-specific PROs, there is a need to also characterize self-perceived impairments with generic and dimension-specific instruments within individuals with CAI. Evidence of generic HRQL deficits are limited at this time, as only two studies[16,44] have demonstrated that individuals with CAI report more global HRQL deficits using the SF-36 Physical Component Summary[44] and the Disablement of the Physically Active (DPA)[43] scale. Additionally, Houston et al[16] reported increased fear and avoidance beliefs within those with CAI as measured using by the Fear-Avoidance Beliefs Questionnaire (FABQ) and the Tampa

Scale of Kinesiophobia (TSK-11) indicating this is a focused dimension of HRQL which warrants additional research. Cumulatively, these self-perceived impairments highlight the need for continued emphasis on HRQL as well as the development and evaluation of interventions to improve multiple facets of HRQL in people with CAI.

Chronic Ankle Instability: Interventions

Due to the multifactorial nature of CAI,[13] there is a need for interventions that are capable of addressing several of the disease- and patient-oriented impairments associated with the health condition. Within the literature, intervention studies have focused on targeting isolated impairments thus there are a number of rehabilitation strategies that are successful at improving a limited number of the aforementioned impairments. To date, two of the most investigated interventions are joint mobilizations[45-49] and balance training[50-52] programs. Joint mobilizations have demonstrated efficacy to improve DFROM,[45-47,49,53] postural control,[46] and HRQL.[46,48,53] Similarly, balance training protocols have enhanced postural control[54-59] as well as HRQL.[57-59] Another common intervention is the use of strength training programs, which have improved ankle strength in those with CAI.[40,41,60,61] Additionally, several studies have evaluated the combined effect of several interventions[51,62-64] on the common deficits associate with CAI. While these studies combined multiple interventions to create a more comprehensive rehabilitation protocol, they failed to utilize the previously mentioned evidence-based protocols. Cumulatively, the intervention studies demonstrate that many rehabilitation strategies can be used to improve common clinical impairments associated with CAI. However, there is a need for an investigation that would evaluate the combined effects of several evidence-based interventions to address the common impairments and HRQL deficiencies identified with CAI.

With the emergence of evidence-based practice (EBP) there has been an increased emphasis on incorporating patient-centered evidence into the clinical decision making process.[65] Patient-centered evidence evaluates the effect of a condition on a patient's HRQL and the efficacy of treatment based on the patient's perspective.[65] The patient's perception of their own HRQL can be evaluated using PRO instruments throughout the rehabilitation process. Generic, region-specific, and dimension-specific can be used to capture a multi-dimensional HRQL profile of those with CAI. The increased use of PROs is evident within the CAI literature by the increasing number of new studies[23,40,46,48,50,51,53,57-59,66-68] that are incorporating PROs within their protocols. Additionally, the International Ankle Consortium[69] has directed clinicians and scientists to include PROs within CAI research. While there are a variety of investigations that evaluate the effect of an intervention on HRQL in individuals with CAI, there is a lack of consensus regarding the impact of these treatments. At this time there is a need for a critical and systematic synthesis of the existing literature on HRQL changes following an intervention in those with CAI. A summation of the available literature will provide clinicians and scientists with concrete recommendation regarding which interventions produce meaningful patient-centered effects.

Response Shift Theory

Due to the increased emphasis on the inclusion of PROs throughout the rehabilitation process, there is a growing demand to ensure accurate evaluation of these outcomes. Accurate assessment of patient change is vital to the proper evaluation of patient progress throughout a rehabilitation program and to assist clinicians in making sound clinical decisions. The utilization of PROs to evaluate HRQL relies heavily on an individual's perception of their quality of life, function, disability and fears. The accuracy of PROs assessing these dimensions may be influenced by a concept known as “response shift” in which a patient reconceptualizes their condition during the rehabilitation process.[70] Response shift is described as a shift in an individual’s self-evaluation of a construct due to changes in internal standards of measurement (recalibration), changes in values (reprioritization), or a personal redefinition of a construct (reconceptualization).[70] Changes in values, standards or priorities throughout the rehabilitation process are hypothesized to lead to new conceptualization of PRO constructs which could lead to inaccurate determinations of HRQL alterations.[70] Consequently, response shift may interfere with the ability to detect change in a construct or PRO with accuracy.

The phenomenon of response shift has traditionally been evaluated in chronic, life threatening conditions where a patient’s physical health deteriorates, yet their self-reported HRQL remains stable.[71] Furthermore, the patients included in these evaluations have reported levels of HRQL that are similar to or higher than healthy controls.[70] Recently, response shift has gained attention as a possible phenomenon within chronic musculoskeletal conditions. Patients with arthritis,[72] spinal conditions,[73] rotator cuff tears,[74] and cartilage lesions in the knee[75] have all demonstrated response shift phenomenon following surgical management. Formal synthesis regarding the magnitude and direction of the aforementioned response shifts within musculoskeletal conditions has yet to be completed which limits the determination of response shift’s potential to impact clinical outcomes. Furthermore, at this time there are no evaluations regarding the potential response shift that may occur after conservative care. It is plausible that individuals with chronic conditions will experience response shift as conservative care improves their level of function. Individuals with CAI present a potential population to experience response shift after conservative care due to the chronic nature of the condition and the activity modifications associated with the condition.[16] The presence of response shift could affect true evaluation of an interventions efficacy and result in an impaired ability to make proper clinical decisions.

The Problem

After one ankle sprain, at least one in three individuals develop CAI.[76] CAI is associated with mechanical, functional, and HRQL impairments.[16,30,33] The staggering occurrence of CAI in combination with the myriad of impairments associated with the condition suggest that there is a need for efficient evidence-based interventions to modulate the consequences of developing CAI. Furthermore, these interventions should be focused on returning individuals to their previous level of function and improving their HRQL. Within this overarching problem, this dissertation plans to address two problem areas which contribute to advancing intervention delivery and outcomes collection for patients with CAI.

Problem 1

There are many factors that contribute to the continuum that is CAI.[13] These factors include ROM, strength, sensation, and postural control impairments.[13] Several interventions have been developed to target specific impairments individually such as joint mobilizations for DFROM deficits,[24,46,47] strength programs for strength deficits,[40,60,64] and balance training for postural control.[57-59] Each of these interventions has demonstrated the ability to improve the function of those with CAI from a clinical manifestation and patient-centered perspective when used in isolation.[40,45,59] However, there is a lack of a systematic synthesis regarding the overall effectiveness of the available CAI interventions to improve patient-oriented outcomes which would allow for definitive clinical recommendations. Additionally, the effectiveness of these interventions when used in concert has not been evaluated. The combination of these targeted evidence-based interventions may create a comprehensive approach that addresses a multitude of the factors that contribute to CAI. By targeting various factors a comprehensive intervention may generate a larger magnitude of change in HRQL and functional improvement in those with CAI then obtained from a single, targeted intervention strategy.

Problem 2

EBP is an emergent topic within healthcare. It incorporates clinical expertise, patient values and the best available evidence to develop individualized treatment plans for patients.[65] EBP has led to the increased use of patient-oriented outcomes, such as PROs, to aid in the clinical decision making process throughout rehabilitation.[65] As with any measurement tool, it is vital to ensure PROs accurately capture patient change as a result of the rehabilitation. If the PROs used to assess change do not accurately reflect the constructs they claim to measure then the precise evaluation of a rehabilitation program cannot be achieved. At this time there is some evidence that response shift occurs within many chronic orthopedic conditions undergoing surgical intervention.[72,74,75,77-81] However, there has been no systematic and critical synthesis of this evidence. Additionally, it is unclear if response shift occurs for patients with a chronic condition that undergoes conservative care such as those with CAI. It is essential to examine the potential for response shift in those with CAI following conservative care to ensure accurate assessment of patient-oriented outcomes.

Purposes

Based on the two identified problem areas, there were four purposes of this dissertation. The first purpose was to systematically review and meta-analyze the literature to examine the efficacy of current CAI interventions on HRQL. The second purpose was to systematically review the literature to examine the presence of response shift in patients with various musculoskeletal conditions after surgical intervention and or rehabilitation. The third purpose was to assess the effect of a 4-week comprehensive evidence-based intervention on disease-oriented outcomes in those with CAI. The fourth purpose was to assess the effect of a 4-week comprehensive evidence-based intervention on patient-oriented outcomes in those with CAI and determine if individuals with CAI who undergo this treatment experience response shift.

Experimental Aims and Hypotheses

Aim 1: To systematically review the literature to examine the efficacy of current conservative CAI interventions to improve patient-reported HRQL.

Hypotheses for Aim 1: Within the literature, there will be strong and consistent evidence that individuals with CAI will exhibit HRQL improvements following conservative intervention.

Aim 2: To systematically review the literature to examine the presence and magnitude of response shift following surgical intervention and/or rehabilitation in patients with various musculoskeletal conditions.

Hypotheses for Aim 2: Within the literature, there will be moderate and consistent evidence that response shift is exhibited in those with chronic musculoskeletal conditions following treatment.

Aim 3: Examine the effects of a 4-week comprehensive evidence-based intervention for individuals with CAI on:

a) Clinician-oriented measures of DFROM and dynamic postural control.

b) Laboratory-oriented measures of static postural control.

Hypotheses for Aim 3: Following a 4-week comprehensive intervention clinician- and laboratory-oriented measures will improve in those with CAI.

Aim 4: Examine the effect of a 4-week comprehensive evidence-based intervention on patient-oriented outcomes in those with CAI and determine if individuals with CAI who undergo this treatment experience response shift.

Hypotheses for Aim 4: Individuals with CAI will experience improvements in patient-oriented outcomes and response shift following a 4-week comprehensive evidence-based intervention.

Clinical Implications

Individuals with CAI suffer from a myriad of mechanical, functional, and HRQL impairments[13,39,43] as well as are at an increased risk for long-term consequences such as osteoarthritis.[14] Thus the creation and assessment of effective multimodal rehabilitation strategies to combat the impairments of CAI is paramount. Ultimately, the improved treatment algorithm will better modulate the patient- and disease-oriented impairments associated with CAI.

It is believed that there are a multitude of impairments that contribute to the functional deficits associated with CAI.[13] Currently, there is a lack of evidence regarding the effectiveness of a comprehensive rehabilitation protocol designed to target a myriad of contributing factors. The proposed dissertation would be the first to evaluate the efficacy of a comprehensive rehabilitation protocol that incorporates multiple evidence-based interventions. The multifaceted nature of the intervention has the potential to generate robust improvements in common mechanical and functional impairments as well as several facets of HRQL. This will provide strong evidence for the utilization of this comprehensive evidence-based intervention protocol for those with CAI and add to the treatment strategies for the condition.

The evaluation of response shift phenomenon within orthopedics has traditionally been evaluated in individuals with chronic conditions that undergo surgical intervention.[72,74,75,77-81] Similarly to these patients, individuals with CAI suffer from long-term and recurrent dysfunction due to their condition.[13,69] Such adaptions may repolarize individuals with CAI into believing their limited function is normal and provide the potential for response shift. The presence of response shift could lead to inaccurate estimates of HRQL changes and detrimentally affect the course of clinical treatment. By identifying the presence and magnitude of response shift in individuals with CAI, recommendations for use of these instruments in clinical practice can be made. Furthermore, the evaluation of and identification of response shift in those with CAI would be the first following conservative care. This investigation has the potential to be a catalyst for more accurate measurement of the patient's perspective of changes in function due to a more global recognition of response shift within orthopedic conditions.

Operational Definitions

Chronic Ankle Instability (CAI): A health condition characterized by the occurrence of repetitive bouts of giving way and instability resulting in numerous ankle sprains and functional loss that occurs following one or more ankle sprains.[13,69,82]

Disease-Oriented Measures: Outcomes that capture the physical manifestation of a condition (e.g. range of motion, strength) at the tissue/organ level.

Dimension-Specific Patient-Reported Outcomes: A PRO used to evaluate a specific health dimensions such as fear of re-injury or pain.[16]

Dorsiflexion Range-of-Motion (DFROM): A type of motion at the talocrural joint that occurs within the sagittal plane when the angle between the dorsum of the foot and the anterior lower leg is decreased.

Dynamic Postural Control: Attempting to maintain the body's center of mass within its base of support while a functional activity is completed.[83]

Evidence-Based Practice (EBP): An approach to clinical practice that incorporates the best available evidence, clinical expertise, and patient values to make clinical decisions.[65]

Generic Patient-Reported Outcomes: A PRO used to evaluate overall health and well-being.[16]

Health-Related Quality of Life (HRQL): A broad, multidimensional concept that refers to the self-reported assessment of physical, psychological, and social domains of health.[42,84] HRQL is often affected by individual experiences, expectations, and perceptions.[42,84]

Joint Mobilization: Is a manual therapy intervention where passive force is applied to a synovial joint. Mobilizations incorporate low-velocity, high-amplitude motions.

Laboratory-Oriented Measures: Outcome measures completed within the laboratory setting using instruments that are not commonplace in clinical practice (e.g. forceplate).

Patient-Oriented Measures: Outcomes that are based on the patient's perspective and self-evaluation of their wellbeing (e.g. PROs). These outcomes are of most importance to the patient.

Patient-Reported Outcomes (PROs): Questionnaires that ask patients to self-assess their function, injury, health status, and/or fear. PROs are categorized into three domains: generic, region-specific and dimension-specific.[16] These instruments are used to assess the impact of the health condition on the personal and societal domains of function.

Region-specific Patient-Reported Outcome: A PRO specific to a joint or body region.[16]

Response Shift: The change in the meaning of one's self-evaluation of a target construct as a result of recalibration, reprioritization, reconceptualization.[70]

Static Postural Control: Attempting to maintain the body's center of mass within its base of support while standing in a quite stance.[56]

Then-Test: A retrospective self-assessment of an individual's HRQL prior to an intervention that is completed after the completion of the intervention.[85]

Assumptions

The primary assumptions of this dissertation were the following:

For Chapter IV:

1. Subjects with a self-reported history of CAI had the condition of interest.
2. Subjects clearly understood and followed the instructions of all outcome measures.
3. Subjects provided honest answers and best effort when completing all outcome measures.
4. Changes in all outcome measures were related to ankle health and no other, unknown, unreported, or underlying causes.
5. All subjects were honest when reporting compliance with home and clinical interventions protocols.
6. Subjects did not receive other forms of rehabilitation during the study and maintained their normal level of physical activity throughout the study.

For Chapter V:

1. Assumptions 1-6 for Chapter IV.
2. Subjects recalled their pre-intervention function to the best of their ability.
3. Subjects were able to clearly understand and comprehend questionnaires.

Delimitations

For Chapter IV:

1. Subjects were males and females between the ages of 18-65 years of age.
2. Subjects were physically active.

   a. Qualified by a score of 24 or higher on the Godin Leisure-Time Exercise Questionnaire.

3. Subjects had self-reported CAI.
   a. Qualified by having a history of ≥1 ankle sprain, report ≥1 episodes of giving way in the past three months, answered "yes" to ≥ 5 questions on the Ankle Instability Instrument, ≤24 on the Cumberland Ankle Instability Tool.
4. Subjects had not sustained an ankle sprain six weeks and no other lower extremity injuries six months prior to enrollment or during enrollment.
5. Subjects had no history of lower extremity surgery or condition that could affect balance.

For Chapter V:

1. Delimitations 1-5 for Chapter IV.
2. The "then-test" method was used to test for response shift.
3. Subjects were able to complete questionnaires in English independently.

Limitations

For Chapter IV:

1. Relied on retrospective self-reporting to establish condition of CAI.
2. Individuals with bilateral CAI were included, preventing bilateral comparison.
3. The intervention was only applied to the limb of interest.
4. Subjects were not required to have specific deficits and an intervention tailored to those deficits.
5. Only the immediate and two week effects of the intervention were evaluated. The long term effects could not be established.

For Chapter V:

1. Limitation 1-5 for Chapter IV.
2. "Then-test" method was used to test for response shift. This method may be susceptible to recall bias.

CHAPTER II
REVIEW OF THE LITERATURE

The purpose of this chapter is to systematically review the literature regarding 1) the efficacy of conservative rehabilitation to enhance health-related quality of life (HRQL) in those with chronic ankle instability (CAI) and 2) to examine the phenomenon of response shift after rehabilitation for patients with orthopedic conditions. Chapter II Project IA, The Effectiveness of Rehabilitation for Improving Health-Related Quality of Life Detriments in Individuals with Chronic Ankle Instability: Meta-Analysis, critically appraises the literature to evaluate the efficacy of the current evidence-based interventions to enhance self-reported function of those with CAI. Chapter II Project IB, Examination of Response Shift After Rehabilitation for Patients with a Variety of Orthopedic Conditions: A Systematic Review, critically appraised the literature to evaluate the potential response shift that occurs within those undergoing care for orthopedic conditions. Overall, this chapter provides a synthesis of the literature regarding the enhancement of HRQL in those with CAI and the potential confounding of HRQL assessment in those undergoing care for orthopedic conditions due to response shift.

PROJECT IA: THE EFFECTIVENESS OF REHABILITATION FOR IMPROVING HEALTH-RELATED QUALITY OF LIFE DETRIMENTS IN INDIVIDUALS WITH CHRONIC ANKLE INSTABILITY: META-ANALYSIS

Introduction

Chronic ankle instability (CAI) is a condition characterized by residual symptoms following one or more acute ankle sprains.[13] These residual symptoms include episodes of "giving way," sensation of instability, recurrent ankle sprains, and functional deficits.[13] Acute ankle sprains, which provide the impetus for the development of CAI, are one of the most common orthopedic injuries as over 600,000 occur each year in the United States.[86] While ankle sprains are considered minor injuries with about 50% resolving within 7 days,[4] between 32 and 74% of sufferers will develop CAI.[10,11] This fact in concert with the commonality of ankle sprains creates a scenario for an enormous healthcare burden.[2,86] This burden is further exacerbated by the association between CAI and decreased physical activity levels[15] and increased risk of post-traumatic ankle osteoarthritis.[14] Therefore, there is a need for evidence-based rehabilitation interventions capable of mitigating the impact of CAI.

Conventionally, conservative rehabilitation for those with CAI has focused on addressing disease-oriented measures related to the mechanical and sensorimotor impairments that are the common clinical manifestations of this condition. However, the growing adoption of evidence-based practice (EBP) has emphasized the need to incorporate patient-oriented outcomes when evaluating the efficacy of an intervention.[65] Patient-oriented outcomes evaluate the patients' health status and the efficacy of a treatment based on the patient's perspective.[65] One of the essential aspects of patient-oriented outcomes is the evaluation of health-related quality of life

(HRQL), a multidimensional concept that incorporates physical, psychological and social domains and is often affected by individual experiences and perceptions.[42]
Patient-reported outcomes (PRO) are often utilized to capture individuals with CAI's perception of their health status. PRO instruments that assess ankle-specific function, overall health, and fear of re-injury have identified HRQL impairments within those with CAI compared to healthy individuals.[43] An array of investigations have also used PROs to examine the effects of rehabilitation for individuals with CAI to gain a patient-oriented perspective. Despite the multitude of investigations that have used PROs to assess the effects of rehabilitation, it is difficult to draw conclusions regarding the patient-oriented effects of these interventions as a wide variation of rehabilitation strategies and PRO instruments have been examined within the literature. To our knowledge, a comprehensive systematic review examining the effect of conservative rehabilitation on PROs in individuals with CAI has not been performed. The completion of a systematic review of the literature with a corresponding meta-analysis may offer a deeper understanding of the efficacy of the currently available CAI rehabilitation interventions to improve HRQL. Therefore, the purpose of this systematic review with meta-analysis was to collect, critically appraise, and provide a synthesis of the published evidence investigating the effect of CAI rehabilitation interventions on HRQL.

Methods

Search Strategy

The PRISMA guidelines were followed to perform a systematic search to locate studies that investigated the effect of a conservative rehabilitation intervention on PROs in those with CAI.[87] PubMed and EBSCO Host (CINAHL, MEDLINE, SportDiscus) were searched from their inception through January 27th, 2016. Electronic databases were searched using combinations of key words related to the research question (Table II.IA.1). Boolean operators “OR,” “AND,” and “NOT” were utilized to combine search terms and the search was limited to humans and manuscripts written in English. The reference list of articles screened during the systematic search were hand searched for additional publications. The constructed Boolean phrase, systematic search, and hand search were completed by two investigators (CJP, MCH).

Selection Criteria

The eligibility of articles obtained by the systematic search was determined by two authors (CJP, MCH) using the inclusion and exclusion criteria listed below. Initially, the titles and abstracts of all articles were screened for eligibility. When eligibility could not be determined during the initial screen, the full text of the manuscript was examined.

<u>Inclusion Criteria</u>

The following inclusion criteria were used to select and screen studies for inclusion into the systematic review:

- Articles in which the primary aim of the investigation was to examine the effect of a conservative rehabilitation intervention for individuals with CAI.
- Articles that included human participants described as having a history of at least one ankle sprain, classified as having CAI, functional ankle instability, mechanic ankle instability, or recurrent ankle sprains.
- Articles that utilized validated multi-item PROs to quantify the patient’s perceived change due to treatment.
- Articles that were peer-reviewed and full text.

<u>Exclusion Criteria</u>

The following exclusion criteria were used to screen studies for their inclusion into the systematic review:

- Articles that did not use validated PROs to assess self-perceived function pre and post a conservative rehabilitation program.
- Articles that did not report or provide sufficient data to calculate ESs (mean, standard deviation, etc.).
- Articles that evaluated treatments that included only the application of tape, braces, orthotics, or therapeutic modalities.
- Articles that evaluated the effect of an intervention immediately after a single application.
- Articles not published in English.
- Articles that were case-studies, case-reviews, editorials, commentaries, guidelines, or review articles.

Methodologic Quality

The Physiotherapy Evidence Database (PEDro) scale[88] was used to assess the methodologic quality of the included studies. This scale has demonstrated acceptable reliability (ICC=0.68).[88] The PEDro is a 10-items scale designed to determine the methodological quality of randomized-control trials by assessing their internal validity. Each item is scored as either a yes or a no. Studies that were scored with ≥60% of the PEDro items as yes were deemed high quality evidence.[30] Included studies were initially scored independently by two reviewers (CJP, MCH). Following independent scoring the two reviewers met to resolve any disagreements. If disagreements could not be resolved a third reviewer (JMH) was consulted. The percent agreement between the reviewers was calculated for each PEDro item. Studies were then classified into levels based on the Oxford Center of Evidence-Based Medicine levels of evidence.[89]

Data Extraction

During the initial review of the included studies, two independent reviewers (CJP, MCH) extracted data including: study aims, study designs, study quality, inclusion criteria, participant characteristics, clinician details, intervention procedures, outcome assessments, statistical techniques, conclusion and relevant methodological limitations. Discrepancies in interpretation were resolved by discussion until a consensus was achieved. If a consensus could not be achieved a third reviewer (JMH) was consulted.

The primary outcome of interest for this systematic review was PRO scores. Only pre- and post-intervention PRO scores were extracted for intervention groups. During the extraction of PRO scores Foot and Ankle Disability Index (FADI) Sport subscales identified in the literature were reported as Foot and Ankle Ability Measure (FAAM) Sport within this review. This was due to the two instruments being comprised of the same questions.

To further classify the included studies, a moderator variable was created to examine specific types of rehabilitation that are reported in the literature. The moderator variable *rehabilitation type* refers to the nature of interventions that were completed. Four levels were coded for rehabilitation type: balance training, manual therapy, strength training, and combination. Balance training rehabilitation type was used to describe studies that included rehabilitation protocols that involved tasks which challenged the subject's ability to maintain static or dynamic balance. Manual therapy studies investigated an intervention in which hands-on manual therapy techniques (e.g. mobilizations, massage) were applied to the lower extremity. Strength training studies investigated interventions primarily designed to strengthen the lower extremity. Finally, studies classified as combination utilized a combination of rehabilitation approaches where participants underwent conservative rehabilitation that included two or more of the above mentioned interventions. Studies included in this review may have incorporated multiple intervention groups within the study; therefore the outcomes were categorized according to the different rehabilitation types.

Statistical Analysis

Separate meta-analyses were performed for the overall effect and each rehabilitation type. For each meta-analysis, a random-effects model was used in which individual measures were pooled from the included studies using bias-corrected Hedges *g* effect sizes (ESs) and 95% confidence intervals (CI) to determine the magnitude of change in patient-oriented outcomes in those with CAI from pre-intervention to post-intervention. Hedges *g* ES is a unitless measure that is corrected for sample size to represent an effect that exists on a parametric distribution.[90] A positive ES indicated improved PRO scores at post-intervention from pre-intervention. In most studies, investigators used both the FAAM/FADI-ADL and the FAAM-Sport. When this occurred the values were pooled for analysis to reduce sample size inflation. Studies in which multiple rehabilitation types were examined, each group was treated independently within the analyses. All meta-analysis procedures were performed in Comprehensive Meta-Analysis (version 2.0; BioStat, Englewood, NJ). Effect sizes were interpreted as weak ($\leq$0.40), moderate (0.41-0.69), or strong ($\geq$0.70).[90] The alpha level was set *a priori* at $p < 0.05$. Further analysis of the data was performed via a qualitative assessment of effect-size estimates between rehabilitation types and determining if CIs crossed zero.

Assessment of Publication Bias

Assessment of the robustness of the observed overall effect on PRO change was completed using Orwin's fail-safe *N* test. This test determines the number of studies with trivial findings that would be needed to nullify the pooled ES of the included studies. A funnel plot of all included comparisons was generated to assess the likelihood of publication bias. To further assess publication bias, the trim-and-fill method of imputing missing studies was also used.

Level of Evidence

We assessed the grade of recommendation for the included studies using the approach described the Oxford Center of Evidence-Based Medicine.[91] This approach suggests using four levels of recommendation ranging from Grade A (strong evidence) to D (weak or conflicting evidence). A grade of recommendation of A is given when there are consistent high quality or level 1 studies. Consistent findings among moderate quality or level 2 or 3 studies are considered grade B evidence. Evidence from low quality or level 4 studies constitutes grade C evidence. Lastly, grade D evidence is quantified as inconsistent studies or level 5 evidence only.

Results

Literature Search

The initial search strategy identified 446 potential articles (Figure II.IA.1). Hand search of references identified an additional three potential articles. Of the 449 articles screened 399 were excluded based on title or abstract and 36 were excluded based on relevance or inadequate data reporting. Fifteen articles met the inclusionary criteria for this systematic review and provided 24 participant groups for analysis.[23,46,48,50,51,53,57-59,62,66-68,92,93] One participant group[50] was included after hand measuring the mean and standard deviation from a figure. The 15 articles were classified into the following categories based on rehabilitation type: balance training,[50,57-59,66,92] manual therapy,[23,46,48,53,93] and combination.[51,62,66-68,92] Strength training was not included as a rehabilitation type as only one study[62] investigated the isolated effects of a strength training protocol. Several participant groups were included in the analysis for each moderator variable: balance training (n=8), manual therapy (n=9), and combination (n=5). A methodologic summary of the included studies is presented in Table II.IA.2.

Methodological Quality

The two reviewers agreed initially on 141/150 (94.00%) of the PEDro items. All but one disagreement was resolved through discussion between the two reviewers. Overall, quality scores of the included studies ranged from 10.00% to 80.00% with a median of 50.00%. There were a total of seven high quality studies[23,53,57,67,68,92,93] and eight low quality studies.[46,48,50,51,58,59,62,66] Six studies were classified as level 1b evidence,[23,53,57,68,92,93] six as level 2b evidence,[50,51,59,62,66,67] and three as level 4 evidence.[46,48,68] The individual item, quality scores, and level of evidence can be found in Table II.IA.3.

Data Synthesis

Overall Summary Effect

Across all the included studies and subgroups, the overall effect of pre-intervention to post-intervention comparisons was 1.11 (95% CI = 0.76, 1.46; $p < 0.001$) indicating that those with CAI demonstrated strong improvements in HRQL following rehabilitation. The forest plot and table containing the individual ESs and the cumulative effect is presented in Figure II.IA.2 and Table II.IA.4.

Summary Effects for Rehabilitation Type

There were no differences between the three levels of rehabilitation type ($Q = 0.086$, $p = 0.958$) (Figure II.IA.3). Studies labeled as balance training demonstrated a strong effect with a CI that did not encompass zero (ES = 1.22; 95% CI = 0.79, 1.65; $p < 0.001$). Studies labeled as manual therapy demonstrated a strong effect (ES = 1.10; 95% CI = 0.09, 2.11; $p = 0.032$). Lastly, studies labeled as combined demonstrated a strong effect with a CI that did not encompass zero (ES = 1.14; 95% CI = 0.67, 1.60; $p < 0.001$).

Publication Bias

The likelihood of publication bias was assessed with a funnel plot (Figure II.IA.4). It is unlikely that publication bias played a role in the results of the meta-analyses based on the relative symmetry and even distribution of the studies within the funnel plot. This was further indicated via the trim-and-fill method as no studies were inputted or removed. The results of the Orwin fail-safe N test indicated that a range of 214 to 451 additional studies (based on a trivial effect range of Hedges *g* of 0.10 to 0.05) would be needed to nullify the overall summary effect. Based on the aforementioned results, the effect of publication bias is highly unlikely.

Sensitivity Analysis

<u>Overall Sensitivity Analysis</u>

The results of the one-study-removed method indicated that the overall ES remained strong and ranged from 0.94 to 1.16 (95% CI = 0.70, 1.52). All *p* values were < 0.001, which indicates no single participant group substantially influenced the overall summary effect.

<u>Rehabilitation Type Sensitivity Analysis</u>

The one-study-removed analysis for balance training and combination group indicated the ES remained strong and ranged from 1.01 to 1.35 (95% CI = 0.69, 1.77) and 1.00 to 1.25 (95% CI = 0.55, 0.73) respectively. All *p* values were < 0.001, which indicates there was no single ES that substantially influenced the overall summary effect for these groups. However, the one-study-removed analysis for manual therapy rehabilitation type indicated that the ES ranged from 0.44 to 1.30 (95% CI = -0.03, 2.46) and *p* values ranged from 0.002 to 0.056 with three of the seven *p* values indicating non-significance ($p > 0.053$). This indicates that a single participant group substantially influenced the ES for this rehabilitation type. When Cruz-Diaz et al[53] was removed the pooled ES dropped from 1.10 to 0.44 and the 95% CI was narrow signifying that this study had a significant influence on the pooled ES and subsequent recommendation.

Level of Evidence

Overall, there is Grade B evidence to support HRQL improvements in those with CAI following conservative rehabilitation. This recommendation is based on consistent findings from six level-1b,[23,53,57,68,92,93] six level-2b,[50,51,59,62,65,67] and three level-4[46,48,58] studies. For balance training, there is Grade B evidence to supports that this rehabilitation type improves HRQL based on consistent findings from two level-1b,[57,92] four level-2b,[50,59,66,67] and one level-4[58] studies. For manual therapy, Grade C evidence supports its efficacy to improve HRQL based on inconsistent findings from three level-1b[23,53,93] and two level-4[46,48] studies. For combination interventions, Grade B evidence supports its use to improve HRQL based on consistent findings from two level-1b[68,92] and four level-2b[51,62,66,67] studies.

Discussion

The purpose of this systematic review with meta-analysis was to determine the effect of different rehabilitation interventions on HRQL in individuals with CAI. After critically appraising and synthesizing the literature, our findings indicate that published rehabilitation strategies are effective at improving HRQL in subjects with CAI (Overall ES = 1.20). There is Grade B evidence to support this result as indicated by consistent findings from level 1 to level 4 evidence. Furthermore, the evidence suggests that balance training, manual therapy, and a combination of interventions can be used to improve patient-oriented outcomes. This indicates that any of these rehabilitation strategies could be used in clinical practice to improve HRQL in those with CAI.

Balance Training

We found Grade B evidence that a balance training rehabilitation protocol is effective at improving HRQL, as measured by patient-oriented outcomes, in individuals with CAI. Moderate-to-strong effects sizes (pooled = 1.22; range = 0.59 to 2.10) indicated improvement when pre-intervention outcomes were compared to post-intervention outcomes. Three[59,66,92] of the seven[50,57-59,65,67,92] studies were based on a program developed by McKeon et al.[59] These interventions were 4-weeks in length and involved progressive single-limb balance and hopping tasks. The remaining balance interventions[50,57,58,67] used progressive exercises with intervention lengths that ranged from 4 to 8 weeks. The largest ES was demonstrated by Cruz-Diaz et al[57] (ES = 2.10) who also had one of the longest intervention length (6 weeks). The lowest ESs (ES = 0.59 and 0.61) were from the only studies that employed a home-based balance training program.[58,67] These results in combination may imply that supervised balance training interventions may be more effective at improving HRQL, as measured by PROs, compared to non-supervised home-based programs.

Manual Therapy

Based on our systematic review with meta-analysis, we found Grade C evidence that a manual therapy focused intervention program was able to improve patient-oriented outcomes in patients with CAI.[23,46,48,53,93] This finding should be interpreted with caution however, as a single participant group substantially influenced the summary ES for this intervention type. With Cruz-Diaz et al[53] removed (ES = 5.41), the summary ES became moderate (ES = 0.44). Therefore, we believe it is more likely that there is moderate improvement in PROs following isolated manual therapy interventions.

The manual therapy techniques investigated included talocural anterior-to-posterior Maitland Grade III joint mobilizations,[46,53,93] Mulligan's talocural mobilizations-with-movement,[48,53] fibular manipulations,[23] and plantar massage.[93] Fibular manipulations demonstrated the weakest ESs (range = -0.03 to 0.23)[23] compared to the 4 studies[46,48,53,93] that investigated talocural mobilizations (range = 0.45 to 5.41). This indicates that manual therapy techniques that aim to improve talar mobility and positioning may be more effective, from the patient's perspective, when compared to the other manual therapy techniques. The talocural mobilization protocols that were included in this review ranged from 2-weeks[46,48,93] (ES = 0.45 – 0.86) to 3-weeks[53] (ES = 5.41) in duration with 3[48] (ES = 0.45) to 6[46,53,59] (ES = 0.64 – 5.41) mobilization sessions being completed during those time frames. Mobilizations-with-movement protocols varied as one[53] completed 2 sets of 10 repetitions and the other[48] employed 2 sets of 4 repetitions with 30 second holds at end range of dorsiflexion. Maitland mobilization techniques were implemented using 2[93] and 4[46] sets of 2-minute applications. Additionally, plantar cutaneous massage had a moderate effect on PROs (ES = 0.54).[93] This finding however was accompanied with 95% CI that crossed zero. Together, these results in combination indicate there is a continued need to determine the patient characteristics, manual therapy techniques, and treatment volume and dosage that optimize improvements in HRQL in those with CAI.

Combined Interventions

We found Grade B evidence that rehabilitation programs that employed two or more targeted interventions improved PRO measures in those with CAI. The summary effect (ES = 1.14) indicated that combined interventions had a strong effect on PROs from pre-intervention to post-intervention. The combined interventions included stretching,[51,66] strength training,[51,62,67,68] balance training,[51,62,66-68,92] vestibular-ocular reflex training,[92] soft-tissue mobilization,[66] dry needling,[68] and strain-counterstrain.[67] All, combined rehabilitation protocols included a balance training component with two[66,92] completing a balance training program based off McKeon et al[59] Five studies investigated the combined effect of two interventions[62,66-68,92] and two studies investigated the combined effect of three interventions.[51,68] Combined interventions demonstrated a slightly lower summary effect compared to isolated balance training. This may indicate that the addition of other interventions to balance training may not result in greater HRQL gains for those with CAI.

Practical Implications

The results of this systematic review with meta-analysis demonstrated that the available rehabilitation strategies are effective at improving ankle-specific PROs for those with CAI. This was indicated by a strong overall effect for the improvement of region-specific PROs, specifically the FAAM-ADL, FAAM-Sport, FADI, FADI-Sport, and Cumberland Ankle Instability Tool. Despite variations in rehabilitation strategy, dosage, and rehabilitation length, improvements were consistently demonstrated. Of the available rehabilitation strategies, supervised balance training programs demonstrated the greatest efficacy to improve PROs in those with CAI. This was true when balance training was used in isolation or in combination with other treatment modalities. Additionally, balance training used in combination with other rehabilitation strategies demonstrated similar summary effects as compared to isolated balance training. This indicates that supplementing balance training with other interventions may not further improve HRQL when compared to the isolate use of balance training.

Limitations of Review

Although this review was conducted based on the PRISMA guidelines[87] it is not without limitations. Our electronic search was conducted to find articles written in English within databases thought to be most relevant to journals that frequently publish articles relevant to CAI. Due to this it is possible that there may be articles relevant to this review that were not identified and included in this review. Additionally, there was limited evidence regarding the isolated effects of strength training interventions despite their common use in clinical practice. Due to this no recommendation could be made regarding the effect of strength training on HRQL. Lastly, individuals with CAI have reported decreased HRQL as measured using region-specific, dimension-specific, and global outcome measures.[43] Thus a multidimensional profile of HRQL should be used to evaluate the effectiveness of CAI rehabilitation strategies. The evidence presented in this review only included studies that used region-specific PROs due to limited evidence assessing other domains of HRQL. Future research should continue to examine the effects of common CAI rehabilitation strategies using a multidimensional HRQL profile to examine the effectiveness of these rehabilitation programs from the whole-person perspective.

While the included studies all used similar inclusion and exclusion criteria, history of ankle sprains and subsequent episodes of giving way, none of the studies implemented intervention protocols that were designed based off of clinician-oriented measured impairments. For all included studies in this review, the interventions were delivered using blanket procedures regardless of the presence of measureable deficits. This “cookie cutter” approach to CAI rehabilitation is contradictory to developing CAI treatment paradigms.[17] Donovan et al’s[17] rehabilitation paradigm suggests that CAI rehabilitation should be conducted using an assess, treat, and reassess model. They theorize that by treating individual-specific deficits, greater health improvements may be attained.[17] By focusing on deficits specific to the individual, clinicians may create an environment most conducive to achieving HRQL improvements from the patient's perspective. To promote patient-centered care and to mimic a realistic model of clinical care, CAI intervention research should look to adopt impairment based treatment paradigms. Furthermore, to mimic true clinical care there is a need for research to move away from laboratory based intervention studies to point of care research.

Conclusion

This synthesis of the available evidence suggests that several rehabilitation strategies effectively improve ankle-specific HRQL in individuals with CAI. Balance training demonstrated the highest Grade of evidence as well as the largest summary effect indicating that it may be the most appropriate rehabilitation strategy to improve HRQL in those with CAI. Furthermore, manual therapy may have a degree of clinical efficacy as an intervention to improve HRQL. Future research is needed to examine the isolate effects of other common rehabilitation strategies (i.e. strength training) to decipher how these strategies contribute to the overall treatment effect. Additionally, investigations should explore the efficacy of impairment based treatment paradigms on improving HRQL in individuals with CAI.

Table II.IA.1. Search Strategy

Step	Search Terms	Boolean Operator	EBDCO Host	PubMed
1	Chronic Ankle Instability Functional Ankle Instability Ankle Instability	OR	1,933	733
2	Rehabilitation Treatment Balance Postural Control Mobilization Strength	OR	2,875,934	7,288,050
3	Surgery Surgical	OR	1,885,167	2,404,068
4	1, 2	AND	624	577
5	3, 4	NOT	421	242
Duplicates				217*
Total Identified				446

*Total number of duplicates between EBSCO and PubMed.

Table II.IA.2. Methodologic Summary of the Included Studies

Author and Design	Sample Size/ Group	Subject Characteristics	Intervention	Intervention Frequency	Outcome Measures	Results
Hale et al 2007 RCT	29 CAI, 19 healthy CAI-Control = 12/13, CAI-Rehab = 13/16, Healthy = 17/19	Unilateral CAI, history of ankle sprain, chronic weakness/pain, episodes of giving way in last 6 months.	HEP/Supervised – gastrocnemius/soleus stretching, ankle strengthening, SL balance training. Supervised – box hops, carioca, figure of eight.	4-weeks, 6 supervised sessions, HEP 5 per week. Weeks 1/2=2 sessions a week, Weeks 3/4=1 session per week.	FADI (%) FADI-Sport (%)	Rehab had significantly greater FADI, FADI-Sport change scores compared to Control, Healthy
Mckeon et al 2008 RCT	31 CAI BT = 16/16, Control = 15/15	History of more than one ankle sprain, giving way, ≥4 "yes" on AII.	Progressive Dynamic Balance Training – hop to stabilization, hop to stabilization and reach, unanticipated hop to stabilization, single-limb stance with eyes open and close (20 min per session).	4-weeks, 12 supervised sessions (20min).	FADI (%) FADI-Sport (%)	BT had significantly greater post scores compared to pre and Control post.
Beazell et al 2012 RCT	43 CAI PTFM = 15/15, DTFM = 14/15, Control = 13/13	History of ankle sprain, episodes of giving way, <85% on FAAM-Sport or ≥3 "yes" on modified AII, 5° dorsiflexion deficit compared bilaterally.	Proximal tibiofibular joint manipulations - 1 to 2 thrusts per session. Distal tibiofibular joint manipulations - 1 to 2 thrusts per session.	3-weeks, 4 supervised sessions.	FAAM-Sport (%)	There were no significant changes in FAAM-Sport scores over time or compared to controls in the PTFM and DTFM groups

Table II.IA.2. Continued.

Author and Design	Sample Size/ Group	Subject Characteristics	Intervention	Intervention Frequency	Outcome Measures	Results
Hilgendorf et al 2012 RCT	16 CAI BT = 8/8, VOR = 8/8	History of ≥2 ankles sprains, ≥1 episode of giving way in last 6 months.	Progressive Dynamic Balance Training - with and without vestibular-ocular reflex training.	4 weeks, 12 supervised sessions.	FAAM-ADL (%) FAAM-Sport (%)	Significant improvements in the FAAM-ADL, -Sport from pre-to-post for both groups. No differences between groups were found.
Hoch et al 2012 Prospective Cohort	12 CAI	History of an ankle sprain, ≥2 episodes of giving way in past 3 months, ≥4 "yes" on AII, ≤90% on the FAAM-ADL, ≤80% on the FAAM-Sport.	Maitland grade II talocrural joint traction (2 sets of 2 min), Maitland grade III anterior-to-posterior talocrural joint traction (4 sets of 2min).	2 weeks, 6 mobilizations sessions.	FAAM-ADL (%) FAAM-Sport (%)	FAAM-ADL, -Sport significantly improved at post and 1 week follow-up compared to pre.
Schaefer and Sandrey 2012 RCT	36 CAI BT/GISTM = 13/15, BT/S = 12/15, BT/Control = 11/15	History of inversion ankle sprain, repeated injury, perception of giving way.	Dynamic flex-band stretching warm-up (10min), progressive dynamic balance training, GISTM.	4-weeks, 8 supervised sessions (45min).	FAAM-ADL (%) FAAM-Sport (%)	FAAM-ADL, -Sport significantly improved from pre-to-post for all groups.
Gilbreath et al 2013 Prospective Cohort	11 CAI	History of an ankle sprain, ≥1 episode of giving way in past 3 months, ≤25 on the CAIT, participate in physical activity 20 min a day 3 times a week.	Weight-bearing talocrural MWM (2 sets of 4 repetitions with 30s holds).	2-weeks, 3 mobilization sessions.	FAAM-ADL (%) FAAM-Sport (%)	Significant improvement in FAAM-Sport. No changes in FAAM-ADL.

Table II.IA.2. Continued.

Author and Design	Sample Size/ Group	Subject Characteristics	Intervention	Intervention Frequency	Outcome Measures	Results
Collins et al 2014 NRCT	36 CAI SCS = 13/13, Sham = 14/14	History of ankle sprain at least 3 months prior, ≥3 episodes of giving way in past year.	SCS of tender points of the pelvis and lower extremity (90s holds). HEP of strengthening and proprioceptive training.	4-weeks, 4 SCS or Sham sessions, 12 days of HEP.	FAAM-ADL (%) FAAM-Sport (%)	SCS and Sham groups both had significantly greater FAAM-ADL, -Sport scores post compared to pre.
Hale et al 2014 NRCT	34 CAI BT = 13/17, Control = 14/17	History of >1 ankle sprain, reported feeling of giving way.	Progressive Balance Training Program – dynamic and static single-limb stance activities. Program completed on stable ankle only.	4-weeks, 8 supervised sessions (30min).	FADI-ADL (%) FADI-Sport (%)	BT significant improved from pre-to-post on the FADI-Sport. No changes in FADI-ADL.
Kim et al 2014 RCT	30 CAI Strength = 10/10, Strength/PE = 10/10, Control = 10/10	Episodes of giving way as result of previous ankle sprain, ≤ 24 on the CAIT.	TheraBand ankle strengthening (10min), proprioceptive exercises involving SL balance and marching in place (10min).	4-weeks, 12 supervised sessions.	CAIT (score)	CAIT scores significantly improved in Strength and Strength/PE compared to control. Strength/PE significantly improved compared to Strength.
Cruz-Diaz et al 2015 RCT	70 CAI BT = 35/35, Control = 35/35	History of ankle sprain ≥6 months prior with subjective feeling of instability, <27 on the CAIT.	Individually tailored balance training –static single- or double-limb stance tasks. Control group completed general lower extremity strengthening program.	6-week, 18 supervised sessions.	CAIT (score)	Both groups had significant improvement in CAIT scores. BT significantly greater change score than control.

Table II.IA.2. Continued.

Author and Design	Sample Size/ Group	Subject Characteristics	Intervention	Intervention Frequency	Outcome Measures	Results
Cruz-Diaz et al 2015 RCT	90 CAI MWM = 29/30, Sham = 28/31, Control = 21/29	History of ankle sprain, ≥2 sprains on same side in last 2 years, feeling of giving way, >2cm WBLT asymmetry, no ankle sprain on contralateral side.	Weight-bearing MWM according to the Mulligan "no pain rule" (2 sets of 10 reps). Sham consisted of a fixed ankle while knee was flexed and extended (2 sets of 10 reps).	3-weeks, 6 supervised sessions.	CAIT (score)	Significant differences in the CAIT were found for MWM compared to control and sham at post-treatment and 6-month follow up.
De Ridder et al 2015 Case-Control	39 CAI, 31 Healthy BT = 33/39, Healthy = 31/31	History of ≥2 ankle sprains, one ankle sprain associated with 3-weeks of activity restriction, sensation of giving way, decreased functional participation, physically active.	Progressive balance training program – single-limb and some double-limb tasks. Tasks were progressed by changing arm position, visual status and surface.	8-weeks, 24 home balance sessions.	FADI (%) FADI-Sport (%)	Individuals with CAI indicated significantly higher FADI and FADI-Sport scores at post compared to pre balance training.
Salom-Moreno et al 2015 RCT	27 CAI BT/Strength = 13/13, BT/Strength/DN	History of ankle sprain, ≥1 episode of giving way in past 6 months, pain >3 points on an 11 point scale, and <26 on the CAIT.	Progressive theraBand ankle strengthening and balance training tasks. Trigger point dry needling to the lateral peroneus muscle.	8-weeks, 16 supervised sessions. DN completed over first 4 weeks, 8 sessions.	FAAM-ADL (%) FAAM-Sport (%)	Both groups significantly increased FAAM scores from base line with BT/Strength/DN increasing more.

Table II.IA.2. Continued.

Author and Design	Sample Size/ Group	Subject Characteristics	Intervention	Intervention Frequency	Outcome Measures	Results
Mckeon et al 2015 RCT	80 CAI Mobilization = 19/20, Massage = 19/20, Stretching, 18/20, Control = 19/20.	History of ≥2 episodes of giving way in past 6 months, ≥5 on the AII, ≤90% FAAM, ≤80% FAAM Sport.	Maitland grade III anterior-to-posterior talocrural joint mobilizations (2 sets of 2min). Petrissage and effleurage plantar massage (2 sets of 2min). Heel cord stretching with knee slightly bent (3 sets of 30s).	2 weeks, 6 supervised sessions.	FAAM-ADL (%) FAAM-Sport (%)	FAAM-ADL improvements following Massage and Stretching. FAAM-Sport improvements following Massage and Mobilizations.

RCT=Randomized Control Trial, NRCT=Non-Randomized Control Trial, CAI=Chronic Ankle Instability, BT=Balance Training, PTFM=Proximal Tibiofibular Manipulations, DTFM=Distal Tibiofibular Manipulations, VOR=Vestibular-Ocular Reflex, GISTM=Graston Instrumented Soft Tissue Mobilization, SCS=Strain-Counter-Strain, PE=Proprioception Exercises, MWM=Mobilization with Movement, DN=Dry Needle, AII=Ankle Instability Instrument, FAAM=Foot and Ankle Ability Measure, CAIT=Cumberland Ankle Instability Tool, WBLT=Weight Bearing Lunge Test, HEP=Home Exercise Program, SL=Single Leg, FADI=Foot and Ankle Disability Instrument

Table II.IA.3. PEDro Individual Items and Quality Index Scores for the Included Articles

Questions	Hale et al (2007)	Mckeon et al (2008)	Beazell et al (2012)	Hilgendo et al (2005)	Hoch et al (2012)	Schaefer et al (2012)	Gilbreath et al (2013)	Collins et al (2014)	Hale et al (2014)	Kim et al (2014)	Cruz-Diaz et al (2015)	Cruz-Diaz et al (2015)	De Ridder et al (2015)	Salom-Moreno et al (2015)	McKeon et al (2015)
1. Random Allocation	Yes	Yes	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	No	Yes	Yes
2. Allocation Concealed	No	Yes	No	Yes	No	Yes	No	No	No	No	Yes	Yes	No	Yes	Yes
3. Similar at Baseline	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
4. Blinding of all Subjects	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No
5. Blinding of all Therapists	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
6. Blinding of all Assessors	No	No	Yes	No	No	No	No	Yes	No	No	Yes	Yes	No	No	No
7. More than 85% of Follow-up	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes
8. Intention to Treat	No	No	No	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes
9. Between-Groups Statistical Comparison	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
10. Point Measures and Variability	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11. Eligibility Criteria Indicated	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Percentage of Yes (%)	5/10 = 50.00	5/10 = 50.00	6/10 = 60.00	6/10 = 60.00	4/10 = 40.00	4/10 = 40.00	4/10 = 40.00	7/10 = 70.00	3/10 = 30.00	4/10 = 40.00%	8/10 = 80.00	8/10 = 80.00	1/10 = 10.00	7/10 = 70.00	7/10 = 70.00
Level of Evidence	2b	2b	1b	1b	4	2b	4	2b	2b	2b	1b	1b	4	1b	1b

Table II.IA.4. Effect Size and 95% Confidence Intervals of Participant Groups

Study	Rehabilitation Type	Outcome	Hedges *g*	95% CI	*p* - value
Mckeon et al 2008	Balance	Combined	1.06	(0.35, 1.77)	0.004
DeRidder et al 2015	Balance	Combined	0.59	(0.11, 1.07)	0.017
Hilgendorf et al 2012	Balance	Combined	1.13	(0.16, 2.09)	0.023
Schaefer et al 2012	Balance	Combined	1.44	(0.56, 2.31)	0.001
Schaefer et al 2012 Sham	Balance	Combined	1.66	(0.78, 2.54)	< 0.001
Collins et al 2014 Sham	Balance	Combined	0.61	(-0.12, 1.33)	0.102
Hale et al 2014	Balance	FAAM-Sport	1.28	(0.45, 2.11)	0.003
Cruz-Diaz et al 2015a	Balance	CAIT	2.10	(1.53, 2.67)	< 0.001
Summary Balance			1.22	(0.79, 1.65)	< 0.001
Hale et al 2007	Combination	Combined	0.73	(0.01, 1.45)	0.047
Hilgendorf et al 2012	Combination	Combined	1.01	(0.06, 1.96)	0.038
Schaefer et al 2012	Combination	Combined	1.81	(0.94, 2.68)	< 0.001
Collins et al 2014	Combination	Combined	0.51	(-0.23, 1.25)	0.179
Salom-Moreno et al 2015 Dry Needle	Combination	Combined	1.54	(0.74, 2.34)	< 0.001
Salom-Moreno et al 2015	Combination	Combined	0.56	(-0.19, 1.31)	0.141
Kim et al 2014	Combination	CAIT	2.17	(1.14, 3.20)	< 0.001
Summary Combination			1.14	(0.67, 1.60)	< 0.001
Hoch et al 2012	Manual Therapy	Combined	0.86	(0.07, 1.65)	0.033
Gibreath et al 2013	Manual Therapy	Combined	0.45	(-0.35, 1.25)	0.269
Beazell et al 2012 Proximal	Manual Therapy	FAAM-Sport	-0.03	(-0.71, 0.65)	0.932
Beazel et al 2012 Distal	Manual Therapy	FAAM-Sport	0.23	(-0.47, 0.93)	0.518

Table II.IA.4. Continued.

Study	Rehabilitation Type	Outcome	Hedges *g*	95% CI	*p* - value
Cruz-Diaz et al 2015b	Manual Therapy	CAIT	5.41	(4.32, 6.50)	< 0.001
Mckeon et al Mob	Manual Therapy	Combined	0.64	(0.01, 1.27)	0.048
Mckeon et al 2015 Massage	Manual Therapy	Combined	0.54	(-0.09, 1.16)	0.095
Summary Manual Therapy			1.10	(0.09, 2.11)	0.032
Kim et al 2014		CAIT	1.03	(0.16, 1.90)	0.021
Mckeon et al 2015 Stretch		Combined	0.56	(-0.09, 1.20)	0.091
Overall Summary			1.11	(0.76, 1.46)	< 0.001

Figure II.IA.1. Flow Chart of Literature Review

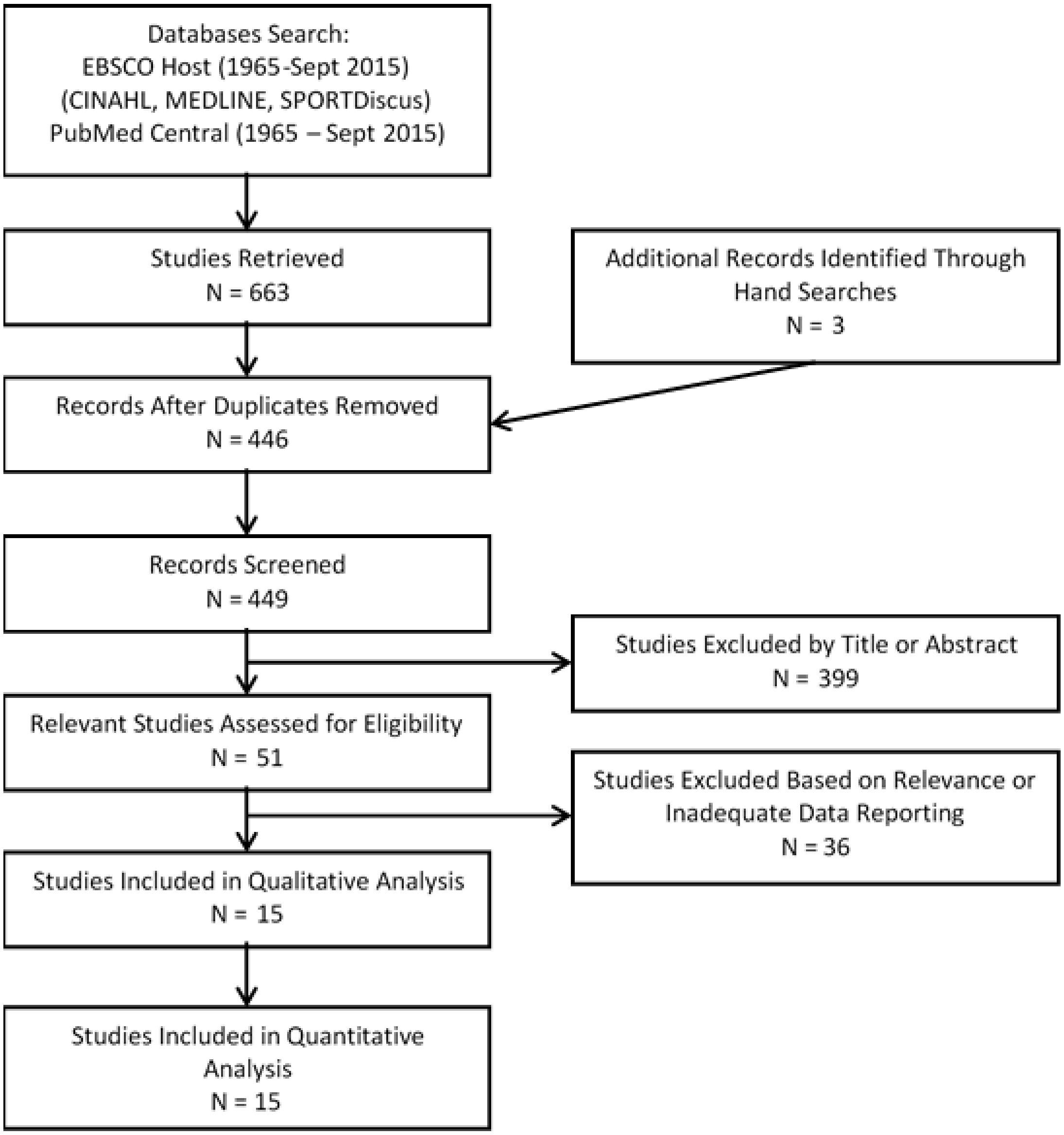


Figure II.IA.2. Summary of Hedges *g* Effect Sizes and 95% Confidence Intervals for the Included Participant Groups

Study	Rehabilitation Type	Outcome
Mckeon et al. 2008	Balance	Combined
DeRidder et al. 2015	Balance	Combined
Hilgendorf et al. 2012	Balance	Combined
Schaefer et al. 2012	Balance	Combined
Schaefer et al. 2012 Sham	Balance	Combined
Collins et al. 2014 Sham	Balance	Combined
Hale et al. 2014	Balance	FAAM-Sport
Cruz-Diaz et al. 2015a	Balance	CAIT
Hale et al. 2007	Combination	Combined
Hilgendorf et al. 2012	Combination	Combined
Schaefer et al. 2012	Combination	Combined
Collins et al. 2014	Combination	Combined
Salom-Moreno et al. 2015 Dry Needle	Combination	Combined
Salom-Moreno et al. 2015	Combination	Combined
Kim et al. 2014	Combination	CAIT
Hoch et al. 2012	Manual Therapy	Combined
Gibreath et al. 2013	Manual Therapy	Combined
Beazell et al. 2012 Proximal	Manual Therapy	FAAM-Sport
Beazel et al. 2012 Distal	Manual Therapy	FAAM-Sport
Cruz-Diaz et al. 2015b	Manual Therapy	CAIT
Mckeon et al. Mob	Manual Therapy	Combined
Mckeon et al. 2015 Massage	Manual Therapy	Combined
Kim et al. 2014	Strength	CAIT
Mckeon et al. 2015 Stretch	Stretch	Combined
OveralL Summary Effect		

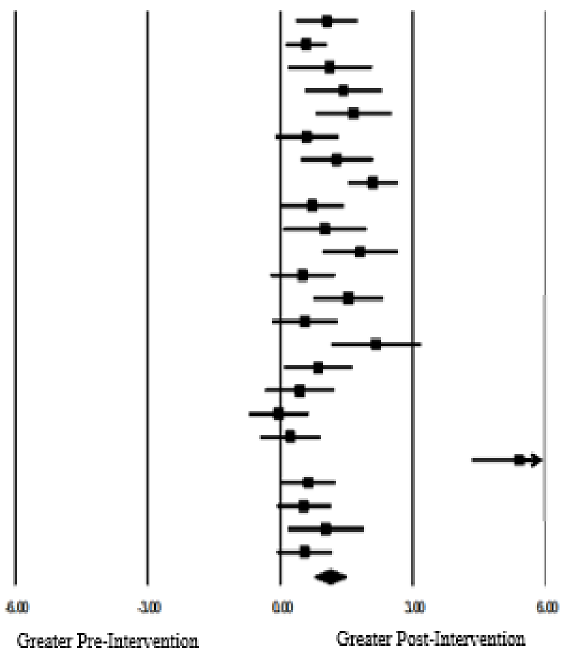


Figure II.IA.3. Summary of Hedges *g* Effect Sizes and 95% Confidence Intervals for Rehabilitation Type

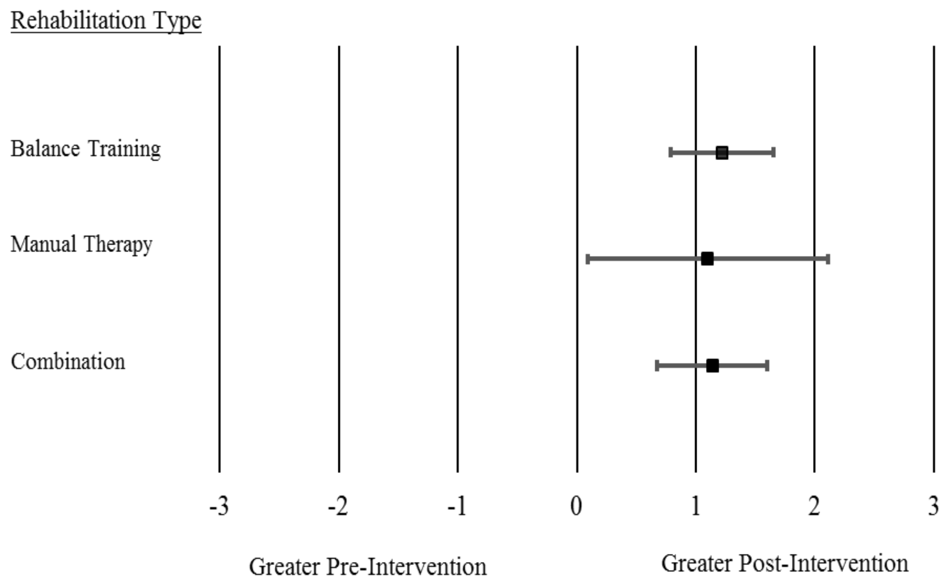
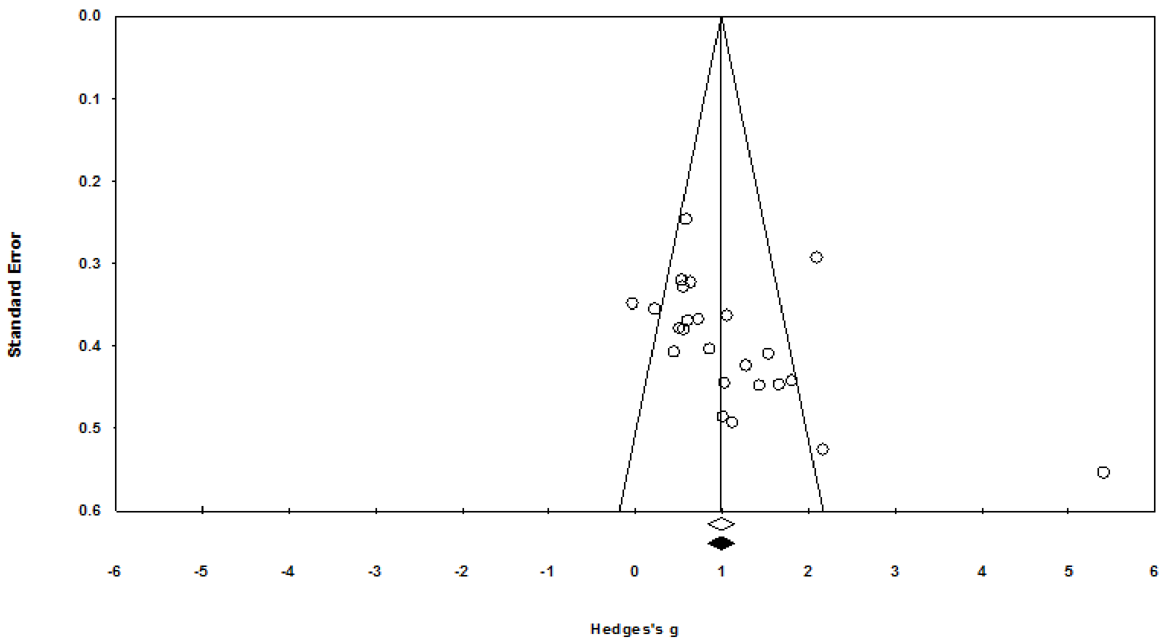


Figure II.IA.4. Funnel Plot Analysis for Publication Bias



PROJECT IB: EXAMINATION OF RESPONSE SHIFT AFTER REHABILITATION FOR PATIENTS WITH A VARIETY OF ORTHOPEDIC CONDITIONS: A SYSTEMATIC REVIEW

Introduction

The evaluation of change in patient status throughout and after the cessation of orthopedic rehabilitation is a vital component of healthcare. Traditionally, it has been common to document changes using disease-oriented measures such as range-of-motion or strength. While these measures are important to examine the effect of the health condition at the body function and structural level, these measures are often not meaningful to the patient and do not allow for the provision of patient-centered care. Patient-based outcomes are often used to assess the effect of the health condition on function at the personal and societal levels while examining concepts related to health-related quality of life (HRQL). There is an increased emphasis regarding the collection of patient-based outcomes to facilitate patient-centered care and quantify change in HRQL status from the patient's perspective.[65,70] HRQL is a broad, multidimensional concept that refers to the synthesis of physical, psychological, spiritual, economic and social domains of health that is affected by an individual's experiences, expectations, and perceptions.[70] Clinicians often measure HRQL through the utilization of a variety of patient-reported outcomes (PROs) which can be categorized as generic, region/disease-specific, or dimension-specific. Each of these instruments are constructed to measure different aspects of HRQL and the effects of the health condition and interventions on these aspects of HRQL, from the patient's perspective. The use of PROs to identify and categorize HRQL treatment responses is important because the measurement of patient perceived change, or lack of change, is key to the development of treatment algorithms and the provision of patient-centered care.[17]

The increased emphasis on PROs to capture HRQL and make clinical decisions that incorporate the patient's perspective suggests that there is an increased demand to ensure accurate documentation of these outcomes. Because the concept of HRQL is firmly rooted in the individual's perception, the commonly used measures automatically assume that the intra-individual standards remain stable throughout the rehabilitation process.[85] However, this may not be true, as it is reasonable to believe that patient values can change, particularly in cases where the condition is present for a prolonged period of time prior to intervention.[85] The change in the person's beliefs, values and experiences as it relates to the impact of the health condition on their function is often referred to as the Response Shift (RS) phenomenon.[70,71] Response shift phenomenon is when an individual's self-evaluation of a construct is altered due to changes in internal standards of measurement (recalibration), changes in values (reprioritization), or a personal redefinition of the construct (reconceptualization).[70,71] The changes in self-evaluation may be a direct or indirect result of the rehabilitation that the patient is receiving due to their health condition. The changes in an individual's values, standards, or priorities throughout the rehabilitation process are hypothesized to lead to new conceptualization of the constructs in which the PROs are used to measure. If a patient shifts their responses on the PROs due to this change, an inaccurate estimate of treatment effects may occur and unfavorable clinical decisions could be made.[70]

Response shift has been extensively evaluated in individuals with chronic, life-threatening conditions such as cancer.[71] Recently, there has been an increase in the number of studies which examine RS phenomenon in individuals with chronic musculoskeletal conditions. The studies have included patients with arthritis,[72] spinal conditions,[73] rotator cuff tears,[74] and cartilage lesions in the knee[75] whom have all demonstrated RS after surgical intervention and subsequent rehabilitation. However, formal synthesis of the aforementioned literature has not been completed to evaluate the magnitude of RS throughout orthopedic rehabilitation. The completion of a systematic review of the literature would improve our understanding of RS's effect on the evaluation of HRQL following orthopedic rehabilitation. Thus, the purpose of this systematic review was to compile, critically appraise, and synthesize the published evidence which investigated the presence of RS following orthopedic rehabilitation.

Methods

Search Strategy

A systematic search was conducted to locate studies which assessed RS after rehabilitation for an orthopedic condition.[94] Online databases were searched with a combination of key words related to RS and self-reported outcomes (Table 1). Boolean operators "OR" and "AND" were utilized to combine search terms and the search was limited to peer-reviewed, full-text manuscripts written in English.

Two investigators (CJP, JMH) derived the Boolean phrase and completed the systematic search. PubMed, EBSCO Host (CINAHL, MEDLINE, SportDiscus, Psychology and Behavioral Sciences Collection) were searched from their inception through April 14th, 2016. Additionally, the reference lists of articles screened for inclusion were hand searched for publications that were not identified through the electronic search.

Eligibility Criteria

Two authors (CJP, JMH) reviewed the articles identified by the systematic search for possible inclusion in the review. The titles and abstracts of all identified articles were screened for inclusion based on the criteria listed below. In cases of inclusion uncertainty, the full text of the manuscript was screened for inclusion.

Inclusion Criteria

The inclusion criteria used to select and screen studies for inclusion into the systematic review were as follows:

- Studies that aimed to examine the presence of RS in individuals with orthopedic conditions after an intervention.
- Studies that included human participants who underwent rehabilitation for an orthopedic condition.
- Studies that utilized PROs to quantify subjective change in HRQL. No restrictions were made to the type of PRO used in the study.

Exclusion Criteria

The exclusion criteria used to screen studies for their suitability for exclusion were as follows:

- Articles that did not report or provide sufficient data to calculate the magnitude and direction of RS following an intervention.[95]
- Articles that included subjects whose rehabilitation was not for an orthopedic condition such as spinal cord surgery, cancer treatment, or rheumatoid arthritis.[96,97]
- Articles not published in English.
- Articles that were case-studies or case-reviews.

Assessing Quality of Studies

Two reviewers (CJP, JMH) independently assessed the quality of each of the included studies using a 16-item version of the original Downs and Black Quality Index (DBQI).[30,98] The DBQI, developed to critically appraise both randomized and non-randomized studies, has demonstrated acceptable reliability and internal consistency.[98] Disagreements between reviewers were resolved by discussion or through a third reviewer (MCH). Studies that met ≥60% of the criteria were deemed high quality and those that meet <60% were considered limited quality.[30]

Data Extraction

Two reviewers (CJP, JMH) extracted data during the initial review which included: study aims, study design, participant details, intervention details, outcome assessments, RS technique, statistical technique, and conclusions. Discussion or a third reviewer (MCH) was used to resolve discrepancies in interpretations and achieve consensus. The evaluation of RS was further categorized based on type of PRO that was used to capture patient-perceived function and HRQL. The three categories of PROs used in the included studies were generic, region-specific, and other. Generic outcomes are designed to assess the patient's overall health and can be used to assess detriments to HRQL at the personal and societal level (eg., SF-36). Region-specific outcomes are designed to assess the effect of a health condition as it relates to function of a specific joint or region of the body (eg., International Knee Documentation Committee). Outcomes categorized as other either fell outside the scope of the region-specific, dimension-specific and generic or it could not be determined what aspect of health was evaluated.

Statistical Analysis

The magnitude of RS was examined through reported[77] and calculated Hedges *g* effect sizes[74,75,79-81] and standardized response mean effect sizes[72,99] with 95% confidence intervals (CI). Hedges *g* and standardized response mean effect sizes are unitless measures that represents the effect that exists on a parametric distribution.[90] For this analysis effect sizes were oriented so that positive effect sizes indicated that participants overestimated their disablement at their pretest assessment. Conversely, negative effect sizes would indicate that participants underestimated their disablement at their pretest assessment. Effect sizes were interpreted as weak (≤0.40), moderate (0.41-0.69), or strong (≥0.70).[90] To synthesize effect sizes across studies, point estimates for overall RS as well as generic, region-specific, and other outcomes were examined descriptively using mean, median, minimum, and maximum.

Level of Evidence

The quality of evidence was assessed using the Strength-of-Recommendation Taxonomy (SORT).[100] Level 1 evidence is considered good quality, patient-oriented evidence; Level 2 evidence is considered limited-quality, patient-oriented evidence and Level 3 is considered other evidence.[100] The strength of recommendation for the SORT considers a grade of A as consistent, good-quality patient-oriented evidence, B as inconsistent or limited-quality patient-oriented evidence and C as consensus, disease-oriented evidence, etc.[100]

Sensitivity Analysis

The effect of methodologic quality criteria on the strength of recommendation was tested by subjecting the quality of evidence scores, as assessed using the DBQI, to changes of ±10%.[101] After the scores were subjected to this change, the potential modification in the strength of recommendation was determined to assess the sensitivity of the overall recommendation.

Results

Literature Search

The flow of articles through the search and review process is illustrated in Figure 1. Of the 12 articles assessed for eligibility, eight[72,74,75,77,79-81,99] met the inclusion criteria for this systematic review. Of the 4 studies that were excluded, one study was excluded due to methodology that did not allow for RS effect size calculation,[95] one was excluded as it was a clinical commentary,[78] and two were excluded because of subject populations did not undergo rehabilitation for orthopedic musculoskeletal conditions.[96,97] A summary of study characteristics for all included studies can be found in Table 2.

Methodological Quality

The results of the quality assessment can be found in Table 3. The two reviewers initially agreed on 108 out of 128 (84.38%) items on the DBQI. All disagreements were resolved by discussion among the two reviewers. The overall quality scores of the included studies was a median of 72.52% and a range of 52.94% to 82.35%. Six[74,75,77,80,81,99] high quality (>60%) and 2[72,79] low quality studies were included. The recruitment component of the DBQI had a median of 100.00% (71.43-100.00%), the internal validity component had a median of 64.29% (42.86-85.71%), and the external validity had a median of 0.00% (0.00-50.00%).

Study Characteristics

The characteristics of the included studies are displayed in Table 2. In all studies, subjects underwent a surgical intervention and or rehabilitation program for an orthopedic condition. Interventions completed included autologous chondrocyte implantation,[75] total knee arthroplasty,[72,80,81] knee microfracture,[77] arthroscopic rotator cuff repair or decompression,[74] open rotator cuff repair,[74] lumbar spinal decompression surgery,[99] and unspecified rehabilitation for chronic low back pain.[79] The then-test method was used to evaluate response shift 6 weeks,[99] 3 months,[99] 6 months,[72,75,80] 12 months,[72,75] 18 months,[81] 24 months,[74] and an unspecified amount of time[77,79] after baseline. The then-test method involves participants retrospectively rating their pre-rehabilitation function at the completion of the rehabilitation process or at select time-points throughout the rehabilitation process.[102] The type of PRO used to capture the patients perception of their health and RS were categorized as generic,[72,75,81,99] regional,[72,74,75,77,80,99] and other.[77,79] None of the included studies used dimension-specific PROs.

Overall the included studies demonstrated a weak to negative strong effect size for RS with a mean of -0.46, median of -0.34 (range of -1.58 to 0.33). Of the 56-point estimates 20 (35.7%) were strong negative effect sizes, 4 (7.1%) were moderate negative, and 31 (57.1%) were weak negative or positive. Generic instruments demonstrated a weak to strong effect size for RS with a mean of -0.70, median of -0.79 (range of -1.31 to 0.19). Of the 24 generic point estimates 14 (58.3%) were strong negative effect sizes, 4 (1.7%) were moderate negative, and 6 (25.0%) were weak negative or positive. Region-specific instruments demonstrated a weak to strong effect size with mean of -0.28, median of -0.13 (range of -1.58 to 0.33). Of the 21 region-specific point estimates 5 (23.8%) were strong negative effect sizes and 16 (76.2%) were weak negative or positive. Other instruments demonstrated a weak to strong effect size with a mean of -0.28, median of -0.19 (range of -0.92 to -0.15). Of the 11 other point estimates 1 (9.1%) was a strong negative effect size and 10 (90.9%) were weak negative or positive. Individual effect sizes can be found in Table 4.

Level of Evidence

The results of the systematic review (Table 4) indicate there is Grade B evidence that a moderate RS, in which patients initially underestimated their disability, may occur in patients with orthopedic conditions undergoing care.[72,74,75,77,79-81,99] This recommendation is based on limited-quality Level 2 patient-oriented evidence. When further examining the results of this review according to PROs type; generic, region-specific, and other. There is Grade B evidence that a strong RS, in which patients initially underestimate their disability, may occur in patients with orthopedic conditions undergoing care when HRQL is measured using generic instruments.[72,75,81,99] Also, when evaluating response shift using region-specific PROs[72,74,75,77,80,99] or other instruments,[77,79] there is Grade B evidence that a weak RS, in which patients initially underestimate their disability, may occur. However, these values should be interpreted with caution. This is because effect sizes not only cross 0, indicating there is no effect, but also span from both negative to positive. This indicates that the individuals included in the studies were inconsistently identifying their then-test scores compared to their pre-test scores.

Sensitivity Analysis

The sensitivity analysis, where the criterion for study quality was subjected to a ±10%, did not affect the grade of recommendation for any of the analyses. Therefore the grade of recommendation is not affected by the quality of the included evidence.

Discussion

Summary of Results

The purpose of this systematic review was to critically synthesize the published evidence which investigated the presence of RS in orthopedic conditions who underwent rehabilitation. The review found that there is Grade B evidence that moderate RS (ES = -1.83 to 0.33) may occur in patients with orthopedic conditions undergoing rehabilitation. The nature of this RS was that patient's initially underestimated their disability prior to rehabilitation. This grade is indicated due to consistent findings from level 1 and 2 evidence. Furthermore, the presence of RS was strongest when HRQL was captured using generic PROs. While no recommendation is being made to utilize a then-test method to assess RS in routine clinical practice, these findings indicate that clinicians should be cognizant of RS when capturing HRQL during the rehabilitation process for orthopedic conditions.

Methodological Considerations

A wide range of orthopedic patient populations undergoing various types of care were included within this systematic review. Care ranged from total knee replacement[72,80,81] and autologous chondrocyte implantation[75] to chronic back pain rehabilitation[79,99] and rotator cuff tear repair.[74] All but one study[79] evaluated RS following a care plan that included surgical intervention.[72,74,75,77,80,81,99] These articles primarily indicated that patients underestimated their initial disability prior to care. The one study[79] that investigated RS during conservative care primarily reported weak ES indicating that a reconceptualization may not have occurred within their chronic low back pain population. It is believed that for RS to occur a catalyst is needed to change an individual's condition.[75] This may indicate that conservative rehabilitation alone was not a substantial enough catalyst to initiate RS. Further research is needed to understand the impact of care type and to examine if RS occurs following conservative care. Additional consideration should be made to the length of symptoms prior to care or surgical intervention. It is possible the length of symptoms followed by conservative care or surgical intervention in combination could serve as the catalyst for RS.

Regardless of the PRO type used to evaluate HRQL there was a trend toward orthopedic patients underestimating their disability prior to rehabilitation. Overall, a larger RS was demonstrated when HRQL was evaluated using generic PROs compared to region-specific and other PROs. This was indicated by greater ES for generic PROs (mean= -0.78) than region-specific (mean= -0.31) and other (mean= -0.28). From these findings it is reasonable to hypothesize that specific PRO types may be more susceptible to RS.[80] This may be due to the constructs evaluated within the varying PRO types. Generic PROs often focus on societal and personal factors of HRQL, whereas region-specific PROs focus on physical function of a specific body part. The focused concepts of region-specific PROs may provide greater context for patients, reducing room for varying interpretation and in turn reducing the potential for RS when compared to the global nature of the questions found on generic instruments. Future investigations should look to examine the effect of PRO type on the phenomenon of RS and include generic, region-specific, and dimension-specific instruments in their investigations.

Practical Implications

The results of this systematic review indicated that RS occurs in those with orthopedic conditions undergoing rehabilitation after surgery and or conservative care. This was reflected by mostly moderate to large ES supporting that individuals initially underrate their HRQL deficits prior to orthopedic rehabilitation. The notion of underestimating HRQL deficits was most notable when HRQL was captured using generic instruments, most commonly the SF-36, and some region-specific PROs. The presences of RS during orthopedic rehabilitation is noteworthy as it can affect the determination of HRQL changes due to the care provided to the patient. RS can inhibit a clinician's ability to accurately identify improvement or deterioration in HRQL and make the appropriate adjustments to the care provided.[102] Clinicians should be cognizant that RS has the potential to confound the determination of HRQL changes and employ strategies to combat its effects.[71] Howard et al[102] suggested that clinicians should evaluate an individual's frame of reference over the course of care in order assess RS that may alter a patients frame of reference. This could be completed through continual reevaluation of patient goals and expectations as to provide a standardized frame of reference throughout the rehabilitation process.[102] The implementation of then-tests, as used within the included studies,[72,74,75,77,79-81,99] may help clinicians identify potential confounding due to RS and to make proper clinical decisions.[102] Further research is needed however, to develop and validate clinical strategies to mitigate the potential effect of RS in order to enhance the ability to use PRO data in clinical decision-making.

Limitations of Review

This systematic review was not without limitation. The electronic search was conducted within databases thought to be most relevant to RS and orthopedics. It is possible that articles relevant to this review were not located within these databases and subsequently failed to be identified during the search. The articles included primarily focused on chronic orthopedic conditions undergoing a surgical intervention and a lengthy rehabilitation program. Due to this no recommendation can be made regarding the potential for RS during the conservative care of chronic or acute orthopedic conditions. Furthermore, factors such as length of symptoms, rehabilitation type, and the length of rehabilitation may all influence the potential for RS. Due to limitations in the reporting of these factors we were unable to assess the impact of these factors on RS in the included studies. Additionally, there was a lack of consistency in the data reported by the included studies, which limited the ability to complete a unified synthesis of the data. Future RS studies should place emphasis on providing consistent data reporting to facilitate comparisons between investigations. Lastly, there was a lack of literature regarding RS when HRQL is captured using dimension-specific PROs. Future research should examine the potential for RS within HRQL concepts such as fear and avoidance beliefs to examine the presence of RS within a multidimensional profile of HRQL.

Conclusion and Future Recommendations

There is grade B evidence that RS, in which individuals initially underestimate their disability, occurs in people undergoing rehabilitation for an orthopedic condition. The magnitude of RS was largest when HRQL was evaluated using generic PROs that are designed to assess a patient's overall health as well as detriments to HRQL at the personal and societal level. It is important for clinicians to be aware of the potential shift in their patients' internal standards as it can affect the evaluation of HRQL changes during the care of orthopedic conditions. This misclassification of HRQL changes can in turn adversely affect clinical decision-making. Clinicians can consider the use of a frame of reference standard when implementing the instruments in practice to abate some of these changes. At this time there is need for further research pertaining to RS as to provide clinicians with the tools to identify and disentangle the influence of RS on HRQL assessment.

Table II.IB.1. Search Strategy

Step	Search Terms	Boolean Operator	EBSCO Host	PubMed
1	Response Shift Recalibration Reprioritization Reconceptualization	OR	2,132	1960
2	Health-related quality of life Quality-of-life Self-reported Patient-Reported	OR	346,064	336,368
3	2 + 3	AND	253	253
Duplicates*				216
Hand Search				1
Total Identified				291

*Total number of duplicates between EBSCO and PubMed.

Table II.IB.2. Methodologic Summary of the Included Studies

Author	Sample	Subject Characteristics	Intervention	Data Collection Time Points	Response Shift Measurement	Outcome Measures	Results
Howard et al 2014	48 patients (29 male, 35±8.0yrs, 180.7±31.7cm, 92.4±20.3kg)	Inclusion: Planned ACI surgery to the knee, willingness to participate, and no uncorrectable contraindications to ACI. Exclusion: Undergoing concomitant meniscal transplant.	Two-step ACI procedure, standardized rehabilitation protocol following surgery.	Pre-operation, 6 months, 12 months	Then-test (6 and 12 months)	SF-36 PCS, WOMAC, IKDC, Lysholm	No significant group-level response shift for any of the outcome measures
Finkelstein et al 2014	169 patients (51.96±16.46yrs)	Inclusion: Undergoing posterior lumbar spinal decompression surgery for spinal stenosis or disc herniation. Exclusion: Unable to complete questionnaires in English, visual or cognitive impairments, disability that prevents independent completion.	Posterior lumbar spinal decompression surgery.	Pre-operation, 6 weeks, 3 months	Then-test (6 weeks, 3 months)	ODI, 8 subscales of the SF-36	Significant differences from in pre-operation and 6 week and 3 month then-tests for all outcomes but SF-36 MHS.
Zhang et al 2012	74 patients (14 male, 68[63-76]yrs)	Inclusion: Undergoing total knee replacement. Exclusion: Cognitive impairment, unable to speak English or Mandarin, undergoing additional surgery.	Total knee replacement surgery.	Pre-operation, 18 months	Then-test (18 months)	SF-6D, EQ-5D	There was a significant difference in then-test scores and pre-operation scores for both the SF-6D and EQ-5D.

Table II.IB.2. Continued.

Author	Sample	Subject Characteristics	Intervention	Data Collection Time Points	Response Shift Measurement	Outcome Measures	Results
Nagl and Farin 2012	189 patients	Inclusion: Chronic low back pain.	Unspecified rehabilitation	Pre- and post-rehabilitation	Then-test (post-rehabilitation)	Self-devised questionnaire with one question to address pain, mobility, activities, emotional well-being, knowledge, cognitive coping, behavioral coping, behavior, family, work. Based on FESV, ODI and SF-12.	Then-test scores were significantly less then pre-rehab scores. Indicating that response occurred.
Razmjou et al 2010	107 patients (66 males; 57±12yrs)	Inclusion: patients returning for 2-year follow-up after rotator cuff surgery, unremitting pain in shoulder for 6 months prior to surgery.	Arthroscopic decompression, arthroscopic rotator cuff repair, or open rotator cuff repair.	Pre-operation and 2 years	Then-test (2 years)	ASES (Pain, ADL)	Significant difference in pre-operation and then-test was identified in the pain domain of the ASES. No response shift occurred in the functional ability domain.

Table II.IB.2. Continued.

Author	Sample	Subject Characteristics	Intervention	Data Collection Time Points	Response Shift Measurement	Outcome Measures	Results
Razmjou et al 2009	236 patients (82 males, 67±10yrs)	Inclusion: candidates for total knee replacement arthroplasty.	Total knee replacement arthroplasty	Baseline, 6 months, and 1 year.	Then test (6 months, 1 year)	WOMAC, SF36-PCS, SF36-MCS	There were significant differences in baseline and then-test scores 6 month and 1 year for the WOMAC and SF36-PCS. Significant differences were identified at 1 year for the SF36-MCS.
Balain et al 2009	53 patients (36 males, 42[32-48]yrs)	Inclusion: undergoing knee microfracture surgery.	Knee microfracture surgery	Pre-test, >6 months	Then-test (mean 34 months)	VAS-Pain, Lysholm, IKDC-SA, IKDC-S	Significant differences in pre-test and then-test were identified in each instrument.
Razmjou et al 2006	125 patients (34 males, 68±9.5yrs)	Inclusion: individuals undergoing total knee replacement between November 2004 and October 2005. Exclusion: Previous total joint arthroplasty, required language translation, visual or cognitive problems, or were unable to complete questionnaires independently.	Total knee replacement arthroplasty	Pre-test, 6 months	Then-test (6 months)	WOMAC	Significant differences in pre-test and then-test were identified for the overall WOMAC score as well as pain and physical function domains.

FESV=Questionnaire to Assess Pain Processing Fragebogen Zur Erfassung der Schmerzverarbeitug, ASES=American Shoulder and Elbow Surgeons score, VAS=Visual Analog Scale, GH=General Health, WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index, IKDC=International Knee Documentation Committee, SA=Subjective Assessment, S=Symptom

Table II.IB.3. Downs and Black Quality Index for the Included Articles

Author	Quality Index Score, %	Reporting Score, %	Internal Validity Score, %	External Validity, %	Level of Evidence
Howard et al 2014	81.25 (13/16)	100.00 (7/)	57.14 (4/7)	50.00 (1/2)	2b
Finkelstein et al 2014	75.00 (12/16)	100.00 (7/7)	57.14 (4/7)	0.00 (0/2)	2b
Zhang et al 2012	81.13 (13/16)	100.00 (7/7)	71.43 (5/7)	0.00 (0/2)	2b
Nagl and Farin 2012	56.25 (9/16)	71.43 (5/7)	42.86 (3/7)	0.00 (0/2)	4
Razmjou et al 2010	81.25 (13/16)	100.00 (7/7)	71.43 (5/7)	0.00 (0/2)	2b
Razmjou et al 2009	56.25 (9/16)	71.43 (5/7)	42.86 (3/7)	50.00 (1/2)	4
Balain et al 2009	75.00 (12/16)	85.71 (6/7)	71.43 (5/7)	0.00 (0/2)	2b
Razmjou et al 2006	87.50 (12/16)	100.00 (7/7)	85.71 (6/7)	0.00 (0/2)	2b

Table II.IB.4. Effect Size and 95% Confidence Intervals for Included Point Estimates

Author	Participants (#)	Time Points	Outcome Measure	Effect Size	95% CI
Generic Patient-Reported Outcomes					
Howard et al 2014	ACI (48)	6 months	SF36-PCS	0.13	(-0.31, 0.56)
Howard et al 2014	ACI (48)	12 months	SF36-PCS	0.19	(-0.24, 0.62)
Finkelstein et al 2014	Lumbar Decompression (169)	6 weeks	SF36-PF	-1.31*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	6 weeks	SF36-RP	-0.64*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	6 weeks	SF36-BP	-1.30*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	6 weeks	SF36-GH	-0.67*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	6 weeks	SF36-V	-0.94*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	6 weeks	SF36-SF	-0.98*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	6 weeks	SF36-RE	-0.52*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	6 weeks	SF36-MH	-0.80*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	3 months	SF36-PF	-1.16*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	3 months	SF36-RP	-0.81*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	3 months	SF36-BP	-1.26*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	3 months	SF36-GH	-0.61*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	3 months	SF36-V	-0.98*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	3 months	SF36-SF	-0.82*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	3 months	SF36-RE	-0.78*	NR
Finkelstein et al 2014	Lumbar Decompression (169)	3 months	SF36-MH	-0.85*	NR
Zhang et al 2012	Total knee replacement (74)	18 months	SF-6D	-0.70	(-1.04, -0.36)
Zhang et al 2012	Total knee replacement (74)	18 months	EQ-SD	-0.96	(-1.32, -0.61)
Razmjou et al 2009	Total knee replacement (236)	6 months	SF36-PCS	-0.21*	NR
Razmjou et al 2009	Total knee replacement (236)	6 months	SF36-MCS	-0.04*	NR
Razmjou et al 2009	Total knee replacement (236)	12 months	SF36-PCS	-0.40*	NR
Razmjou et al 2009	Total knee replacement (236)	12 months	SF36-MCS	-0.31*	NR

Table II.IB.4. Continued

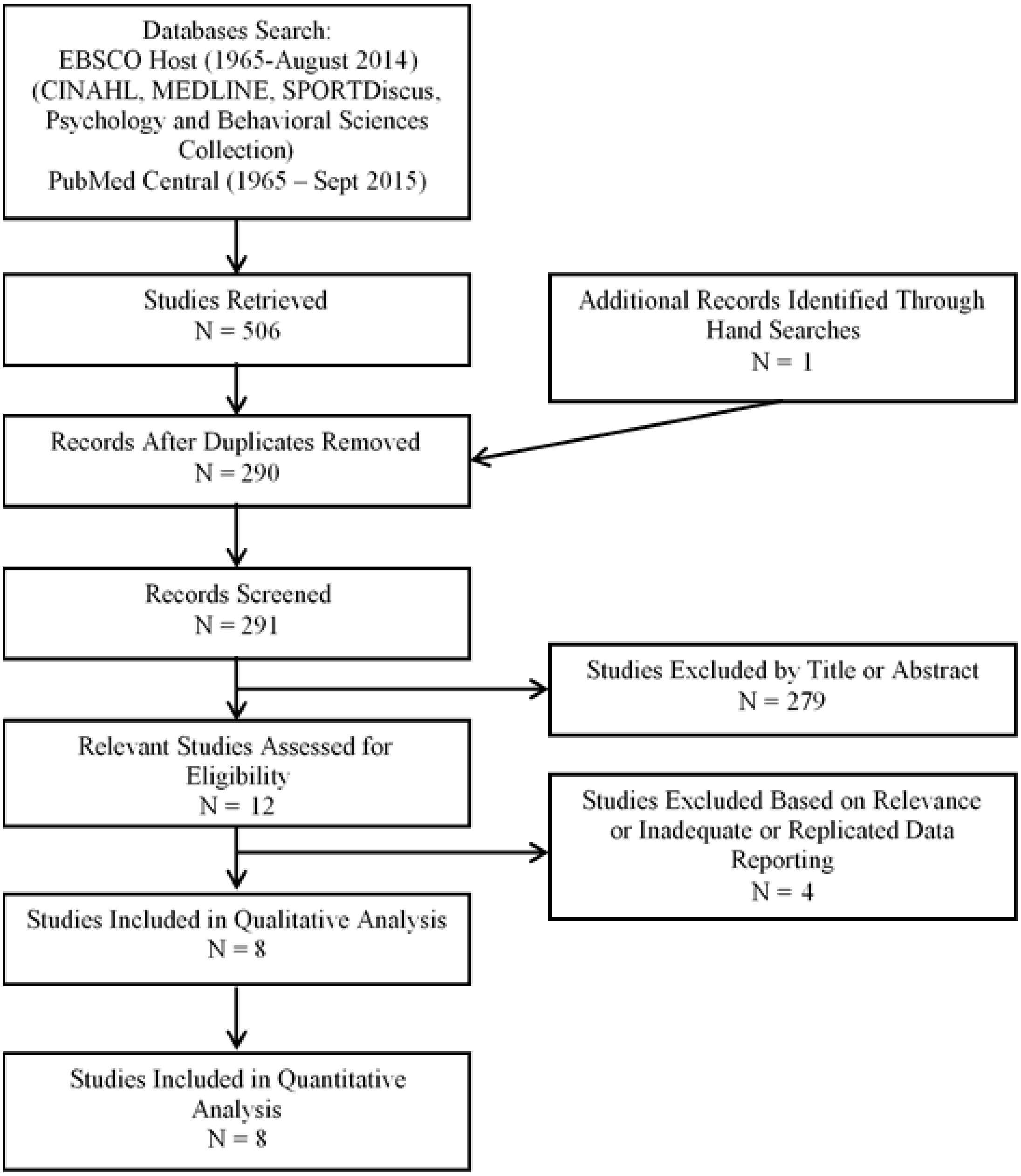
Author	Participants (#)	Time Points	Outcome Measure	Effect Size	95% CI
Region-Specific Patient-Reported Outcomes					
Howard et al 2014	ACI (48)	6 months	WOMAC	0.25	(-0.18, 0.68)
Howard et al 2014	ACI (48)	6 months	IKDC	0.11	(-0.32, 0.54)
Howard et al 2014	ACI (48)	6 months	Lysholm	-0.29	(-0.72, 0.15)
Howard et al 2014	ACI (48)	12 months	WOMAC	0.11	(-0.32, 0.55)
Howard et al 2014	ACI (48)	12 months	IKDC	0.08	(-0.35, 0.51)
Howard et al 2014	ACI (48)	12 months	Lysholm	-0.17	(-0.61, 0.26)
Finkelstein et al 2014	Lumbar Decompression (169)	6 weeks	ODI	-1.22*	(1.20, 1.92)
Finkelstein et al 2014	Lumbar Decompression (169)	3 months	ODI	-1.58*	(1.41, 2.13)
Razmjou et al 2010	RC Surgery, full tear (44)	24 months	ASES-Pain	-1.26	(0.80, 1.72)
Razmjou et al 2010	RC Surgery, full tear (44)	24 months	ASES-ADL	-0.13	(-0.55, 0.29)
Razmjou et al 2010	RC Surgery, partial tear (62)	24 months	ASES-Pain	-0.95	(0.57, 0.29)
Razmjou et al 2010	RC Surgery, partial tear (62)	24 months	ASES-ADL	-0.03	(-0.38, 0.32)
Razmjou et al 2009	Total knee replacement (236)	6 months	WOMAC	-0.32*	NR
Razmjou et al 2009	Total knee replacement (236)	12 months	WOMAC	-0.40*	NR
Balain et al 2009	Knee microfracture surgery (53)	6 months	Lysholm	0.33**	NR
Balain et al 2009	Knee microfracture surgery (53)	6 months	IKDC-SA	-0.71**	NR
Balain et al 2009	Knee microfracture surgery (53)	6 months	IKDC-S	-0.36**	NR
Razmjou et al 2006	Total knee preplacement (125)	6 months	WOMAC	0.19	NR
Razmjou et al 2006	Total knee preplacement (125)	6 months	WOMAC-Pain	0.18	(-0.05, 0.45)
Razmjou et al 2006	Total knee preplacement (125)	6 months	WOMAC-Stiffness	0.01	(-0.24, 0.25)
Razmjou et al 2006	Total knee preplacement (125)	6 months	WOMAC-Physical Func	0.22	(-0.03, 0.47)

Table II.IB.4. Continued

Author	Participants (#)	Time Points	Outcome Measure	Effect Size	95% CI
Other Patient-Reported Outcomes					
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Pain	-0.15	(-0.5, 0.38)
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Mobility	-0.16	(-0.04, 0.37)
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Activities	-0.16	(-0.05, 0.37)
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Emotional Well-Being	-0.19	(-0.02, 0.39)
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Knowledge	-0.36	(0.15, 0.57)
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Cognitive Coping	-0.30	(0.09, 0.51)
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Behavioral Coping	-0.29	(0.09, 0.50)
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Behavior	-0.20	(0.00, 0.42)
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Family	-0.18	(-0.03, 0.39)
Nagl and Farin 2012	Chronic low back pain (189)	Unknown	Work	-0.15	(-0.19, 0.31)
Balain et al 2009	Knee microfracture surgery (53)	6 months	VAS	-0.92**	NR

Effect sizes calculated as Hedges *g* unless otherwise noted
* Standardized Response Mean
** Effect size reported by article
ACI=Autologous Chondrocyte Implantation, RC=Rotator Cuff, FESV=Questionnaire to Assess Pain Processing Fragebogen Zur Erfassung der Schmerzverarbeitug, ASES=American Shoulder and Elbow Surgeons score, VAS=Visual Analog Scale, GH=General Health, WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index, IKDC=International Knee Documentation Committee, SA=Subjective Assessment, S=Symptom

Figure II.IB.1. Flow Chart of Literature Review



CHAPTER III

PROJECT II: THE EFFECTIVENESS OF A 4-WEEK COMPREHENSIVE INTERVENTION ON DISEASE-ORIENTED MEASURES IN THOSE WITH CHRONIC ANKLE INSTABILITY

Introduction

Ankle sprains are common orthopedic injuries experienced by physically active individuals as they accounting for 10 to 30% of all athletic injuries.[3] Additionally, 23,000 ankle sprains occur each day within the United States resulting in over $4 billion in annual aggregated healthcare costs.[1] The health and economic burden of ankle sprain may be more robust as up to 55% of individuals do not seek treatment from a medical professional.[6] This lack of reporting may be due to ankle sprains being considered innocuous injuries. A perception that has maintained although nearly 65% of individuals modify their physical activity for years following an initial ankle sprain.[7] Furthermore, roughly half of individuals with a history of an ankle sprain will develop CAI.[10,11] CAI is a condition characterized by residual ankle sprain symptoms, repetitive ankle sprains, and recurrent instability.[13] In addition to repeated bouts of acute trauma, CAI has been associated with an increased risk of ankle osteoarthritis, deficits in health-related quality of life, and decreased physical activity levels.[14,15,43] The immediate and long-term consequences of CAI highlight the need to develop interventions that address this complex and multifaceted condition.

Several mechanical and functional impairments may contribute to the residual symptoms, functional loss and decreased HRQL associated with CAI. Traditionally, these deficits have been evaluated using measures that capture physical impairment. Dorsiflexion range of motion (DFROM) deficits have been identified in as many as 74% of individuals with CAI.[103] DFROM restrictions have been associated with dynamic balance impairments,[46] another commonly cited deficit in those with CAI.[29,31] Static balance deficits have also been cited in individuals with CAI alluding to a general decrease in postural control.[29,31] Finally, ankle strength deficits have been commonly identified; particularly in the evertor muscle group of these individuals.[34] The wide range of impairments have led to the understanding that CAI is not merely the result of a single factor such as diminished proprioception, postural control or ligamentous laxity. Rather, individuals with CAI have displayed a myriad of factors that contribute to the development and progression of this condition.

Within the literature, intervention studies have focused on targeting isolated impairments, which has resulted in a number of rehabilitation strategies that are successful at improving a limited number of the aforementioned clinical deficits. For example, isolated joint mobilization interventions have been shown to improve DFROM as well as postural control.[45-49,53] Balance training programs have created improvements in static and dynamic postural control.[57,59] Additionally, ankle strengthening programs have created improvements in ankle strength.[40] A single study[51] has investigated a comprehensive rehabilitation protocol and identified improvements in postural control. While this study was more comprehensive by combining stretching, balance training, and strength training it failed to utilize the previously mentioned evidence-based protocols. Cumulatively, these studies demonstrate that many rehabilitation strategies can improve common clinical deficits within the CAI population. However, there is a need for an investigation that would evaluate the combined effects of these evidence-based interventions due to the myriad of factors that contribute to CAI.

The purpose of this study was to examine the efficacy of a 4-week rehabilitation program, which incorporated multiple evidence-based interventions, to enhance the common mechanical and functional impairments associated with CAI. We hypothesize that the comprehensive rehabilitation program would create statistically significant and clinically relevant improvements in DFROM, isometric strength, and dynamic and static postural control.

Methods

Design

This investigation employed an interrupted time-series design to examine the effect of a 4-week comprehensive intervention on disease-oriented outcomes for those with CAI. All participants completed four data collection sessions (baseline, pre-intervention, post-intervention, 2-week follow-up) and a 4-week intervention. The 4-week intervention consisted of 12 supervised sessions and a daily home exercise protocol. The independent variable was time (baseline, pre-intervention, post-intervention, and 2-week follow-up). The dependent variables were DFROM, isometric strength, and dynamic and static postural control.

Subjects

Twenty-two subjects with self-reported CAI (5 M; age = 24.91±7.33 yrs; height = 169.18±9.66 cm; weight = 70.62±12.27 kg) volunteered to participate in the study. Subjects were recruited using electronic and poster advertisements at a large public university over a 4-month period. Subjects were included if they were physically active (≥24 on the Godin Leisure-Time Exercise Questionnaire) adults (18-45yrs) with a history of ≥1 ankle sprain at least 6 months ago and ≥2 episodes of “giving way” in the past 3 months. Additionally, subjects had to answer “yes” to ≥5 questions on the Ankle Instability Instrument and ≤24 on the Cumberland Ankle Instability Tool (CAIT). In the case of bilateral CAI, the limb with the lower CAIT score was included in the study. Exclusion criteria consisted of an ankle sprain within the past 6 weeks, lower extremity injury within the past 6 months, history of lower extremity surgery and a condition that may affect balance. All subjects provided written informed consent in compliance with the institutional review board.

Testing Procedures

Upon enrollment, subjects completed the baseline and pre-intervention data collection sessions which were separated by 4 weeks of normal activity. Baseline and pre-intervention data were used to determine reliability and the minimal detectable change (MDC) for all dependent variables. Following the pre-intervention session, subjects began the 4-week intervention that consisted of both home and supervised exercise components. The post-intervention data collection session occurred within 48 hours of the intervention's cessation. Additionally, a follow-up session occurred two weeks after the post-intervention data collection session (2-week follow-up). During each data collection session dependent measures, DFROM, isometric strength, and dynamic and static postural control, were collected in a counterbalanced order using a Latin Square. This order was maintained across all data collection sessions for each subject. One athletic trainer with 5 years of experience completed all data collection sessions. Three athletic trainers with 5-10 years of experience conducted the interventions.

Dorsiflexion Range of Motion

The weight-bearing lunge test (WBLT), an assessment that has previously identified dorsiflexion improvements following interventions,[45,46,93] was performed to measure ankle dorsiflexion. The WBLT was completed using the knee-to-wall principle in which subjects kept their involved heel firmly planted on the floor while they lunged forward to bring their knee to the wall.[104] The uninvolved limb was positioned in a comfortable position that allowed subjects to maintain stability. When the subject was able to maintain heel and knee contact, they were progressed away from the wall. If subjects could no longer maintain both heel and knee contact while lunging they were progressed closer to the wall. Maximum DFROM was indirectly measured as the distance (cm) from the great toe to the wall based on the furthest distance the foot was able to be placed without losing heel and knee contact.[104] Subjects performed one practice trial followed by three analysis trials on the involved limb that were averaged for analysis. The WBLT has demonstrated high test-retest reliability (ICC=0.80-0.99) and an average minimal detectable change (MDC) of 1.9 cm.[104]

Dynamic Balance

Dynamic balance was measured using the of the Y-Balance test (Professional Y-Balance Test Kit, Functional Movement Systems, Inc., Chatham, VA).[105] After verbal instruction and demonstration participants stood on the center of the footplate, with the great toe of the involved limb at the starting line. While balancing on the involved limb, the subject reached with the uninvolved limb in the anterior (ANT), posteromedial (PM), and the posterolateral (PL) directions by pushing the indicator box as far as possible. Subjects completed four practice trials followed by three collection trials in the ANT direction, followed by the PM, and then the PL direction. Collection trials were discarded and repeated if the subject failed to maintain balance, removed hands from hips, used the reach indicator for support, kicked the indicator, or failed to return the uninvolved limb to the starting position. Collection trials were averaged and normalized to leg length for analysis (%). The Y-Balance test has demonstrated high test-retest reliability in the ANT (ICC=0.93), PM (ICC=0.91), and PL (ICC=0.85) directions.[105]

Static Balance

One practice and three collection trials of quiet single limb stance on a forceplate was used to assess static postural control during eyes open and closed conditions.[106] Prior to assessment, each participant's foot was measured and meticulously centered on the forceplate.

Subjects were instructed to stand quietly with their hands on their hips and their uninvolved limb positioned at 45° of knee flexion and 30° of hip flexion during each 10s trial. If participants were unable to maintain the stance position for the entire 10s, touched down, or opened eyes during eyes closed trials the trial was discarded and repeated. For analysis, center of pressure data was separated into its anterior-posterior (AP) and medial-lateral (ML) components and analyzed separately as time-to-boundary (TTB) using a custom MatLab code (Version R2015a, MathWorks Inc., Natick, Massachusetts).[106] The TTB variables included the mean of TTB minima (TTB-mean) and the standard deviation of TTB minima (TTB-SD) in both the AP and ML directions, which estimate the time available to make a postural control correction and the number of solutions available to maintain postural control respectively. TTB variables have demonstrated poor to good test-retest reliability (ICC=0.34-0.69).[106]

Isometric Strength

A handheld dynamometer (MicroFET2™, Hoggan Health Industries Inc., West Jordan, UT) was used to assess DF, plantarflexion (PF), inversion, and eversion isometric strength at the ankle as well as hip abduction, adduction, flexion, and extension.[107] All procedures were conducted based on previous methods found to have high test-retest reliability (ICC=0.77-96).[107] For all strength tests subjects were instructed to ramp into a 3 second maximal effort contraction with the examiner applying resistance. Peak forces were recorded to the nearest 0.1 N. One practice trial followed by 3 collection trials were recorded, normalized to body weight, and averaged for analysis for each motion.

Intervention

The 4-week rehabilitation program consisted of home and laboratory components completed on the involved limb. The home intervention was completed daily and consisted of gastrocnemius-soleus complex (GSC) stretching and ankle strengthening. The laboratory component involved 12 sessions in which talocrural joint mobilizations, balance training, and ankle strengthening were completed. All components of the home and laboratory intervention were based on previously established rehabilitation programs for those with CAI.[40,46,59] During laboratory interventions subjects were reminded and refreshed regarding the home intervention procedures. Interventions and instructions were executed by athletic trainers with a minimum of 5-years of clinical experience. Prior to the initiation of the study the lead investigator held a training session to promote treatment consistency.

Home Intervention

The GSC stretching component consisted of three sets of 30-seconds of stretching on a half foam roller with the knee in full extension as well as three sets slight knee flexion. These stretches were selected as to target both the gastrocnemius and soleus muscles. Subjects were instructed to hold stretches at the point of mild discomfort. Strengthening exercises for DF, PF, inversion, and eversion of the ankle were completed using Thera-Band resistance bands (Thera-Band®, The Hygenic Corporation, Akron, OH).[40] The number of sets completed were 3, 4, 3, and 4 for weeks 1, 2, 3, and 4 respectively with 10-repetitions completed per set. Subjects used a Blue, heavy resistance band during the first 2 weeks and a black, special heavy resistance band during the last 2-weeks of the intervention. All subjects were provided instructions, demonstrations, half foam roller, Thera-Band, and an intervention journal prior to leaving the laboratory after the pre-intervention data collection session. The intervention journal was used to track compliance with the home intervention program.

Laboratory Intervention

Joint mobilizations consisted of 4, 2-minute sets of Maitland Grade III anterior-to-posterior talocrural joint mobilizations with 1-minute of rest between sets.[46] During joint mobilization treatments, subjects were supine with the involved ankle off of a plinth. The investigator stabilized the distal tibia and fibula with one hand and directed force posteriorly over the talus with the opposite hand. Large amplitude, 1-second oscillations from the joint's mid-range to end-range of accessory motion were applied.[46] The balance training program consisted of activities designed to challenge single-limb balance after perturbation.[59] Five activities were implemented that progressively increased in difficulty as the subject became proficient at the task. The activities included: hop to stabilization, hop to stabilization and reach, hop to stabilization box drill, static single-limb stance balance activities with eyes open and with eyes closed.[59] Lastly, a slow-reversal PNF technique comprised of concentric contraction of the antagonist muscle followed by a concentric contraction of the agonist muscle was used to strengthen the ankle in the D1 and D2 patterns.[40] Manual resistance and stabilization was applied by the investigator. Subjects completed 3 sets if 10 repetitions during the first 3 intervention sessions, 4 sets of 10 repetitions during the 4^{th} through 6^{th}, 3 sets of 15 repetitions during the 7^{th} through 8^{th}, and 4 sets of 15 repetitions during the last three intervention sessions.

Statistical Analysis

For each dependent variable minimal detectable change (MDC) scores were calculated to determine the minimal change required to achieve change beyond the error of the measurements. Intraclass correlation coefficients (ICC 2, 1) and the standard error of measurement (SEM) from the data collected during the baseline and pre-intervention sessions were used to calculate MDC scores. The formula SEM x $\sqrt{2}$ was used for MDC scores calculation.[108]

Separate one-way ANOVAs were used to examine differences in the WBLT, each normalized reach direction on the Y-Balance, and for each isometric strength motion over time (pre-intervention, post-intervention, 2-week follow-up). Additionally, separate 2 x 3 ANOVAs were used to assess change in each TTB variable over time for each visual condition (open, closed). Sidak post hoc comparisons were completed in the presence of significant main effects or interactions. The significance level for all analyses was set *a priori* at $p < 0.05$. Standardized response mean effect sizes (ES) and corresponding 95% confidence intervals (CI) were calculated for each dependent variable.[109] A positive ES indicated improvement following the intervention. ES were interpreted as weak (≤0.39), moderate (0.40-0.69), and strong (≥0.70).[110]

Results

Baseline characteristics of the included subjects can be found in Table II.1. Of the 22 individuals enrolled in the study, 20 completed the study in its entirety. Due to unrelated injury, the 2 subjects that did not complete the study self-withdrew during the intervention phase. Due to the high completion rate an intention to treat analysis was not performed and data were simply removed from the analysis for the subjects that did not complete the study. Table II.2 displays means (± standard deviations), change scores, and MDCs for all analyses.

Intervention Compliance

Overall subjects were 91.86% compliant with the home-based intervention. Specifically, subjects completed on average 92.74% of the home stretching and 91.48% of home strengthening. The lowest individual level of compliance with either portion of the home-based intervention was 74.49%. Overall, there was a 97.50% laboratory-based session completion rate as all but 2 subjects completed every session. The subjects that failed to complete each session completed 11 and 7 out of 12 sessions. Lastly, one subject completed a modified balance training program consisting of only the static balance and reaching components due to muscle soreness and injury-related fear with the hopping tasks. The study acquired an overall balance training completion rate of 95.11%.

Statistical Results

A significant time main effect was found for the WBLT ($p < 0.001$). Post hoc analysis revealed that post-intervention ($p < 0.001$) and 2-week follow-up ($p < 0.001$) were significantly improved compared to pre-intervention. These differences exceeded the MDC (Table III.2.) and were associated with large ES that had CIs that did not cross zero (Figure III.1.). No differences were identified between post-intervention and 2-week follow-up ($p = 0.348$).

Significant main effects were found for each reach direction of the Y-Balance test ($p < 0.001$). The ANT, PM, and PL reaches of the Y-Balance test were all significantly improved at post-intervention ($p < 0.001$) and 2-week follow-up ($p < 0.001$) compared to pre-intervention. These differences exceeded the MDC (Table III.2.) and were associated with large ES that had CIs that did not cross zero (Figure III.1.). No significant differences were identified between post-intervention and 2-week follow-up ($p > 0.603$).

Significant main effects were found for each ankle strength direction ($p < 0.004$). Post hoc analysis revealed significant improvements in inversion, eversion, DF, and PF strength at post-intervention ($p < 0.015$) and 2-week follow-up ($p < 0.014$) compared to pre-intervention. These differences exceeded the MDC (Table III.2.) and were associated with ES that had CIs that did not cross zero (Figure III.1.). No significant differences were identified between post-intervention and 2-week follow-up ($p > 0.083$).

Significant main effects were found for each hip strength direction ($p < 0.038$). Post hoc analysis revealed significant improvements at post-intervention compared to pre-intervention for adduction ($p = 0.012$), flexion ($p = 0.033$), and extension ($p = 0.003$). Additionally, significant improvements were identified at 2-week follow-up compared to pre-intervention for abduction ($p = 0.001$), adduction ($p < 0.001$), and extension ($p = 0.002$). All significant differences exceeded the MDC (Table III.2.) and were associated with large ES that had CIs that did not cross zero (Figure III.1.). No significant differences were found between post-intervention and 2-week follow-up ($p > 0.542$).

Significant vision main effects were found for all TTB variables ($p < 0.001$). Significant time main effects were found for TTB MM-AP ($p = 0.008$ and TTB SD-AP ($p = 0.012$). Significant vision by time interaction was found for TTB MM-AP ($p = 0.007$) and TTB SD-AP ($p = 0.037$). No other significant main effects or interactions were found ($p > 0.054$). Post hoc analysis revealed that during eye open conditions TTB MM-AP significantly increased at 2-weeks compared to pre-intervention ($p = 0.002$) and post-intervention ($p = 0.003$) when vision was pooled. These changes exceeded the MDC (Table III.2.) and were associated with large ES that had CIs that did not cross zero (Figure III.1.). Additionally, during eyes open conditions TTB SD-AP significantly increased at 2-weeks compared to pre-intervention ($p = 0.013$) and post-intervention ($p = 0.012$). These changes did not exceed the MDC (Table III.2.) and were associated with moderate ES that had CIs that did not cross zero (Figure III.1.). No other significant post hoc differences were identified ($p > 0.313$).

Discussion

We hypothesized that a 4-week comprehensive rehabilitation program would create statistically significant and clinically relevant improvements in DFROM, isometric strength, and dynamic and static postural control. Our findings supported this hypothesis as we found significant improvements in all outcome measurements, except for TTB MM ML and TTB SD

ML, following the 4-week comprehensive rehabilitation program. Improvements in DFROM, dynamic strength, and almost all isometric strength measures were maintained 2-weeks following the completion of the intervention. Additionally, improvements surpassed the MDCs of the outcome measures and were also associated with primarily large ES (>0.61) indicating that these are clinically meaningful changes. Interestingly, static balance improvements were only identified at the 2-week follow up session. Cumulatively, our results suggest that a 4-week comprehensive rehabilitation program can be used to improve common mechanical and functional insufficiencies associated with CAI.

Dorsiflexion restrictions are one of the most common impairments associated with CAI.[111] Clinically, the enhancement of DFROM is thought to be a primary goal of CAI rehabilitation as it could improve structural adaptions and enhance functional movement patterns.[24,111] We found significant improvements in DFROM as measured with the WBLT immediately following our comprehensive rehabilitation as well as at 2-weeks ($p < 0.001$). These improvements were associated with large ES (post=1.29, 2-weeks=1.27) and change scores (post=1.17 cm, 2-weeks=1.54 cm) that exceeded the MDC of the WBLT (0.54 cm). These findings are comparable to other CAI investigations which used joint mobilizations targeted to improve posterior talar glide (1.4 – 2.23 cm).[45,46,53,93] Additionally, our findings of sustained DRFOM improvements after the cessation of our intervention is similar to previous 1-week[46] and 6-month[53] follow-up investigations on the effect of joint mobilizations. These findings cumulatively indicate that the application of multiple bouts of joint mobilizations can produce clinically meaningful improvements in DFROM that remain after completion of the treatment program for up to 6-months.

Significant improvements were identified for each of the Y-Balance test reach distances both at post-intervention and 2-week follow up compared to pre-intervention. These findings are comparable to the isolated effects of joint mobilizations[46] and balance training[59] on Star-Excursion Balance Test reach distances. Hoch et al[46] theorized that joint mobilization treatment resulted in improved reach distances due improved DFROM and the subsequent improved mechanical freedom to complete the assessment. McKeon et al[59] also identified improvements in reach distances using the Star-Excursion Balance Test. McKeon et al[59] suggested that their improvements in PM and PL reach distances may have been due to balance training's ability to decrease the constraints on the sensorimotor system. It is possible that our intervention was able take advantage of the effects of both interventions. We found robust increases in the ANT reach similar to an investigation of isolated joint mobilization.[46] Additionally, large improvements in the PM and PL reaches were comparable to the effects of an isolated balance training program.[59] Overall, our large effect sizes (ES > 0.72), with CIs that did not cross zero, indicate that our comprehensive intervention produced meaningful comprehensive improvements in dynamic balance.

While we found consistent improvements in dynamic balance the same findings did not hold true for static balance assessment. We found no pre-intervention to post-intervention differences in any TTB variables in either visual condition ($p > 0.313$). Comparison of 2-weeks to pre-intervention demonstrated significant improvements in TTB MM AP and TTB SD AP during eyes open conditions. These changes were similar to improvements in these specific TTB variables following a single talocrural joint mobilization intervention.[45] However, another investigation of the effects of a 2-week talocrural joint mobilization intervention demonstrated no immediate or 1-week follow-up changes in TTB variables. Furthermore, these differences varied considerably to the findings of McKeon et al[59] who found improvements in TTB variables during eyes closed conditions following the same balance training program used in this investigation. It is also important to note that previously identified changes in TTB have occurred immediately following the completion of the intervention.[45,59] This investigation revealed improvements in TTB only 2-weeks after the intervention was completed. Our findings suggest that it may take a period of time for sensorimotor alterations to manifest improvements in TTB. Future research is needed to further examine the effects of rehabilitation on static postural control in those with CAI and to incorporated longer follow ups as to evaluate the adaptations of the sensorimotor system over time.

Significant improvements in ankle and hip strength were identified at post-intervention and 2-weeks compared to pre-intervention measurements. The identified improvements in ankle strength were associated with large effect sizes (ES > 0.72) and CIs that did not cross zero. These finding are consistent with previous strength training investigations[41,112] as well as a recent multimodal CAI intervention investigation.[17] These similarities confirm that strength training programs as well as combined CAI interventions can result in large improvements in ankle strength immediately following a 4- or 6-week protocol. Additionally, our findings demonstrate that improvements in ankle strength are still present 2 weeks after a 4-week protocol indicating that our comprehensive intervention may produce lasting improvements in ankle strength. Lastly, to our knowledge we are one of the first investigations to examine the effect of a comprehensive rehabilitation program on hip strength in those with CAI. Although our intervention did not target hip strength directly we found immediate improvements in hip strength following our 4-week intervention. These changes were most likely the result of the functional activities incorporated in the balance training program. The evaluation of how these improvements in hip strength contribute to enhancement of the deficits associated with CAI is beyond the scope of this investigation but should be further evaluated.

Limitations of this study were the lack of a control group, a lack of blinding, and the relatively short follow up period. By not including a control group we were unable to compare the effects of the 4-week intervention to the natural progression of CAI. The introduction of a control or sham group would add rigor to the study design and help to confirm the efficacy of the intervention. Additionally, by having a control or sham group there would be greater opportunity for blinding. Enhanced blinding could reduce the potential bias within the study due to treatment expectations. Due to this limitation, we chose to examine the changes following the intervention in multiple ways; ES, CI, MDC. Our investigation included a 2-week follow up period. While this follow up period was able to confirm that many of the improvements due to the intervention lasted beyond the completion of the intervention it failed to confirm exactly how long the effects lasted. Future studies should investigate how long treatment effect last and explore if maintenance exercises are needed to prolong these effects. Lastly, we did not employ an intervention that was based on identified deficits. All subjects received every aspect of the intervention no matter their baseline status. Perhaps the treatment efficacy and clinician burden could be improved if interventions for CAI were targeted to identified deficits as proposed in a new treatment paradigm for CAI.[17]

Conclusion

Following a 4-week comprehensive rehabilitation program that incorporated joint mobilizations, balance training, ankle strengthening, and ankle stretching those with CAI demonstrated improvements in DFROM and dynamic balance as well as ankle and hip strength. These improvements were identified immediately following the intervention and 2-weeks after its completion. Large effect sizes and improvements that exceeded the MDC of our measures indicated that not only are these changes statistically significant but may also be clinically meaningful. This evidence supports the incorporation of a multifaceted evidenced-based intervention for the treatment of CAI.

Table III.1. Participant Demographics and Inclusion criteria.

N = 20	Mean ± SD
Gender	Male = 5; Female = 15
Ankle	Right = 9, Left = 11
Age (years)	24.35 ± 6.95
Height (cm)	169.29 ± 10.10
Weight (kg)	70.58 ± 12.90
Previous Ankle Sprains (#)	2.95 ± 1.50
Episodes of Giving Way (3 Months)	5.6 ± 6.54
Time Since Last Sprain (Months)	18.5 ± 17.22
Ankle Instability Instrument ("yes")	6.85 ± 1.31
Cumberland Ankle Instability Tool	16.05 ± 5.55
Godin Leisure-Time Exercise Questionnaire	63.65 ± 25.86

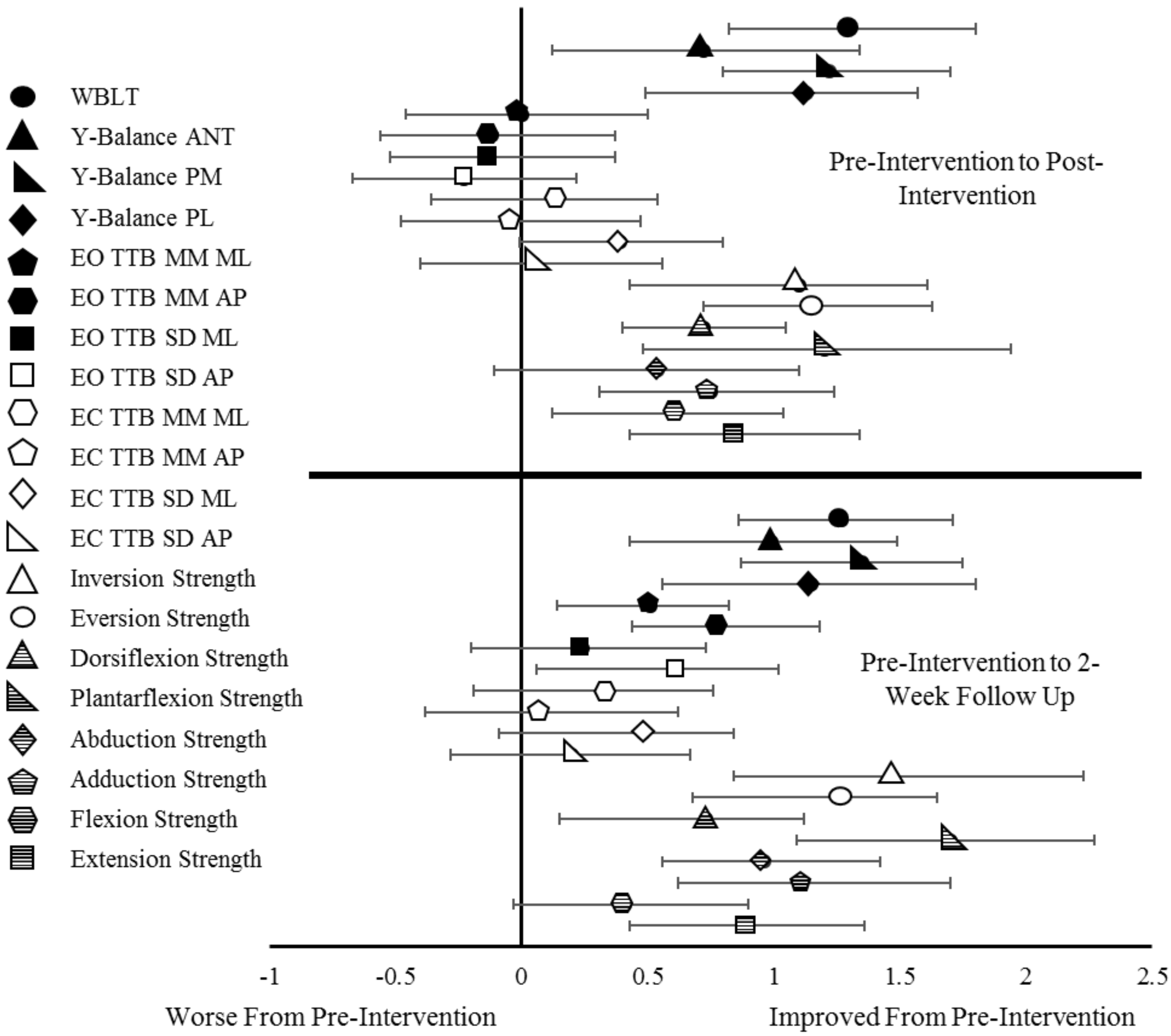
Table III.2. Means (± Standard Deviations), Change Scores, and Minimal Detectable Change Scores (MDCs) for all Dependent Variables.

	Baseline	Pre-Intervention	Post-Intervention	2-Week Follow-up	Pre to Post Δ	Pre to 2-Week Δ	MDC
Weight-Bearing Lunge Test (cm)	8.53±3.38	8.59±3.54	9.75±3.49[a]	10.13±3.49[a]	1.17±0.90	1.54±1.22	0.54
Y-Balance Test (%)							
Anterior	57.99±5.72	58.82±7.29	61.57±5.89[a]	62.19±5.07[a]	2.75±3.81	3.37±3.41	3.11
Posteromedial	98.44±7.40	99.03±6.96	105.97±6.02[a]	106.00±6.42[a]	6.95±5.68	6.98±5.16	4.57
Posterolateral	95.49±6.72	97.78±6.38	104.04±5.37[a]	104.67±5.98[a]	6.25±5.52	6.89±5.98	4.48
Time-to-Boundary (s)							
Eyes Open							
MM-ML	1.88±0.46	1.84±0.47	1.84±0.53	2.07±0.65	-0.00±0.45	0.23±0.45	0.24
MM-AP	5.04±1.59	5.02±1.82	4.88±1.27	5.83±2.06[ab]	-0.14±1.14	0.81±1.04	0.71
SD-ML	1.52±0.43	1.44±0.57	1.35±0.60	1.58±0.61	-0.09±0.74	0.14±0.57	0.52
SD-AP	3.29±1.02	3.22±1.12	3.00±0.91	3.73±1.39[ab]	-0.22±0.97	0.51±0.84	0.92
Eyes Closed							
MM-ML	0.79±0.23	0.82±0.22	0.85±0.26	0.89±0.28	0.03±0.22	0.06±0.19	0.14
MM-AP	2.24±0.78	2.44±0.89	2.42±0.77	2.50±0.81	-0.03±0.70	0.06±0.75	0.53
SD-ML	0.64±0.25	0.59±0.20	0.70±0.29	0.72±0.31	0.11±0.29	0.13±0.26	0.24
SD-AP	1.44±0.50	1.51±0.59	1.53±0.43	1.61±0.60	0.02±0.49	0.1±0.53	0.35
Isometric Strength (N/kg)							
Ankle							
Inversion	3.38±1.01	3.8±1.01	4.57±0.75[a]	4.78±0.83[a]	0.77±0.70	0.98±0.67	0.55
Eversion	3.23±0.76	3.66±0.81	4.47±0.81[a]	4.53±0.82[a]	0.81±0.70	0.86±0.68	0.35
Dorsiflexion	3.62±0.66	3.86±0.72	4.24±0.91[a]	4.23±0.75[a]	0.38±0.53	0.37±0.52	0.29
Plantarflexion	4.57±0.85	4.41±1.06	5.37±1.01[a]	5.92±1.13[a]	0.97±0.81	1.51±0.89	0.56
Hip							
Abduction	2.02±0.26	2.02±0.33	2.2±0.31	2.29±0.33[a]	0.19±0.29	0.27±0.29	0.26
Adduction	1.89±0.31	1.85±0.33	2.07±0.39[a]	2.09±0.37[a]	0.22±0.29	0.24±0.22	0.23
Flexion	2.07±0.36	2.09±0.33	2.21±0.38[a]	2.21±0.38	0.12±0.20	0.12±0.28	0.24

	Baseline	Pre-Intervention	Post-Intervention	2-Week Follow-up	Pre to Post Δ	Pre to 2-Week Δ	MDC
Extension	2.62±0.48	2.59±0.38	2.87±0.47[a]	2.88±0.43[a]	0.28±0.34	0.29±0.32	0.26

[a]=Significantly different from pre-intervention at $p<0.05$, [b]=Significantly different from post-intervention at $p>0.05$, MM=Mean Minima, ML=Medial-Lateral, AP=Anterior-Posterior, SD=Standard Deviation of Mean Minima

Figure III.1. Standardized Response Mean Effect Sizes and 95% Confidence Intervals



CHAPTER IV

PROJECT III: THE EFFECTIVENESS OF A 4-WEEK COMPREHENSIVE INTERVENTION ON PATIENT-ORIENTED MEASURES IN THOSE WITH CHRONIC ANKLE INSTABILITY

Introduction

Chronic ankle instability (CAI) is a condition characterized by residual symptoms, recurrent ankle sprains, and repetitive episodes of giving way during functional activities.[13] The repetitive trauma that accompanies CAI is believed to contribute to long-term consequences such as ankle osteoarthritis[14] and reductions in physical activity.[15] Traditionally, CAI investigations have focused on the identification of mechanical and functional insufficiencies from a disease-oriented perspective, such as dorsiflexion range of motion restrictions and balance impairments. With the emergence of evidence-based practice there has been a push to capture patient-oriented evidence that evaluates the effect of a condition, from the patient's perspective, on their health status. This evolution in the CAI literature is evident as an increasing number of studies incorporate patient-reported outcomes (PROs) and the directive from the International Ankle Consortium[69] to include PROs in CAI research. This emphasis has led to numerous investigations which have been recently summarized, suggesting that those with CAI report functional deficits during activities of daily living (ADL) and sport, in addition to increased fear of re-injury.[43] Consequently, there is a need to develop interventions capable of mitigating the self-perceived impact of CAI.

A multitude of investigations have evaluated the ability of targeted interventions to enhance self-reported function of individuals with CAI.[23,46,48,50,51,53,57-59,66-68,92,93] These interventions include balance training, balance training using in combination with other treatments, and joint mobilizations. However, the current evidence is primarily limited to measuring self-reported function using region-specific PROs. Specifically, the current evidence-based interventions have demonstrated the ability to enhance ankle-specific PROs including the Foot and Ankle Ability Measure (FAAM) subscales (ADL and Sport),[23,46,48,67,68,92,93] the Foot and Ankle Disability Index (ADL and Sport),[50,51,58,59] and the Cumberland Ankle Instability Tool (CAIT).[53,57] While these findings indicate that current rehabilitation strategies are effective and enhance the physical component of HRQL specific to the ankle, they failed to capture a multidimensional view of HRQL. Beyond ankle-specific function, impairments in overall health and fear of re-injury have been identified within individuals with CAI.[43] This indicates that there is a need to examine the impact of rehabilitation on a multidimensional profile of HRQL in this population.

With the need to evaluate a complex profile of HRQL throughout the rehabilitation process there is a growing demand to ensure accurate documentation of these outcomes. The accurate determination of patient change is vital to the evaluation of patient progression and subsequent clinical decisions. Due to the subjective nature of HRQL and PROs, there is an assumption that the intra-individual standards remain stable throughout rehabilitation in order to measure accurate change in these concepts.[70,102] However, this may not be true, as it is reasonable to believe that patient values can vary as patients reconceptualize their condition during the disease or rehabilitation process.[70,102] This reconceptualization is known as response shift and can alter the conceptualization of perceived HRQL.[70] Response shift is a phenomenon by which an individual's self-evaluation of a construct changes due to: a change in internal standards of measurement (scale recalibration), a change in values or priorities (reprioritization), and or a personal redefinition of the target construct (reconceptualization).[70,102] Consequently response shift may interfere with the ability to accurately detect change in a construct or PRO and in turn lead to improper clinical decisions if not taken into consideration during the treatment process.

Traditionally, response shift has been observed in individuals with chronic, life-threatening conditions where a patient's physical health deteriorates, yet their self-reported HRQL remains stable.[71] It is thought that the stable HRQL experienced by these patients may be a result of changing values, standards, and priorities.[71] More recently, response shift has gained attention as a possible phenomenon within chronic musculoskeletal conditions. The current literature indicates that a response shift phenomenon exists in patients who have undergone surgical intervention and or rehabilitation for conditions such as rotator cuff repair,[74] autologous chondrocyte implantation,[75] total knee arthroplasty,[72,80,81] knee microfracture,[77] lumbar spinal decompression surgery,[99] and unspecified rehabilitation for chronic low back pain.[79] The demonstrated response shifts in these populations have the potential to effect the evaluation of the rehabilitation process and impact clinical decision-making.

Currently, there is limited evidence regarding whether or not response shift occurs following conservative management for their condition. However, patients who underwent conservative care for chronic low back pain reported a small response shift in which they initially underestimated their disability.[79] It is possible that those with CAI may follow a comparable trend after conservative rehabilitation. Similar to chronic low back pain, CAI is a condition associated with prolonged modifications in physical activity to avoid re-injury.[15,43] These prolonged activity limitations and participation restrictions may cause individuals with CAI to repolarize; resulting in the belief that this is their normal level of function and cause them to reconceptualize the activities they deem meaningful. Therefore, during and after a conservative intervention is applied and function is restored, individuals with CAI may experience a response shift because they become aware of the lifestyle changes created by their chronic condition. This would lead to an inaccurate assessment of HRQL constructs and underestimate or overestimate the effectiveness of an intervention. Thus, it is essential to examine the potential for response shift in those with CAI following conservative care to ensure accurate assessment of patient-oriented outcomes. The purpose of this investigation was to evaluate HRQL changes following a 4-week comprehensive rehabilitation program for individuals with CAI and to determine if these individuals experience a response shift. We hypothesize that a 4-week rehabilitation program will result in significant and clinically relevant improvements in HRQL. Additionally, we hypothesize that response shift will occur which indicates that detriments in HRQL may be underestimated in individuals with CAI prior to rehabilitation.

Methods

Design

This investigation employed an interrupted time-series design to examine the effect of a 4-week comprehensive intervention on patient-oriented outcomes and to examine response shift in individuals with CAI. All participants completed 4-data collection sessions (baseline, pre-intervention, post-intervention, 2-week follow-up) and a 4-week intervention. The 4-week intervention consisted of 12 supervised sessions and a daily home exercise protocol. The independent variable was time (baseline, pre-intervention, post-intervention, and 2-week follow-up) and PRO administration (traditional, then-test). The dependent variables were scores on the following PROs: the FAAM-ADL, FAAM-Sport, Quick-FAAM, Modified Disablement of the Physically Active scale (mDPA), and the Fear-Avoidance Belief Questionnaire (FABQ).

Subjects

Twenty-two subjects with self-reported CAI (5 M; age = 24.91±7.33 yrs; height = 169.18±9.66 cm; weight = 70.62±12.27 kg) volunteered to participate in the study. Subjects were recruited using electronic and poster advertisements at a large public university. Subjects were included if they were physically active (≥24 on the Godin Leisure-Time Exercise Questionnaire) adults (18-45yrs) with a history of ≥1 ankle sprain at least 6 months ago and ≥2 episodes of "giving way" in the past 3 months. Additionally, subjects had to answer "yes" to ≥5 questions on the Ankle Instability Instrument and ≤24 on the Cumberland Ankle Instability Tool (CAIT). In the case of bilateral CAI, the limb with the lower CAIT score was included in the study. Exclusion criteria consisted of an ankle sprain within the past 6 weeks, lower extremity injury within the past 6 months, history of lower extremity surgery and any condition that may affect balance. All subjects provided written informed consent in compliance with the institutional review board.

Testing Procedures

Upon enrollment, subjects completed the baseline and pre-intervention data collection sessions which were separated by 4-weeks of normal activity. Baseline and pre-intervention data were used to determine reliability and the minimal detectable change (MDC) for each PRO. Following the pre-intervention session, subjects began the 4-week intervention that consisted of both home and supervised exercise components. The post-intervention data collection session occurred within 48 hours of the intervention's cessation. Additionally, a follow-up session occurred 2-weeks after the post-intervention data collection session (2-week follow-up). During each data collection session traditional PRO administration was completed in a counterbalanced order using a Latin Square. During the last two data collection sessions (post-intervention, 2-

week follow up) then-test PRO administration was also completed (Then, Then 2-weeks). The order of traditional and then-test PRO assessment was counterbalanced. The order of PRO administration was maintained across all data collection sessions for each subject. One athletic trainer with 5 years of experience completed all data collection sessions. Three athletic trainers with 5-10 years of experience conducted the interventions.

Region-Specific Patient-Reported Outcome

Three PROs were utilized to capture ankle-specific self-reported function: FAAM-ADL, FAAM-Sport, and Quick-FAAM. These questionnaires were designed to quantify how foot and ankle conditions impact activity and function.[113,114] The FAAM-ADL is a 21-item scale assessing function during activities of daily living. The FAAM-Sport is an 8-item scale that focuses on sport related activities. The Quick-FAAM is a combined and condensed version of both the FAAM-ADL and FAAM-Sport that contains 12 items and is tailored for those with CAI.[114] Items on each of the FAAM instruments are scored on a 5-point Likert scale (0-4) from *no difficulty at all* to *unable to do*. Scores are transformed into percentages, with 100% representing no functional impairments. The FAAM-ADL and FAAM-Sport have both demonstrated high test-retest reliability (ICC=0.87)[113] and the ability to identify region-specific deficits in those with CAI.

Global Patient-Reported Outcomes

The mDPA was used to asses global function.[115] This PRO assesses overall quality of life and function in physically active people through two subscales, physical summary component (PSC) and mental summary component (MSC). The mDPA-PSC consists of 12 items and addresses impairment, activity limitations and participation restrictions. The mDPA-MSC consists of 4 items and evaluate perceptions of emotional well-being. A 5-point Likert scale (0-4) from *no problem* to *severe problem* is used to evaluate each item. Scores on each item are then combined to create total scores for each summary component (PSC=0-48; MSC=0-16) with higher scores indicating functional limitations and decreased quality of life. The mDPA has demonstrated high test-retest reliability (ICC=0.94) in physically active individuals.[116]

Dimension-Specific Patient-Reported Outcomes

Fear-avoidance beliefs were assessed using the 16 item FABQ.[117] The FABQ is comprised of two subsets, physical activity (PA) and work (W), which evaluate fear beliefs during physical activity and a work environment respectively. The FABQ-PA consists of 5 items and the FABQ-W consists of 11 items. Each item is scored on a 7-point Likert scale from *completely disagree* to *completely agree*. Scores range from 0 to 24 on the FABQ-PA and from 0-42 on the FABQ-W. Greater scores indicated increased injury related fear. High test-retest reliability (ICC>0.77) has been demonstrated for the FABQ.

Assessment of Response Shift

Assessment of response shift was completed using the then-test method.[75] The completion of this approach supplements traditional pre/post assessment with the addition of a then-test assessment at the same time as the post-intervention assessment. The then-test assessment involved subjects completing PROs to retrospectively assess their function at pre-intervention, prior to the completion of the intervention. During this assessment subjects were instructed to complete the PROs based on how they perceived their function before the intervention.[85] By completing the then-test and traditional post-intervention assessment at the same time it is thought that the same frame of reference and standards can be used for both. This would control for shifts in construct interpretation that may develop due to the rehabilitation process.[85]

Traditionally, the only variable of interest is the difference between pre- and post-interventions scores, traditional change (TC). With the implementation of the then-test, multiple comparisons are added: response shift and response shift adjusted change. Response shift is calculated as the difference between the then-test and pre-intervention assessment. Response shift evaluates the potential change in pre-intervention self-perceived function due to a change in internal standards following an intervention.[85] Additionally, response shift adjusted change is the difference between the then-test and the post-intervention assessment. This variable assesses the change in self-perceived function due to the intervention while using the then-test as the pre-intervention time point.[85]

Intervention

The 4-week rehabilitation program consisted of home and laboratory components completed on the involved limb. The home intervention was completed daily and consisted of gastrocnemius-soleus complex (GSC) stretching and ankle strengthening. The laboratory component involved 12 sessions in which joint mobilizations, balance training, and ankle strengthening were completed. All components of the home and laboratory intervention were based on previously established rehabilitation programs for those with CAI.[40,46,59] During laboratory interventions subjects were reminded and refreshed regarding the home intervention procedures. Interventions and instructions were executed by athletic trainers with a minimum of five years of clinical experience. Prior to the initiation of the study, the lead investigator held a training session to promote treatment consistency across all clinicians.

<u>Home Intervention</u>

The GSC stretching component consisted of three sets of 30-seconds of stretching on a half foam roller with the knee in full extension as well as 3-sets with the knee in slight knee flexion. These stretches were selected as to target both the gastrocnemius and soleus muscles. Subjects were instructed to hold stretches at the point of mild discomfort. Strengthening exercises utilized Thera-Band resistance bands to strengthen DF, PF, inversion, and eversion of the ankle.[40] The number of sets completed were 3, 4, 3, and 4 for weeks 1, 2, 3, and 4, respectively. Ten repetitions were completed per set of Thera-Band strengthening. Subjects used a Blue (heavy resistance) band during the first 2-weeks and a black (special heavy resistance) band during the last 2-weeks of the intervention. All subjects were provided instructions, demonstrations, half foam roller, Thera-Band, and an intervention journal prior to leaving the laboratory after the pre-intervention data collection session. The intervention journal was used to track compliance with the home intervention program.

Laboratory Intervention

Joint mobilizations consisted of four, 2-minute sets of Maitland Grade III anterior-to-posterior talocrural joint mobilizations with 1-minute of rest between sets.[46] During joint mobilization treatments, subjects were positioned in supine with the involved ankle off of a plinth. The investigator stabilized the distal tibia and fibula with one hand and directed force posteriorly over the talus with the opposite hand. Large amplitude, 1-second oscillations from the joint's mid-range to end-range of accessory motion were applied.[46] The balance training program consisted of activities designed to challenge single-limb balance after perturbation.[59] Five activities, that progressively increase in difficulty as the subject became proficient at the task, were used. The activities included: hop to stabilization, hop to stabilization and reach, hop to stabilization box drill, static single-limb stance balance activities with eyes open and with eyes closed.[59] Lastly, a slow-reversal PNF technique comprised of concentric contraction of the antagonist muscle followed by a concentric contraction of the agonist muscle was used to strengthen the ankle in the D1 and D2 patterns.[40] Manual resistance and stabilization was applied by the investigator. Subjects completed 3-sets of 10-repetitions during the first 3 intervention sessions, 4-sets of 10-repetitions during the 4th through 6th, 3-sets of 15-repetitions during the 7th through 8th, and 4-sets of 15-repetitions during the last three intervention sessions.

Statistical Analysis

Missing items for all PROs were replaced with regression imputation. This method involved establishing the estimated relationship between the missing item to the other items within the PRO using regression and the complete data from other subjects. Values of non-missing items within the PRO, for the subject with missing values, was then inputted into the regression equation to predict the missing items. If participants missed more than 33% of the items in a PRO then the PRO was removed from the analysis.[118,119]

To examine traditional differences in PRO scores over time (pre-intervention, post-intervention, 2-week follow-up) separate one-way ANOVAs were used for each PRO. The presence of response shift (pre-intervention, then post-intervention, then 2-weeks) was evaluated using separate one-way ANOVAs for each PRO. The difference in response shift adjusted change (then post-intervention; then 2-weeks – post-intervention) and traditional change (pre – post-intervention; pre – 2-weeks) was examined using a two-way ANOVA. Sidak post hoc comparisons were completed in the presence of significant main effects or interactions. The significance level for all analyses was set *a-prior* at $p < 0.05$.

Minimal detectable change (MDC) scores were calculated to determine the minimal change required within the outcome variables to achieve change beyond the error of the measurements. Chronbach α and the standard error of measurement (SEM) from the data collected during the baseline and pre-intervention sessions was used to calculate MDC scores. The formula SEM x $\sqrt{2}$ was used for MDC scores calculation.[120]

Standardized response mean effect sizes (ES) and corresponding 95% confidence intervals (CI) were calculated for each dependent variable from pre- to post-intervention and pre-intervention to 2-week follow up scores.[109] A positive ES indicated improved self-reported function following the intervention. Additionally, the magnitude of difference between traditional change and response shift adjust change as well as between pre-intervention and then-test scores was evaluated using standardized response means ES. Positive ES indicated a greater magnitude of self-reported change following the intervention when evaluated using response shift adjusted change as compared to traditional change. Positive ES also indicated greater reported disability on then-tests compared to pre-intervention scores. The interpretation of the ES were interpreted as: weak (0.39), moderate (0.40-0.69), and strong (≥0.70).[110]

Results

Baseline characteristics of the included subjects are provided within Table IV.1. A total of 22 individuals were enrolled, and 20 completed the study. The two subject that did not complete the study self-withdrew during the intervention phase due to non-study related injuries. Due to a high study completion rate (91%; 20/22), the data from the 2 subjects that withdrew was removed and an intention to treat analysis was not performed. The means (± standard deviations), Cronbach's α, and MDCs for all PROs at all time points is displayed in Table IV.2. Traditional change scores, response shift change scores, and two-way ANOVA results are displayed in Table IV.3. ES and 95% CI are displayed in Figure IV.1.

Missing Items

Two subjects' Quick-FAAM data were not included in the MDC analysis as they did not complete baseline assessments on this PRO (N=18). No other data were removed from the analysis for missing more than 33% of the items on a given PRO. The FAAM-ADL was the only PRO with missing data in which 0.71% of the total data and ≤ 2.86% of a session's data had to be imputed. Overall, 0.22% of all PRO data was imputed using regression imputation.

Intervention Compliance

Overall, subjects were 91.86% compliant with the home-based intervention. Specifically, subjects completed on average 92.74% (80.95-100.00%) of the home stretching and 91.48% (74.49-100%) of the home strengthening program. A total of 18 subjects completed all laboratory-based intervention sessions. The 2 subjects that failed to attend all session attend 11 and 7 out of 12 sessions. Overall, there was a 97.50% attendance rate for the laboratory-based sessions. Lastly, one subject completed a modified balance training program consisting of only the static balance and reaching components due to muscle soreness and injury-related fear with the hopping tasks. The study acquired an overall balance training completion rate of 95.11%.

Traditional Assessment of Change

When assessing traditional changes in self-reported function (pre-intervention, post-intervention, and 2-week) a significant time main effect was found for the Quick-FAAM (p = 0.043), FAAM-ADL ($p < 0.001$), mDPA-PSC ($p < 0.001$), and the FABQ-PA, ($p < 0.001$). Post hoc analysis revealed that the FAAM-ADL, mDPA-PSC, and the FABQ-PA were significantly improved at post-intervention ($p < 0.001$) and 2-weeks ($p < 0.001$) compared to pre-intervention measures. Additionally, the Quick-FAAM was significantly improved at post-intervention compared to pre-intervention ($p = 0.000$). The FAAM-ADL was significantly improved at 2-

weeks compare to post-intervention ($p = 0.049$). A significant time main effect was not demonstrated for the FAAM-Sport ($p = 0.071$), mDPA-MSC ($p = 0.087$), or the FABQ-W ($p = 0.160$). Statistically significant changes were associated with change scores that exceeded the MDC (Table IV.2.) and large ES with CIs that did not cross zero (Figure IV.1.).

Assessment of Response Shift

When assessing the presence of response shift following the intervention no significant differences were detected between pre-intervention, then post-intervention or then 2-weeks scores for all PROs ($p > 0.124$). Furthermore, these differences did not exceed the MDC (Table IV.2.) and were associated with weak ES with CIs that crossed zero (Figure IV.1.). These findings indicate that there was a lack of a meaningful response shift or recalibration of the subjects' internal standards.

Traditional Change vs. Response Shift Adjusted Change

A significant change score type main effect was identified for the FAAM-ADL ($p = 0.032$) which indicated a greater amount of identified improvement with response shift adjusted change than traditional change regardless of time (Table IV.3). This difference did not exceed the MDC associated with the FAAM-ADL (Table IV.2). No other change score type main effects were identified ($p > 0.070$) for any other of the PROs. A significant time main effect was found for the mDPA-PA ($p = 0.032$). This indicates that change scores between pre-intervention and post-intervention were significantly less than change scores between pre-intervention and 2-weeks. The magnitude of this difference did not exceed the MDC associated with the mDPA-PA (Table IV.2.). No other time main effects were identified ($p > 0.081$) for the other PROs. Lastly, no significant change score type by time interactions were found ($p > 0.163$).

Discussion

The main finding of this investigation was that a 4-week comprehensive rehabilitation program for individuals with CAI resulted in significant improvements in self-reported function. Specifically, subjects reported improvements on the Quick-FAAM, FAAM-ADL, mDPA-PA, and the FABQ-PA. This indicates that subjects reported improvements in self-reported ankle function and general function as well as reductions in injury related fear during physical activity after they completed the 4-week rehabilitation program. These improvements were primarily identified immediately post-intervention as well as 2-weeks following the intervention, which indicated that there was a lasting effect following the intervention. Additionally, all significant improvements were associated with large ES (Figure IV.1.) at post-intervention (ES >1.38) and two weeks (ES > 1.31) as well as change scores that surpassed the MDCs (Table IV.2.). This indicates that not only where changes significant, they may also clinically meaningful improvements.

We hypothesized that individuals with CAI that participated in a comprehensive rehabilitation program would experience a response shift in which they would initially under estimate their HRQL detriments prior to rehabilitation. Our findings did not support this hypothesis as we found no significant differences between pre-intervention, then post-intervention, and then 2-weeks measures. This indicates that at post-intervention the subjects' retrospective assessment of their disability prior to the intervention was similar to their pre-intervention measurements. Statistically significant differences between traditional change and response shift adjusted change were identified for the FAAM-ADL. However, this difference did not exceed the MDC for the FAAM-ADL indicating that the difference was within the measurement error. These findings suggest that following conservative care those with CAI do not experience a response shift and that traditional pre-to-post testing methods provide an accurate evaluation of treatment effect.

This investigation was one of the first to evaluate the phenomenon of response shift following a conservative intervention. Nagl and Farin[79] investigated the impact of response shift in individuals undergoing conservative rehabilitation for low back pain. While their conclusions indicated that a small response shift occurred, in which individuals underestimated their pre-intervention disability, these findings were associated with weak ES. This indicates their identified response shift may not be clinically meaningful. This would support our findings that following conservative care for CAI individuals do not experience response shift, as we found non-significant differences in change scores and this was also associated with weak ESs for all measures. It has been proposed that in order for response shift to occur a significant catalyst must take place.[70] Traditionally, response shift has been identified following surgical interventions such as knee replacements,[81] rotator cuff repair,[74] and arthroplasty.[72] It is possible that conservative care does not provide a substantial enough catalyst to prime individuals for a potential response shift. As such, the findings of this investigation support the use of traditional pre-to-post methods to evaluate self-reported function following a conservative intervention for those with CAI.

The evaluation of self-reported function following an intervention has primarily been focused on ankle-specific function within the CAI literature assessed using the FAAM-Sport and FAAM-ADL. Investigations have demonstrated improvements in self-reported ankle function following joint mobilizations,[46,53,93] balance training,[57,59,121] stretching,[93] as well as during a combination of these targeted interventions.[17,51] Our investigation found similar changes in the FAAM-ADL (Pre-Post=7.14%, Pre-2week=13.96%), FAAM-Sport (Pre-Post=11.25%, Pre-

2week=12.5%), and Quick-FAAM (Pre-Post=12.5%, Pre-2week=8.57%). While we found a non-significant time main effect for the FAAM-Sport, changes (Pre-Post=11.25%, Pre-2week=12.5%) surpassed the calculated MDC (6.07%) and were associated with large ESs (>1.21). Cumulatively, these findings in combination with the previous literature support the implementation of evidence-based interventions to improve ankle-specific self-reported function in those with CAI.

Previous findings have demonstrated that individuals with CAI report decreased global well-being as well as increased fear of re-injury.[43] These factors may be associated with reports of decreased physical activity levels within the CAI population.[15] Our investigation demonstrated statistically significant improvements in global well-being as measured with the mDPA-PSC and injury related fear measured with the FABQ-PA. These improvements were associated with changes that exceeded the MDC (Table IV.2) and large ES (Figure IV.1.). The findings of global well-being and injury related fear enhancements indicate that our intervention was capable of creating multidimensional improvements to HRQL from a patient-centered perspective.

This investigation is not without limitations within its design. The major limitation was the lack of blinding within the study, which could have introduced bias within the results. However, we chose to incorporate multiple methods of interpreting the results in an effort to protect for the lack of blinding. Additionally, we included a relatively short follow-up period of 2-weeks. Due to this we are unable to draw conclusion regarding the long-term effects of the intervention on HRQL. In addition, it may be possible that time is a factor in the evaluation of response shift as many of the previous investigations of response shift have included 6 to 24-month follow-up periods.[72,74,75,80] Individuals may need time to reconceptualize their new level of function. Future investigations are needed to confirm the findings of this study by including blinding and sham treatments. Additionally, longer follow-up periods after CAI interventions are needed as to evaluate the long-term effects of the intervention on CAI status.

Conclusion

In conclusion, the results of this investigation support the use of traditional pre-to-post methods when evaluating the efficacy of conservative treatment for patients with CAI. Evaluation of traditional change demonstrated that people with CAI immediately and 2-weeks following a 4-week comprehensive rehabilitation program reported improvements in ankle-specific function, global well-being, and injury related fear. Our findings support the implementation of a comprehensive rehabilitation program to enhance a multidimensional profile of HRQL in those with CAI.

Table IV.1. Participant Demographics and Inclusion criteria.

N = 20	Mean ± SD
Gender	Male = 5; Female = 15
Ankle	Right = 9, Left = 11
Age (years)	24.35 ± 6.95
Height (cm)	169.29 ± 10.10
Weight (kg)	70.58 ± 12.90
Previous Ankle Sprains (#)	2.95 ± 1.50
Episodes of Giving Way (3 Months)	5.6 ± 6.54
Time Since Last Sprain (Months)	18.5 ± 17.22
Ankle Instability Instrument ("yes")	6.85 ± 1.31
Cumberland Ankle Instability Tool	16.05 ± 5.55
Godin Leisure-Time Exercise Questionnaire	63.65 ± 25.86

Table IV.2. Means (± Standard Deviations) for all four timepoints and then-test assessments, Cronbach's α, and Minimal Detecatable Change scores (MDCs) for all Dependent Variables

	Baseline	Pre-Intervention	Post-Intervention	2-Week Follow-up	Then Post	Then 2-Week	Cronbach's α	MDC
FAAM-ADL (%)	87.68±8.47	88.63±8.07	95.77±4.69*	97.2±2.95*	86.79±9.66	86.37±9.9	0.890	3.88
FAAM-Sport (%)	74.06±11.74	80.16±10.2	91.41±7.65	92.66±7.04	77.97±13.47	76.41±12.88	0.847	6.07
Quick FAAM (%)	75.12±11.64	79.38±11.33	91.88±7.64*	93.33±6.33	76.88±13.23	75.42±13.58	0.899	4.81
mDPA-PSC	11.85±7.24	13.25±7.75	6.05±6.9*	4.75±5.89*	14.8±8.63	16.45±8.44	0.594	6.76
mDPA-MSC	2.75±2.86	2.3±2.62	1.3±3.05	1.25±3.04	2.25±2.83	2.3±3.39	0.667	2.24
FABQ-PA	13.5±3.52	12.6±4.22	6.5±5.01*	5.65±4.74*	11.5±5.22	10.8±5.31	0.662	3.18
FABQ-W	8.75±7.21	5.2±6.81	2.4±3.02	4.35±5.9	5±5.59	6.35±6.54	0.704	5.39

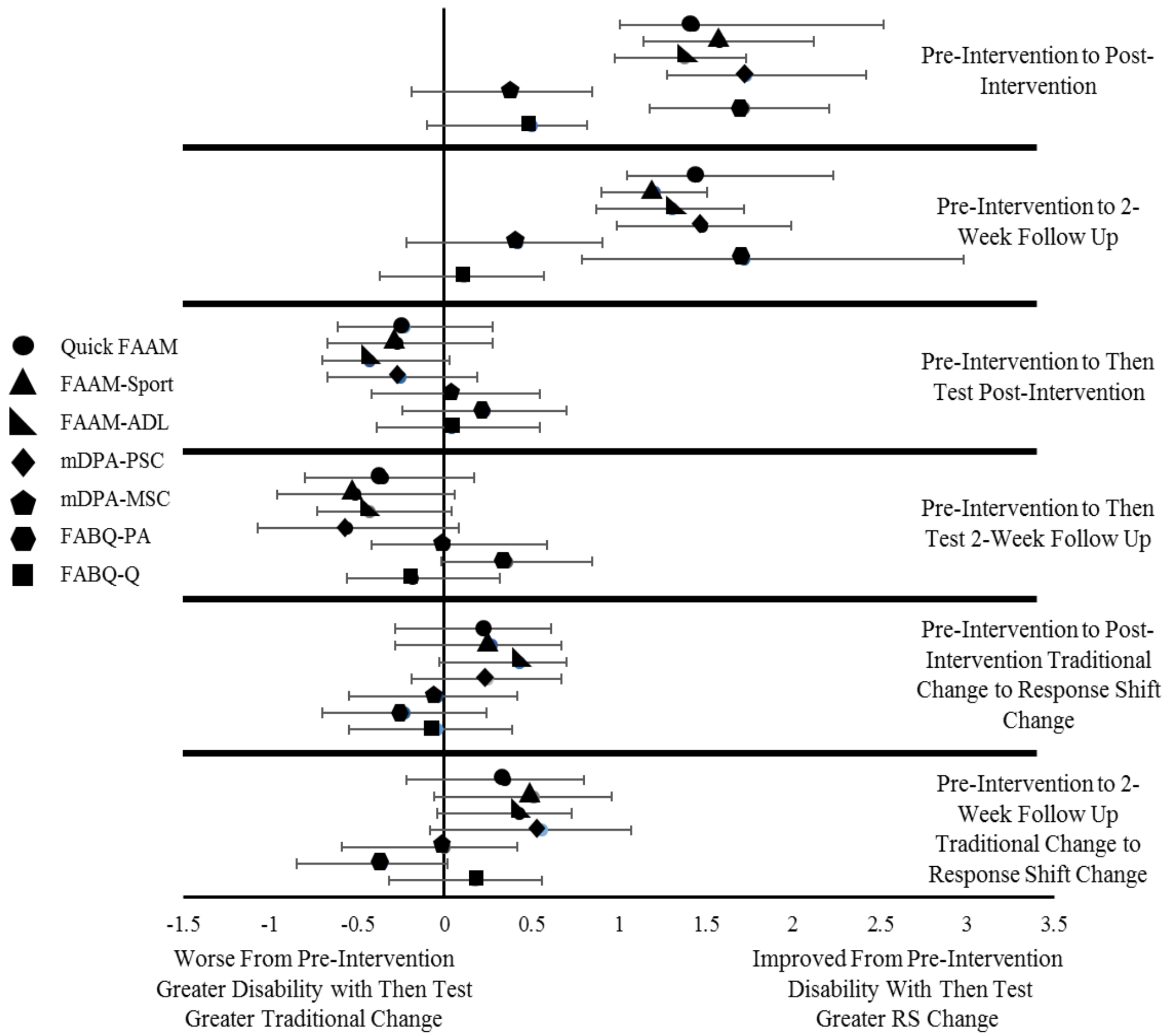
*=Significantly different from pre-intervention at $p<0.05$. FAAM=Foot and Ankle Ability Measure, ADL=Activities of Daily Living, mDPA=Modified Disablement of the Physically Active Scale, PSC=Physical Summary Component, MSC=Mental Summary Component, FABQ=Fear-Avoidance Belief Questionnaire, PA=Physical Activity, Work

Table IV.3. Traditional Change, Response Shift Adjusted Change Scores, and *p*-values

	Traditional Change (Pre to Post Δ)	Traditional Change 2-Weeks (Pre to 2-Week Δ)	Response Shift Adjusted Change (Then Post to Post Δ)	Response Shift Adjusted Change 2-Weeks (Then 2-Week to 2-Week Δ)	Main Effect for Type of Change (*p*)	Main Effect for Time (*p*)	Type by Time Interaction (*p*)
FAAM-ADL (%)	7.14±5.17	8.57±6.54	8.99±6.59	17.92±10.7	0.032	0.081	0.740
FAAM-Sport (%)	11.25±7.13	12.5±10.29	13.44±9.57	16.25±12.57	0.084	0.149	0.163
Quick FAAM (%)	12.5±8.76	13.96±9.61	15±9.43	10.83±8.25	0.192	0.093	0.309
mDPA-PSC	-7.2±4.16	-8.5±5.73	-9.4±5.72	-11.7±6.61	0.070	0.032	0.089
mDPA-MSC	-1±2.6	-1.05±2.48	-0.95±2.01	-1.05±1.76	0.945	0.791	0.921
FABQ-PA	-6.1±3.55	-6.95±4.03	-5±3.64	-5.15±4.23	0.017	0.582	0.410
FABQ-W	-2.8±5.57	-0.85±7.82	-2.6±4.69	-2±3.51	0.698	0.252	0.176

Δ = Change, FAAM=Foot and Ankle Ability Measure, ADL=Activities of Daily Living, mDPA=Modified Disablement of the Physically Active Scale, PSC=Physical Summary Component, MSC=Mental Summary Component, FABQ=Fear-Avoidance Belief Questionnaire, PA=Physical Activity, Work

Figure IV.1. Standardized Response Mean Effect Sizes and 95% Confidence Intervals



CHAPTER V
CONCLUSIONS

The overall purpose of this dissertation was to gain a better understanding of the efficacy of interventions for those with chronic ankle instability (CAI). To achieve this overarching goal, multiple sub-goals were developed. The first goal of this dissertation was to perform a systematic review and meta-analysis of the available literature to examine the efficacy of the current CAI interventions to enhance health-related quality of life (HRQL). Second, was to systematically review the literature to examine the presence of response shift in patients with various musculoskeletal conditions after surgical and or conservative intervention. Third, was to assess the effect of a 4-week comprehensive evidence-based intervention on clinician- and laboratory-oriented outcomes in those with CAI. Lastly, the final purpose was to assess the effect of a 4-week comprehensive evidence-based intervention on patient-oriented outcomes in those with CAI and to determine if individuals with CAI who undergo this treatment experience response shift. To provide a summary of the findings within this dissertation the hypotheses from Chapter I are revisited:

<u>Hypotheses for Aim 1:</u> Within the literature, there will be strong and consistent evidence that individuals with CAI will exhibit HRQL improvements following conservative intervention. *Findings*: The hypothesis was confirmed as the evidence demonstrated that the available conservative CAI interventions were capable of producing meaningful improvements in HRQL. These improvements were specifically made in ankle-specific patient-reported outcomes (PRO) and there was a dearth of information concerning global and region-specific PROs.

<u>Hypotheses for Aim 2:</u> Within the literature, there will be moderate and consistent evidence that response shift is exhibited in those with chronic musculoskeletal conditions following treatment.

Findings: The hypothesis was partially supported as there is evidence of a response shift in those with chronic musculoskeletal conditions following treatment. The findings of response shift were mixed within the literature and the lack of reporting consistency made a summary of the literature difficult.

<u>Hypotheses for Aim 3:</u> Following a 4-week comprehensive intervention clinician- and laboratory-oriented measures will improve in those with CAI.

Findings: This hypothesis was partially confirmed as the dorsiflexion range of motion, dynamic balance and strength scores of the individuals with CAI in this study significant increases at post-intervention and 2-week follow up. However, static balance only improved for a few variables at the 2-weeks follow up signifying that static balance changes were less consistent.

<u>Hypotheses for Aim 4:</u> Individuals with CAI will experience improvements in patient-oriented outcomes and response shift following a 4-week comprehensive evidence-based intervention.

Findings: This hypothesis is partially supported by the findings of the investigation. It was confirmed as significant improvements for the Foot and Ankle Ability Measure (FAAM) activities of daily living (ADL) subscale, the Quick-FAAM, the modified Disablement of the Physically Active Physical Summary Component (mDPA-PSC), and the Fear Avoidance Belief Questionnaire physical activity scale (FABQ-PA) were found at post-intervention and 2-week follow up. It was not confirmed, as response shift was not identified at in any of the PROs.

Summary and Clinical Applications

The systematic reviews within this dissertation (Project IA, IB) provided a valuable synthesis of the available CAI and HRQL literature. Project IA determined that the available evidence-based interventions are effective at enhancing HRQL in those with CAI. However, these results were limited to PROs that focused specifically on ankle-specific function. These findings in combination with findings by Houston et al,[43] which demonstrate the multidimensional nature of HRQL deficits within the CAI population, indicates the need for future investigations to examine the impact of interventions on ankle- and dimension-specific HRQL as well as global HRQL in those with CAI. Additionally, there was a need to ensure the accuracy of traditional methods of assessing of HRQL changes following CAI intervention. The findings from Project IB indicated that there is a potential for response shift to confound HRQL assessment for those receiving care for musculoskeletal conditions. As such, the project identified the need to examine the potential for confounding of traditional HRQL assessment due to response shift within those with CAI.

Projects IA and IB prompted the need for further exploration of the impact of CAI interventions on a multidimensional profile of HRQL as well as the evaluation of response shift phenomenon within a CAI population. As such, Project II was developed were subjects with CAI were asked to complete a comprehensive 4-week intervention to explore these questions. This intervention combined previously established evidenced-based interventions with the goal of creating a robust treatment effect. We theorized that a robust treatment effect or catalyst[70] would be needed to elicit a response shift. Additionally, we hypothesized that such an intervention would be capable of improving the comprehensive profile of the deficits associated with CAI that included disease- and patient-oriented outcomes.

Project II furthered the knowledge associated with interventions to enhance disease-oriented deficits within those with CAI. The project was one of the first to combine multiple evidence-based interventions to create a comprehensive rehabilitation program for those with CAI. The results of this study determined that following a comprehensive intervention of joint mobilizations, balance training, gastroc-soleus stretching, and ankle strengthening individuals with CAI demonstrated improvements at post-intervention and 2-weeks follow-up in dorsiflexion range of motion and dynamic balance as well as ankle and hip strength. These findings are similar to the previously reported effects of the included isolated evidence-base interventions.[40,46,59] Furthermore, Project II is one of the first to identify improvements in hip strength following an intervention for those with CAI. It is possible that improvements in hip strength may allow for the adaption of improved movement patterns for those with CAI. Further research is needed to determine the role of hip strength in the rehabilitation of CAI and if strength training interventions specifically targeting these muscles are warranted. Lastly, Project II determined that improvements in disease-oriented deficits were sustained for two weeks after the completion of the intervention. This indicates that there was a lasting effect of the comprehensive intervention. However, more research is needed to determine the extent to which the improvements are sustained and if maintenance exercises can prolong the effect.

Project III focused on the self-reported changes and the potential for response shift associated with a 4-week comprehensive rehabilitation program for those with CAI. The examination of response shift using the Then-Test method did not identify a significant response shift in individuals with CAI following a comprehensive rehabilitation program. It is possible that the length of the intervention (4weeks) and the follow up period (2 weeks) did not provide sufficient time for individuals to reconceptualize their HRQL. These findings signify that the evaluation of HRQL changes following an intervention in those with CAI is most likely not confounded by response shift. As such, this confirms the accuracy of traditional pre-to-post assessments of HRQL changes. Project III's assessment of traditional HRQL changes demonstrated that the intervention produced significant increases in a multidimensional profile of HRQL. Specifically, ankle-specific self-reported improvements were identified with the

FAAM-ADL and Quick-FAAM, dimension-specific using the FABQ-P, and global well-being using the mDPA-PSC. Similar to disease-oriented measures, improvements in patient-oriented measures were maintained 2-weeks following the completion of intervention. Future investigations are need to evaluate the extent to which these HRQL enhancements are maintained over time.

Due to the multiple factors that contribute to the condition of CAI[13] and the results of this a comprehensive evaluation and intervention need to be employed. The results of the investigations within this dissertation further the evidence regarding the enhancement of the common deficits associate with CAI and support that notion. Following a comprehensive 4-week intervention for those with CAI, improvements were identified in both disease- and patient-oriented outcomes. These improvements were multifactorial and robust in nature, indicating that not only were they statistically significant but also clinically meaningful. Furthermore, this dissertation advocates for the accuracy of traditional pre-to-post evaluation of HRQL changes that were used to come to these conclusions. With this dissertation being one of the first to evaluate injury-related fear changes following an intervention for those with CAI, future research is indicated to confirm the results of this study. Future research should also aim to determine the length of time in which improvements from this intervention last and if maintenance exercises can be used to elongate that time frame. Finally, longitudinal studies are needed to evaluate the effect of this intervention on the risk of reinjury and the development of long-term conditions, such as ankle osteoarthritis and decreased physical activity,[14,15] that have been associated with CAI.

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Research Grants

Powden CJ, Hoch JM, Hoch MC. The Evaluation of Response Shift and Functional Outcomes Following a 4-week Comprehensive, Evidence-Based Rehabilitation Program in Individuals with Chronic Ankle Instability. *Eastern Athletic Trainer's Association, Inc*. Supported Research Program: March 2015. Role: Co-PI. Funding Acquired: $10,000.00. In Progress.

Presentations

Powden CJ, Hoch JM, Hoch MC. The Effectiveness of Conservative Rehabilitation for Improving Patient-Reported Outcomes Associated with Chronic Ankle Instability: A Systematic Review with Meta-Analysis. *National Athletic Trainer's Association Annual Convention and Symposium.* Baltimore, MD, June 2016. Oral Presentation.

Powden CJ. Interventions for Those with Chronic Ankle Instability: A Health-Related Quality of Life Focus. *Virginia Athletic Trainer's Annual Meeting*, Williamsburg, VA. January 2016, Featured Presentation.

Powden CJ, Hoch MC. The Effect of Trial Duration on Instrumented Measures of Single-Limb Stance Postural Control in those with Chronic Ankle Instability. *International Ankle Symposium*. Dublin, Ireland, October 2015. Oral Presentation.