Feasibility of manual therapy in combination with a Dynasplint® for the treatment of trismus in head and neck cancer survivors

by

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Abstract

Introduction: Trismus, defined as an interincisal opening of less than 35mm, is a significant side effect of treatment seen in survivors of head and neck cancer. As this complication can impact a survivor's ability to eat, speak, and maintain oral hygiene, effective methods of managing trismus are needed. In the clinical setting, treatment often includes physical therapy and the use of jaw mobilizing devices such as the Dynasplint®. To date, however, there is limited evidence regarding the effectiveness of manual therapy alone or in combination with a jaw mobilizing device to address trismus once it has developed.

Objectives: The aim of this study was to assess the feasibility of treating survivors of head and neck cancer, presenting with trismus, using a combination treatment comprising manual therapy and home use of a Dynasplint®. Outcomes related to feasibility included feasibility of the intervention process, assessment of resources, personnel and management needs, and safety.

Methods: An 8-week pre-post study design using single subject analysis was conducted with 10 survivors of head and neck cancer. Participants attended manual therapy sessions twice a week and used the Jaw Dynasplint® System at home twice a day starting from week 3-8 of the study. The primary objective outcome, maximal interincisal opening (MIO), was measured at baseline, before and after each manual therapy session, and at the end of the study. Secondary outcomes to assess quality of life and jaw function were completed at baseline and after the 8-week intervention, and included the Short Form-36 Health Survey (SF-36), a Visual Analogue Scale (VAS), and the Gothenburg Trismus Questionnaire (GTQ).

Results: The findings support feasibility with high recruitment (83%), retention (90%), and adherence rates (97% for manual therapy sessions, 70% for Dynasplint® use). The average MIO increase for the nine participants who completed the study was 2.40mm [median improvement of

2.36mm, a range of -1.99mm to 7.42mm]. No severe adverse events related to the study occurred. One minor adverse event related to use of the Dynasplint® was reported (gum pain; n =1). Two participants developed infections in their mouths (unrelated to the study intervention) that impacted their ability to use the Dynasplint®, and one participant withdrew due to ongoing complications with radiation fibrosis syndrome. No changes were observed for outcomes of quality of life, pain, and trismus related symptoms.

Conclusion: Given findings supporting feasibility, larger scale studies comparing the effect of manual therapy alone to manual therapy combined with use of a jaw mobilizing device are warranted.

PREFACE

This thesis is an original work by Joni Nedeljak and Co-Authored by Dr. Margaret L. McNeely, Susan Armijo-Olivo, Dr. Suresh Nayar, and Dr. Ivonne Hernandez. This research study received ethical approval from Health Research Ethics Board of Alberta: Cancer Committee.

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GLOSSARY OF TERMS

Definitions and Abbreviations

Cancer Related:

a) **Head and neck cancer (HNC)-** the term used to describe the different tumors that develop in or around the larynx, pharynx, nose, sinuses, and mouth.[1]

b) **Squamous cell carcinoma-** a form of skin cancer affecting the squamous cells of the epidermis (the outer layer of the skin and mucus membranes).[2]

c) **Head and neck squamous cell carcinoma (HNSCC)-** a form of squamous cell carcinoma that develops in the mucous membranes of the mouth, nose, and throat. Common locations of cancer growth include the oral cavity, pharynx (including the nasopharynx, oropharynx, and hypopharynx), larynx, and nasal cavity and paranasal sinus.[3]

d) **Oral cavity-** this area includes the lining of the lips and cheeks, gums, anterior two-thirds of the tongue, the floor of the mouth under the tongue, the hard palate, and the area of gums behind the wisdom teeth.[3]

e) **Pharynx-** often referred to as the throat. It is a hollow tube that starts behind the nose and leads to the esophagus. It is made up of three parts: the nasopharynx, oropharynx, and hypopharynx. The nasopharynx is the upper portion and is located behind the nose. The oropharynx is the middle portion of the pharynx and includes the soft palate, the posterior third of the tongue, and the tonsils. The hypopharynx is the lower portion of the pharynx.[3]

f) **Larynx-** often referred to as the voice box. It is a hollow tube that is situated above the trachea and includes the vocal cords and the epiglottis.[3]

g) **Paranasal sinus-** spaces between the bones around the nose that are filled with air.[3]

h) **Nasal cavity-** a hollow space inside the nose in which air moves through during breathing. This area is above the bone that creates the roof of the mouth and extends to the throat.[3]

i) **Salivary glands-** glands that release saliva into the mouth to assist with digesting food and protecting against infection. The three paired major salivary glands include: parotid, sublingual, and submandibular.[4]

HNC Treatment:

a) **Radiation therapy or Radiotherapy (RT)-** a form of cancer treatment that uses radiation to destroy cancer cells. Forms of RT include external (at a distance), which uses intense beams of radiation energy to damage the DNA of the cells, or internal, which places radioactive substances directly into the tumour or around the affected area. RT can shrink or completely eliminate a tumour.[5]

b) **Chemotherapy-** a form of cancer treatment that uses drugs to kill cancer cells. The drugs travel in the bloodstream to destroy cancerous cells that are dividing and multiplying rapidly.[6]

c) **Surgery-** a common form of cancer treatment involving manually cutting or stitching tissue to treat cancer. Surgery is used to prevent, diagnose, or remove cancer in the body.[7]

Side effects of HNC treatments:

a) **Trismus-** restricted mouth opening of less than 35mm. This can occur in HNC survivors due to tumour growth or as a side effect of radiation therapy or surgery.[8]

b) **Radiation fibrosis-** a chronic, long term effect of radiation therapy. RT can damage structures – such as vessels, muscles, and nerves – limiting function in the affected areas. In head and neck cancer survivors, radiotherapy-induced trismus can result from radiation fibrosis to muscles and tissues around the jaw.[9]

Trismus Interventions:

a) **Manual therapy (MT)-** techniques- hand-on techniques often used by specialized physical therapists- that are applied to a patient to mobilize joints and soft tissues. The techniques are used to help improve pain and musculoskeletal function, induce relaxation, and decrease edema. MT includes therapist applied tissue manipulation, mobilization, and stretching techniques.[10, 11]

b) **Jaw mobilizing assistive device-** a device used for patient self-management of trismus. The Jaw Dynasplint® System was the assistive device used in this study.[12]

c) **Jaw Dynasplint® System (Dynasplint®)-** a home device used by individuals experiencing trismus. This device applies a low-torque, prolonged duration stretching that aims to lengthen the patient's intra-oral connective tissue permanently.[13]

d) **Slide Caliper-** a measuring device for trismus. In this study, a slide caliper was used to measure the oral opening of the participants.[14]

Study design related:

a) **Pilot feasibility study-** a pilot study is a small version of a study that is completed first, most often to determine feasibility prior to initiation of a larger scale study. A feasibility study is used to evaluate parameters relevant to the design and conduct of a future study but does not evaluate the efficacy of the outcome measures or need to have a primary outcome. Therefore, a pilot feasibility study is a small study that mirrors, and helps provide information on important components of a planned future large-scale study, but has some flexibility in the way in which it is carried out.[15, 16]

b) **Single subject design-** a research design that involves repeated observation of outcomes across time. Each participant serves as their own control. Baseline measurements are taken and then repeated before and during the intervention phases to determine the effectiveness of the treatment protocol.[17]

Outcomes:

a) Recruitment rate- number of participants eligible and consenting divided by the number of participants referred.

b) Retention rate- number of participants completing the study divided by the number of participants starting the study.

c) Adherence to the protocol- the total number of sessions completed divided by the total number of planned sessions for manual therapy and Dynasplint® sessions.

d) MIO- maximal interincisal opening. A measurement of mouth opening between the upper and lower incisors of dentulous participants or between the upper and lower alveolar ridge of edentulous participants.[18]

Questionnaires:

a) **Gothenburg Trismus Questionnaire (GTQ)-** a symptom-specific trismus questionnaire including questions regarding jaw-related problems, eating limitation, and muscular tension.[19]

b) **Pain Visual Analogue Scale (VAS)-** a linear analogue scale used to determine pain intensity in which one end is labeled "no pain" and the other is labeled "worst pain imaginable". [20]

c) Short-Form 36 Health Survey (SF-36)- a survey to determine quality of life. It is composed of 36 items that cover eight health domains including: limitations in social activities because of health problems, limitations in social activities because of physical or emotional problems, limitations in usual role activities because of physical health problems, bodily pain, general mental health, limitations in usual role activities because of emotional problems, and vitality, and general health perceptions.[21]

Participant related:

a) **Dentulous-** possessing teeth in the mouth.[22]

b) **Edentulous-** lacking teeth in the mouth.[23]

c) **Human papillomavirus infection (HPV) positive:** a "high risk" sexually transmitted virus that can lead to cell changes and cancer over time.[24]

Study Acronym:

a) **STRIDE-** Stretching Therapy for patients with Trismus using a Dynasplint® and Exercise

CHAPTER 1: INTRODUCTION

Head and neck cancer (HNC) accounts for approximately 7,000 cancer cases in Canada.[25] This includes cancers of the oral cavity, pharynx, larynx, paranasal sinus and nasal cavity, and salivary glands.[26] The most common causes of HNC are tobacco and alcohol use and the human papilloma virus (HPV).[26] Treatment methods aim to maximize survival and preserve normal oral function and the quality of life (QoL) of the individual. Common treatments include surgery and radiation therapy (RT), which may lead to side effects, such as dysphagia, xerostomia, mucositis, and trismus.[27]

Trismus, or limited mouth opening, is a known complication of oncological treatments for HNC including surgery and radiation therapy. Trismus is defined as an interincisal distance of less than 35 mm and occurs in approximately one third of survivors receiving cancer treatment in the region of oral cavity, oropharynx, nasopharynx and temporomandibular joint.[18, 28] Trismus may occur immediately following surgery, during radiation therapy, or present as a late effect occurring months after cancer treatment.[28] The impact of trismus on quality of life is profound, limiting key functions such as chewing, swallowing and speech, as well as interfering with dental hygiene and management.[26] In the absence of interventions to prevent or attenuate development of trismus, the condition often becomes chronic and can be progressive in nature.[27] Early intervention for trismus is considered key to reduce the risk of long-term morbidity.[28] Multiple physical therapy (PT) modalities are used in the treatment of trismus, with the most common including active exercises, manual therapy and use of a jaw opening devices such as the TheraBite® Jaw Motion Rehabilitation System[3] and the Jaw Dynasplint® System.[27] To address chronic trismus related to radiation fibrosis, significant benefit has been demonstrated with the introduction of the Therabite® and Dynasplint®.[18, 29] The Dynasplint® is a jaw mobilizing device used to help survivors self-manage trismus. It provides low-torque, prolonged-duration stretching with the aim of lengthening the affected connective tissue permanently. Improved mouth opening has been reported following the use of Dynasplint® in patients with trismus.[29]

The evidence is limited regarding the effectiveness of manual therapy alone or in combination with stretching exercises to specifically treat trismus once it has developed. As part of this thesis

work, a scoping review was performed to examine manual therapy and the use of assistive stretching devices for HNC-related trismus and found variability in treatment methods, timing and protocols. No studies have investigated the use of manual therapy, such as joint traction or stretching in combination with a Dynasplint®.

1.1 Statement of the Problem and Purpose of the Thesis

The aim of this study was to fill a gap in knowledge around the feasibility of treating trismus with manual therapy and a Dynasplint® for survivors with HNC. While there have been previous trismus studies, none have evaluated manual therapy (such as traction and jaw stretching) with a Dynasplint®. In addition, all studies involved varying protocols to manage trismus including differences in the type of device, when the intervention was started, and the parameters of the chosen intervention.

The specific aims of this study were to determine the feasibility of study processes (e.g., recruitment rate, completion rate, adherence to protocol, and care pathway), resources, personnel, and safety of intervention (adverse events, mouth opening measurements), as well as the preliminary efficacy of the eight-week trismus intervention protocol to inform future research.

1.2 Objectives

Primary Objectives:
The primary outcome of this study was to determine study feasibility[16] at the following levels:

1. Feasibility of the processes:
    - recruitment rate (number of participants eligible and consenting divided by the number of participants referred)
    - steps in the process from identification of potential participants to study enrollment (description of patient pathway from enrollment to completion of the study)
    - retention rates (number of participants completing the study divided by the number of participants starting the study)

- adherence to the protocol (attendance at sessions, number of sessions with the Dynasplint® at home, minutes completed divided by minutes prescribed, intensity completed divided by intensity prescribed)

2. Assessment of resource needs: time required for assessment including length to complete surveys and manual therapy sessions, dental assessment for mouthpiece, and costs associated with the Dynasplint® device including the mouthpiece.
3. Personnel and management: needed expertise of physical therapist delivering the manual therapy intervention and dentist fabricating the mouthpiece.
4. Scientific: safety of intervention (i.e. serious and non-serious adverse event rates such as tooth damage, dental pain, increase in jaw soreness or stiffness.), determination of protocol feasibility including dose and response, point estimates and measures of variability for treatment effect. The primary objective measure was active maximal interincisal opening (MIO) and repeated measures of oral opening was conducted at the baseline testing session, before and after each treatment session, and at end of the eight-week intervention period.

Secondary Objectives:

In addition, the following secondary measures were evaluated:

1. Questionnaire for trismus symptoms (Gothenburg Trismus Questionnaire)
2. Pain (Visual Analogue Scale)
3. Quality of life (Short-Form 36 Health Survey).

These outcomes were administered at baseline and following the eight-week intervention period.

1.3 Hypotheses

1.3.1 Hypothesis related to feasibility and safety

The primary hypothesis was that the combined intervention of manual therapy and the use of the Dynasplint® would be feasible and safe for survivors with head and neck cancer experiencing trismus.

1.3.2 Hypothesis related to quality of life

A combined intervention of manual therapy and the use of a Dynasplint® would increase participants' MIO and positively impact their quality of life.

1.4 Delimitations

1. The study used a pre-post study design with single-subject analyses to evaluate the feasibility of a combined intervention of manual therapy and the use of an assistive device. No planned follow-up measures were conducted after the study intervention period of eight-weeks.
2. The Dynasplint® protocol was prescribed; however, if a participant was unable to follow the protocol due to pain or discomfort then the prescription was modified accordingly.
3. A slide caliper was used to measure MIO. The procedure was modified to protect the oral tissues by placing the caliper between two popsicle sticks; one popsicle stick placed on the upper incisor/ alveolar ridge and the other on the lower incisor/ alveolar ridge.
4. Trismus symptoms were evaluated using the Gothenburg Trismus Questionnaire (GTQ), pain was evaluated with a Visual Analogue Scale (VAS), and quality of life was evaluated using the Short-Form 36 Health Survey (SF-36).

1.5 Limitations

1. Participants in the study were volunteers, thus limiting generalizability to the larger population of individuals with head and neck cancer related trismus.
2. Sample size: n=10
3. There were no timeline restrictions for the participants regarding the time since the end of their cancer treatment and their eligibility for the STRIDE study. Thus, there was large variability among participants in terms of the time since diagnosis.

1.6 Significance of the Study

The incidence of trismus in HNC is largely unknown with rates ranging from 0% to 100%.[30] Once developed the impact of pain and dysfunction on the survivors eating, swallowing and

speech is considerable.[30] The knowledge gleaned from this research will inform future research in the area. Should the intervention prove beneficial, the protocol has the potential to be implemented clinically.

CHAPTER 2: A SCOPING REVIEW OF INTERVENTIONS FOR TRISMUS IN HEAD AND NECK CANCER- WHERE'S THE MANUAL THERAPY?

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Authors: Joni Nedeljak, Susan Armijo Olivo, Suresh Nayar, Ivonne Hernandez and Margaret L. McNeely

2.1 ABSTRACT

A scoping review of interventions for trismus in head and neck cancer — where's the manual therapy?

Purpose: Trismus, or restricted mouth opening, is a common side effect following treatment for head and neck cancer. We performed a scoping review to examine the characteristics, extent, and nature of existing research on manual therapy and jaw-mobilizing devices to prevent and manage trismus related to HNC.

Methods: Electronic searches were conducted in three databases: MEDLINE, EMBASE and PEDro.

Results: Nine studies were included. Eight studies examined the use of a jaw-mobilizing devices, and one study explored the benefit of remote telephone support. Two studies involved cancer survivors at risk of trismus, five studies examined cancer survivors with trismus, and two studies included cancer survivors both with, and at risk of trismus. No studies were found examining physiotherapist provision of manual therapy. Overall, we found that within-group comparisons supported benefit from use of a jaw-mobilizing device, whereas significant between-group differences were found only in non-RCTs. Issues were identified with study adherence and completion rates.

Conclusion: Findings suggests potential benefit from interventions to manage but not prevent trismus. To address low adherence and completion rates, consideration should be given to survivor symptoms, treatment burden, and enhancing support. Given its potential to enhance outcomes for survivors, research examining manual therapy is warranted.

Keywords: *trismus, scoping review, manual therapy, jaw-mobilizing device, head and neck cancer*

2.2 INTRODUCTION

Approximately 7,000 Canadians develop head and neck cancer (HNC) each year.[31] HNCs are commonly treated through surgery, radiation therapy (RT), chemotherapy (CT) or chemoradiotherapy.[31] These treatments are associated with side effects which can impact the survivor's quality of life (QoL).[12] Trismus, or restricted mouth opening of less than 35mm, is a side effect estimated to occur in 0-100 percent of HNC survivors following treatment.[30, 32] Trismus may develop because of surgery, RT or tumour invasion of the temporomandibular joint (TMJ) and/or local tissues. Symptoms of pain and stiffness are common, and trismus can compromise the survivor's ability to eat, drink, speak, and maintain oral hygiene.[30] Thus, the negative health impact of trismus on the survivor is significant.

Current approaches to address trismus aim to increase the maximal interincisal opening (MIO) of the jaw.[33] In our clinical setting, we teach active exercises to HNC survivors at risk of developing trismus, and prescribe manual therapy (MT) and stretching exercises to survivors if the condition manifests.[34, 35] The aim of MT is to restore function by improving jaw mobility, increasing muscle and tissue length, and reducing pain and inflammation.[36, 37] Moreover, to promote self-management home-based stretching regimens may include use of a jaw-mobilizing device.[33, 38] The prescription of a device is dependent on patient resources, as costs associated with purchase may be prohibitive. Where use of a jaw-mobilizing device is not an option (e.g. survivor resources are limited, or mouth opening is less than 7 mm), we may prescribe stacked tongue depressors instead.

Preliminary evidence from systematic reviews evaluating cancer related trismus support interventions which include jaw-mobilizing devices.[12, 39, 40] At present, however, there is no clear consensus on the optimal approach to prevent or manage trismus related to HNC. Findings of

prior reviews have highlighted issues with trial quality, the large heterogeneity among studies in terms of the type, timing and length of interventions, and the unpredictability of patient-treatment response. The aim of this scoping review was to explore the literature in order to better understand the complexity of the field of research.

2.3 METHODS

This study was designed as a scoping review and followed a rigorous methodology for collecting, synthesizing, and presenting findings from existing research.[41-43] Scoping reviews are especially relevant when an area is emerging or diverse because it examines the extent, range and nature of the research activity; as the primary interest.[44] MEDLINE, EMBASE, and PEDro databases were searched to find articles relating to prevention and treatment of trismus with MT and/or jaw mobilizing devices. The methodology utilized was based on the 5-step procedure created by Arksey and O'Malley.[45, 46] Below, we provide further details on how each step was implemented in this review.

Step 1: Research question

Specifically, we aimed to:

1. Provide a descriptive overview of the characteristics, extent, and nature of existing research on MT and jaw-mobilizing devices to prevent and manage trismus related to HNC.
2. Identify gaps in the literature to inform future research.

Step 2: Identification of relevant studies

A librarian was consulted at the University of Alberta to assist with the development of the search strategy. We searched the databases of MEDLINE and EMBASE using the terms such as "trismus," "head and neck cancer," and "physical therapy" and the associated MeSH terms.

"Trismus and Cancer" were the terms searched in the PEDro database (A detailed search strategy can be found in the Supplementary Material section on page 27).

Step 3: Study Selection

Articles were selected according to the following PICOS criteria:

1. Participants: adults (18 years of age or older) with a diagnosis of HNC, and experiencing, or at risk of developing trismus based on the definition of trismus as less than a 35mm interincisal distance established in 2006.[32]

2. Intervention: prevention or management of trismus through either MT or a jaw-mobilizing device/ tool, or both. MT was defined as the application of hands-on passive techniques to a joint or body region to enhance tissue extensibility and arthrokinematic joint motion.[47] A jaw-mobilizing device/ tool was defined as a patient self-administered device that aimed to stretch the oro-facial tissues and mobilize the TMJ.[48]

3. Comparison: control, usual care, alternative treatment (e.g. other jaw mobilizing devices) or no control group.

4. Outcome: The main outcome of interest was measurement of oral opening defined as MIO. Secondary outcomes included pain, function, and quality of life.

5. Study Design: Study were included if they were prospective randomized controlled trials (RCTs), controlled trials, and single group before and after studies. Retrospective designs and systematic reviews were excluded from this review. Combined interventions (e.g. medication with physiotherapy) were excluded unless the effect of physiotherapy intervention alone could be determined.

6. All articles had to be available in the English language, available in full text, and published between 2006 and March 2020.

Step 4: Data abstraction

After applying the search strategy, two authors (JN, MM) independently identified and evaluated potentially relevant articles for inclusion. A data abstraction table for the studies was created to collect relevant information on the type of study, intervention details, outcome measures, study results, and features.

Step 5: Collating, summarizing and reporting results

To better understand findings, we explored factors related to the intervention delivery, with particular attention to the timing of the intervention (starting the program before, during, or after cancer treatment), adherence, and completion rates, and adverse events.

2.4 RESULTS

A total of 58 articles were retrieved. After screening articles based on titles and duplicates, 25 were deemed ineligible leaving 33 articles for final screening based on inclusion/exclusion criteria. After full text screening, 23 further articles were excluded. One article was obtained from screening a reference list resulting in 11 articles[18, 29, 49-57] , representing 9 unique studies with a total of 460 survivors (Figure 1). Of the included studies, 5 were randomized controlled trials (RCTs)[49, 51, 55-57], 3 were controlled clinical trials[18, 50, 54] and 1 was a single group before and after study.[29] The studies included in the review were divided into three categories: 1) studies including survivors at risk of developing trismus (prevention); 2) studies that included survivors with trismus (management); and 3) studies that included survivors both with, and at risk of trismus (mixed prevention and management). Table 1 provides further description of the included studies.

Intervention Protocols

Eight studies examined the use of a jaw-mobilizing device, and one study explored the addition of remote telephone support to enhance adherence to the intervention. Many different devices were investigated included the Jaw Dynasplint® System (n=3), the Therabite® jaw device (n=5), the Engstrom jaw device (n=1), and the EZBite (n=1). No studies were found examining physical therapist provision of MT for either preventing or managing trismus. Among the included studies there was large heterogeneity in study types and intervention protocols. Differences among studies included the chosen experimental and comparison interventions, the timing and length of the study and secondary outcomes (Table 1).

The number of prescribed stretches, sessions per day, and duration of stretch differed greatly among the included studies. Repetitions ranged from 1 to 30, sessions per day ranged from 1 to 9, and duration of stretch ranged from 15 seconds to 30 minutes. Moreover, interventions ranged from 10 to 52 weeks in duration (Table 2).

Findings related to MIO:

Two studies focussed on the prevention of trismus and both of these studies began the intervention during the early cancer treatment period.[51, 57] Neither study, however, found benefit from use of a jaw-mobilizing device to prevent trismus.

Five studies aimed at managing survivors with trismus.[18, 29, 50, 54, 55] Two of the studies introduced the intervention after completion of cancer treatment[29, 55] and three studies started participants after surgery with, or without, subsequent adjuvant RT or chemotherapy.[18, 50, 54] Of these studies, four reported benefit from use of a jaw-mobilizing device for improving MIO.[18, 29, 50, 54]

Two studies were classified as mixed and including survivors both with, and at risk of trismus.[49, 56] One study involved survivors who were scheduled to undergo RT or chemoradiotherapy.[49] In this study, survivors were included if they perceived stiffness in the jaw, regardless of whether they had established trismus or not. No significant benefit was found from use of a Therabite® when compared to the use of tongue depressors. The second study found a significant benefit from the addition of telephone support to standard care comprising exercises, masseter muscle self-massage and use of tongue depressors when compared to standard care alone.[56]

Findings related to Secondary Outcomes:

Seven studies collected data on secondary outcomes including pain, mandibular function, and quality of life.[18, 29, 49, 50, 55-57] Five studies reported on pain as an outcome [18, 29, 49, 50, 55], with two treatment studies reporting a statistically significant decrease in pain in favour of the experimental intervention.[18, 29] Two management studies evaluated outcomes using the Gothenburg Trismus Questionnaire (GTQ) [18, 50], a trismus-specific self-administered questionnaire. Both studies reported significant improvement on the GTQ in favour of the intervention with a jaw-mobilizing device. Three studies measured mandibular function using the Mandibular Functional Impairment Questionnaire (MFIQ) [29, 55, 56] with one study finding a significant benefit in favour of the group receiving standard care plus telephone support when compared to the group receiving standard care alone.[56] Four studies measured quality of life using the EORTC QLQ-C30 or the EORTC H&N35 questionnaire.[18, 29, 49, 55] Only one study, which was categorized as a management study, reported a statistically significant improvement in quality of life favouring the intervention group using two different jaw-mobilizing devices.[18]

Follow-up findings

Three of the studies included in this scoping review performed follow-up assessments after the completion of the intervention period.[29, 53, 57] One study, included follow-up at both three-months and two-years, and reported significant benefit in favour of the intervention groups (using the Engstrom or Therabite® jaw devices) at each follow-up time point.[53] In addition, this study found a statistically significant benefit at two-year follow-up in favour of the intervention group for jaw-related problems, eating limitations, muscular tension and facial pain. Another study had a 14-week follow-up after completion of an intervention with the Dynasplint®. The authors reported a worsening of 2.3mm in MIO from end of the intervention to the follow-up, however, the MIO was still significantly better than at baseline.[29] The third study, examining the addition of Dynasplint® to standard care for trismus prevention, and included a follow-up at 6 months post-treatment.[57] The authors found no significant differences between groups, and reported that MIO in both groups had returned to near baseline by 6-months post-treatment.

Exploration of intervention parameters, adherence and completion rates and adverse events

Overall, we found that study completion rates ranged from 51% to 100%. Four studies had completion rates below 65%.[49-51, 55, 57] Moreover, where reported, adherence to the intervention was often low [18, 29, 50], even in studies with high completion rates.[18, 50] Protocols varied in terms of the total treatment time per day, ranging from 6.5 minutes to 90 minutes per day. Reported reasons for study withdrawals and poor adherence included disease progression, jaw and dental pain, presence of mucositis, difficulty with use or poor fit of the prescribed device, and time burden related to the intervention protocol.[18, 29, 49, 54, 55, 57] Based on the data abstracted, we identified three key considerations related to the findings of this scoping review: 1) intervention timing; 2) need for personalized care; and 3) enhanced support (Figure 2).

2.5 DISCUSSION

Main review findings

Similar to the findings of prior systematic reviews in the area[39, 40, 58], we found considerable heterogeneity amongst studies for study objectives (prevention, management or both), timing of the intervention relative to cancer treatment, intervention and comparison groups, sample sizes, and findings.[39, 40, 58] Overall, we found that within-group comparisons supported increases in MIO from use of a prescribed jaw-mobilizing device, whereas significant between-group difference were only found in non-RCTs. While we agree with the conclusions of prior reviews supporting preliminary evidence from use of a jaw-mobilizing devices,[39, 40, 58] RCT evidence supporting benefit is currently lacking. The only RCT examining management for existing trismus directly compared two jaw-mobilizing devices without a control/ standard care group and this trial was stopped prematurely due to low recruitment and high study attrition.[55]

Timing of intervention

More recent research suggests a trismus prevalence rate of 23.6%, with higher rates amongst survivors with oropharyngeal tumours, and those undergoing surgical reconstruction (i.e. free flap transfer), radiation therapy, and chemotherapy.[52] As trismus has been found to severely limit daily function and quality of life, a focus on interventions to prevent trismus appears prudent.[52] However, neither of the studies looking at preventing trismus nor the mixed prevention/ management studies were found to show benefit for improving MIO.[49, 51, 56, 57] Moreover, issues with device use and the time burden associated with preventative treatment regimens were found to negatively impact study adherence and completion rates.

Our findings support prior research suggesting that management of trismus may be most effective if commenced earlier in the cancer treatment trajectory.[59] One study divided

participants into two groups based on the time since their primary tumour treatment; a key finding was that treatment response to the Dynasplint® was better in the group less than 36 months from treatment. We concur with Loorents et al (2014) who recommended active surveillance of high-risk survivors, with early intervention at first onset of trismus — a strategy that may enhance outcomes while avoiding unnecessary burden on survivors without the condition.[51]

Many studies reported that participants were less able to comply with the intervention protocol during the later stages of RT due to painful mucositis, a treatment-related side effect of RT resulting in inflammation and ulceration of mucous membranes.[49, 50, 54, 57] In the clinical setting, we often recommend survivors limit or hold exercises until the mucositis has been medically managed or resolved. Future research studies should consider incorporating planned protocol modifications to avoid issues during this treatment time period when mucositis may preclude intervention delivery.

Need for personalized care

This scoping review identified low adherence and completion rates amongst many of the included studies. When we explored adverse events and reasons for withdrawals, many patient-related factors were found. These factors included issues with device fit, comfort, and protocol burden. For example, while the Therabite® was noted to better distribute pressure compared to the Engstrom device, the device was reported as difficult to use for survivors with a large overbite.[18] Three studies reported survivor difficulty when using the Therabite® and Dynasplint® in terms of ill-fitting devices and dental pain.[49, 55, 57] In one study, some participants reported no difficulty using the Dynasplint®, while others reported that the Dynasplint® protocol was burdensome.[29] In another study examining the EZbite, one third of the sample did

not comply with their assigned intervention, despite the fact that all participants were noted to have healthy anterior dentition.[50] At present, there does not seem to be a preferred device; thus, we recommend intervention selection based on survivor preferences, dental status, device fit, and resources.

Need for enhanced support

A single study examined the benefit of enhanced support to monitor progress and promote intervention adherence.[56] While a simple home-based intervention was prescribed, the group receiving regular telephone support was found to have significantly better improvement in MIO and mandibular function when compared to the group receiving standard care alone. The findings of the study highlight the value of close monitoring during the intervention period to allow for early identification of issues such as pain and mucositis, and to promote intervention adherence. Future research should consider the addition of formal support strategies to enhance survivor study adherence and completion.

A notable finding of this review was the lack of studies examining physiotherapist applied MT for trismus. A recent systematic review involving 48 RCTs examining MT and therapeutic exercise for temporomandibular disorders, found that MT alone or in combination with exercise showed promising effects.[36] MT is a safe intervention that helps to restore range of motion, reduce local ischemia, address fibrous adhesions, and stimulate synovial fluid production.[36] In the case of radiation-induced trismus, the mandible is often found to rest in a retracted position (limiting protrusion range of motion) due to fibrosis of the muscles of mastication.[60] MT may be helpful to stretch the adhered tissues and restore forward translation of the TMJ condyle along the articular eminence, allowing progression of MIO beyond 25 mm.[60]

Moreover, inclusion of physiotherapy may allow for closer monitoring of treatment response, side effects and tailoring of interventions to survivor needs.

Limitations

This scoping review involved searches of only three electronic databases. In addition, articles were limited to English language and had to be available in full text. Publication dates of between 2006 and 2020 were selected to align with the changing demographic and treatment of HNCs and improved survival.[61, 62] Thus, some important studies may have been missed. A primary limitation of this review is the large heterogeneity found amongst study designs, interventions, comparisons, and the low reported adherence and completion rates. These findings preclude our ability to make clear conclusions on the optimal intervention to prevent and treat trismus.

2.6 CONCLUSIONS

The findings of this review suggest benefit from the use of jaw-mobilizing devices in the management but not prevention of trismus related to head and neck cancer, with evidence supporting improved outcomes largely from non-RCTs. To address low adherence and completion rates, consideration should be given to the timing of the intervention, personalizing care to address survivor symptoms and treatment burden, and enhancing survivor support. Given its potential to improve trismus, research examining physiotherapist provision of MT alone or in conjunction with a jaw-mobilizing device is warranted.

Table 1: Characteristics of Included Studies

Author/ Year/Design/ Sample size Country/	Timing and Duration of Intervention	Experimental Intervention Details	Control/ Comparison Details	Outcome Measures	Study Results	Issues/ Considerations
	Prevention of Trismus					
Loorents et al (2014)[51] RCT N=66 Sweden	During radiation therapy, up to 12 months after treatment completion	**Therabite®** group: 5 stretches, 5x daily, held for 15s	**Control** group: no training	-MIO	No significant between group differences in MIO	High burden given the low incidence of trismus in study
Zatarain et al (2018)[57] RCT: Feasibility N=40	During radiation therapy, to 3 months after treatment	**Dynasplint®** group: standard care + use of the Dynasplint® for 30 mins, 3x/day during cancer treatment to 3 months posttreatment	**Standard care** group: 1) education 2) interincisal measurement cards for self-monitoring 3) Exercise: opening & lateral movements with a 30s hold,	-MIO	No significant between group differences in MIO	Barriers to adherence (Dynasplint®): mucositis, pain, gagging, fatigue and poor device fit.

USA	Follow-up at 6 months		moving the jaw in a circle for 5 reps each direction, applying downward pressure for 30s, and jaw massage for 30s			
	Management of Trismus					
Ren et al (2013)[54] Controlled Trial N=22 China	1-2 weeks after maxillectomy, with or without neo/ adjuvant RT (or both) for duration of 2-6 weeks	**Therabite®** group: mouth opening exercises 3-5 times a day, 30-40 oscillations each time with a 2 second pause at maximum mouth opening	**Stacked tongue depressors:** same instructions as Therabite® group	-MIO	No significant MIO differences between groups	Barriers to adherence: RT related symptoms
Kamstra et al (2016)[29]	Post-treatment Duration: 16 weeks; Follow-up at 30 weeks	**Dynasplint®** group: 3x/day: 30 min each -Increased intensity every 2 weeks (as tolerated) until	Not applicable	-MIO -Pain: VAS -MFIQ -EORTC QLQ C30	Significant within group improvement in MIO, pain and perceived difficulty in mouth	Patients >36 months could continue to use device for up to 28 weeks

Single group before-and-after study N= 18 Netherlands		a maximum tolerance was reached		-EORTC QLQ- H&N35	opening at end of intervention -Significant improvement in MIO at follow-up	
Li, Chang, Chiang, Lin, Chen (2019)[50] Controlled Trial: 3 groups N=48 with HNC Germany	After surgery with or without RT for 12 weeks	**EZbite** group: active/passive exercises 9x/day. 1) warm up: jaw opening 10x; 2) passive stretching with EZBite device for 30s, repeated 5x; and 3) 5 reps of active biting exercise against resistance of device	**Conventional** group: as per EZbite protocol with tongue depressors/ rubber hose **Control** group: patients who did not comply with assigned group (n =16)	-MIO -HRQL questionnaire -GTQ	Significant improvement in MIO, jaw-related problems, eating limitations and muscular tension in favour of EZBite group compared to conventional and control group	All participants had healthy anterior dentition 1/3 of sample did not comply with assigned intervention

Pauli, et al (2014, 2015, 2016)[18, 52, 53] Controlled Trial N=100 Sweden	Post RT (with or without CT or Surgery) x ≤ 6 months Duration: 10 weeks; Follow-up: 3 month and 2-years	**Intervention** within group randomly allocated to Therabite® or Engström device 1) warm up: jaw opening 10x + lateral movements 10x; 2) passive stretch with assigned device, 30s, 5 repetitions, 5x daily; 3) 5 reps of active exercise with bites towards resistance.	**Control** group: matched patients living outside region. No intervention. NB: 14 controls received treatment for trismus as per standard care	-MIO -GTQ -EORTC QLQ C30 -EORTC QLQ H&N35	Significant improvement in MIO, GTQ domains, functional scales of EORTC QLG-C30 and H&N 35 components in favour of the combined intervention group at 3 month and 2-year follow-ups when compared with control group	No significant differences for between Therabite® and Engström devices

van der Geer, et al (2020)[55]
 	
RCT
N=27
Germany
	Post-treatment
	
	Stratified: < or > 36 months
	
	Duration: 12-weeks
	Follow-up: 26-weeks
		Dynasplint® group: one stretch/session, 3x/day, 30 mins/stretch	**Therabite®** group: 20 stretches per session, 6 times a day, 30 seconds per stretch, OR 30 stretches per session, 4 times a day, 30 seconds per stretch.	- MIO
				-MFIQ,
				EORTC QLQ-C30, EORTC QLQ-H&N35
					No significant differences between groups	Stopped early: poor recruitment and completion
						-Barriers to adherence:
						pain/ soreness (n = 8);
						unable to use device (n =1);
						tooth fracture (n =1);
						protocol intensity (n =1)

	Mixed: Prevention and Management					
Lee et al (2018)[49] Multicentre RCT with qualitative component N=71 England	3 weeks post-surgery (or 1-3 weeks before RT if no prior surgery) – during adjuvant RT or chemoradiotherapy Duration: 6 months	**Therabite®** group: 1) mouth opening exercise: 5 repetitions with 30 second hold, performed 5x/day; 2) recorded mouth opening each day with Therabite® scale	**Wooden spatula** group (tongue depressors): Protocol as per Therabite® group	-MIO - EORTC QLQ-C 30 -EORTC QLQ H&N 35	No significant difference between groups in MIO, quality of life	Included patients with > 35mm opening -Barriers to adherence: mucositis due to RT Therabite®: pain, nausea -Spatula: pain and lack of perceived effectiveness
Wang et al (2019)[63] RCT N=68 Taiwan	Pre-surgery baseline, post-surgery intervention: start – day of hospital discharge. Duration: 3 months	**Standard care & telephone support** at weeks 1, 2, 3,4, 8 and 12 to monitor progress and enhance adherence	**Standard care**: 3x/day for 3 months 1) warm compress on cheek: 15 mins, 2) masseter muscle massage: 5 mins. 3) active jaw ROM and stretching exercises: 5 mins. 3) passive stretching: wooden tongue depressors: 15 mins	-MIO -MFIQ	-Significant between group improvement in MIO and mandibular function in favour of remote support.	76% of sample had surgery alone

Table 2. Synthesis of Study Parameters for Interventions Using Jaw Mobilizing Devices

Author	Time relative to treatment	Device	Total Exercise minutes/day	Intervention duration	Adherence rate	Completion rate	Mean MIO baseline	Within Group Mean Improvement in MIO (95% CI)
Prevention of Trismus								
Loorents et al (2014)[51]	During RT or 12 months	Therabite®	6.25 mins	12 months	32%	70%	NR	-0.3%; *NS*
Zatarain et al (2018) [57]	During RT and for 3 months after	Dynasplint®	90 mins	4 months	25%	50%	46 mm*	42 mm* (IQR: 34.5, 46); *NS*
Management of Trismus								
Ren et al (2013)[28]	Early post-surgical: with or without neo or adjuvant RT	Therabite®	3-6.5 mins	2-6 weeks	91%	100%	17.0 mm	14.0 mm (7.5-20.5)
		Tongue Depressors	3-6.5 mins	2-6 weeks	72%	100%	17.0 mm	15.0 mm (8.5-21.5)
Li et al (2019)[23]	Early post-surgical: no treatment or on RT	EZ bite	22.5 mins	12 weeks	67%	100%	15.7 mm	14.0 mm (12.1-16.7)
		Tongue depressors	22.5 mins	12 weeks	67%	100%	14.8 mm	10.5 mm (6.3-12.5)
Pauli et al (2014)[25-27]	Within 6 months of RT completion	Therabite®	12.5 mins	10 weeks	46%	100%	32.6 mm	7.2 mm (5.18-9.30)
		Engstrom	12.5 mins	10 weeks	63%	100%	31.8 mm	5.5 mm (3.1-8.0)

Kamstra et al (2016)[21]	Post-treatment: 12-54 months	Dynasplint®	90 mins	16 weeks	44%	83%	22.6 mm	7.1 mm (4.9-9.3)
van der Geer et al (2020)[29]	Post-treatment: 7-157 months	Dynasplint®	90 mins	12 weeks	NR	51%	22.0 mm*	1.5 mm (IQR 1.0; 3.0); *NS*
	Post-treatment: 8-132 months	Therabite®	60 mins	12 weeks	NR	51%	27.0 mm*	3.0 mm (IQR 2.0; 4.0); *NS*
Mixed: Prevention and Management								
Lee et al (2018)[22]	During RT up to 6 months after	Therabite®	12.5 mins	6 months	73%	70%	24 mm	Change and final scores: NR Mean difference between groups: -2.43 (-8.15-3.29): *NS*
		Spatula	12.5 mins	6 months	55%	59%	21.8 mm	

Figure 1: Article Search

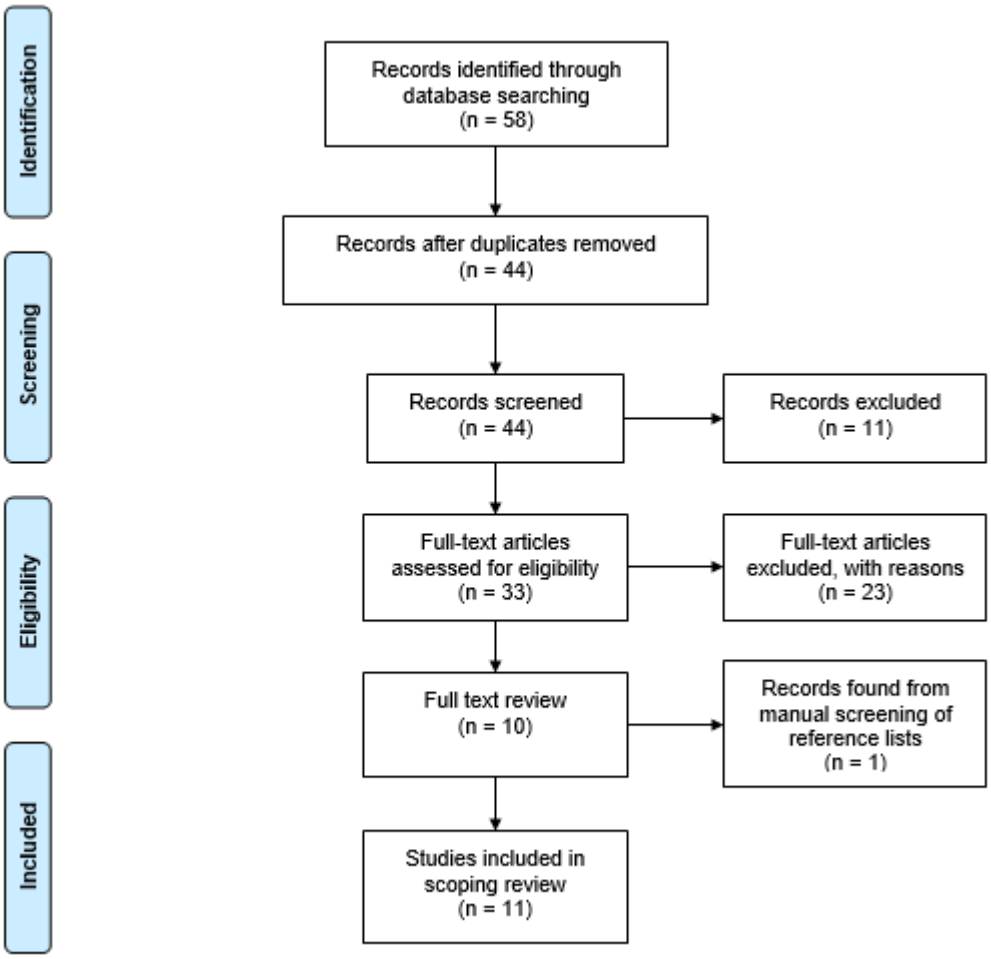
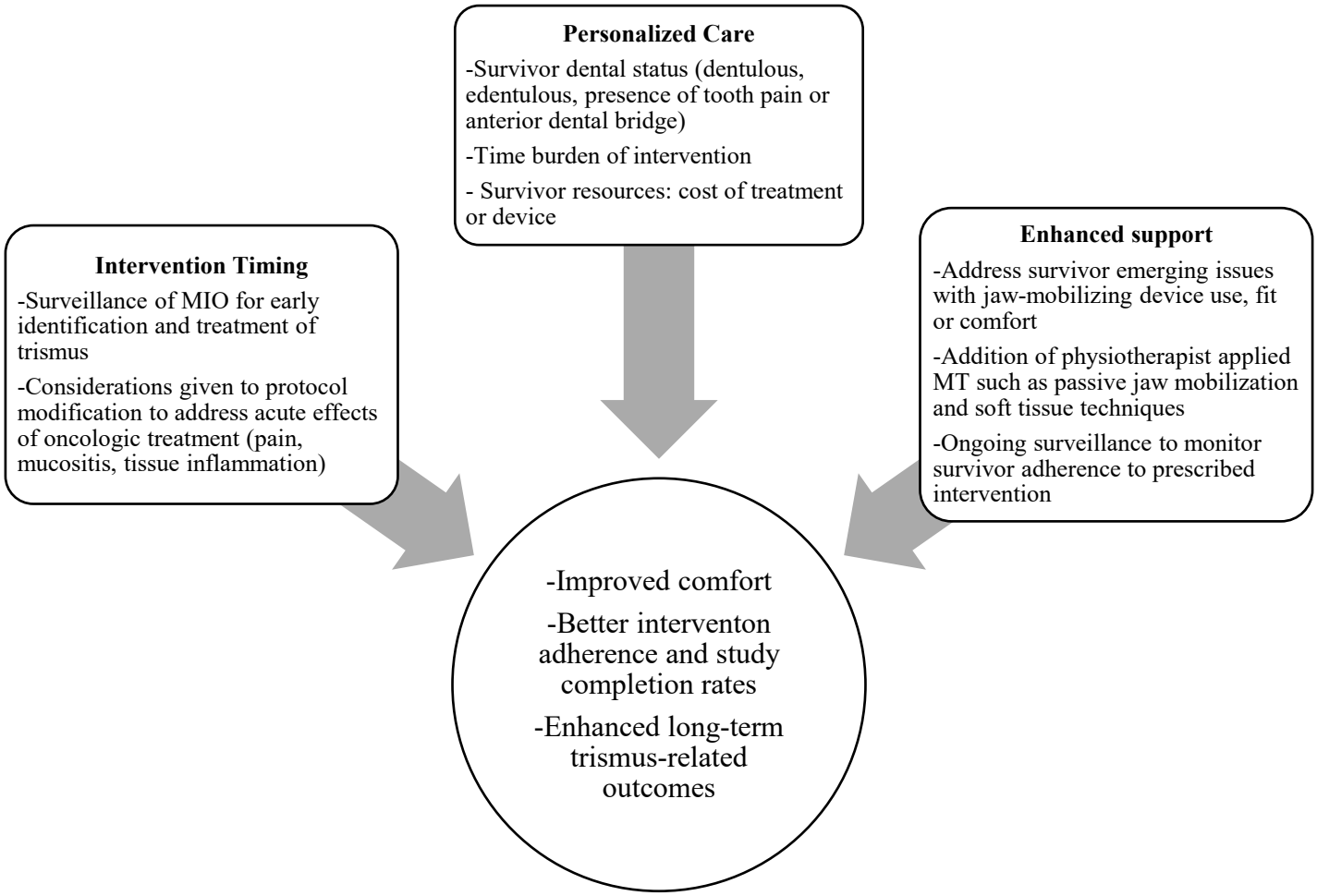


Figure 2: Future trismus intervention considerations to optimize outcomes



Supplementary Material: Example of Medline Search

*all suffixes of the root word
$ all the spellings of the word (ex: tum$r = tumor/tumour)

Concept: HNC

1. ((head and neck neoplasm*) OR (head and neck carcinoma*) OR (head and neck sarcoma*) OR (head and neck tum$r*) OR (neck cancer*).mp.

2. ((head and neck neoplasm*) or (head and neck carcinoma*) or (head and neck sarcoma*) or (head and neck tum$r*) or neck cancer*).mp.

3. (laryngeal cancer* or oropharyngeal cancer* or nasal cavity cancer* or hypopharyngeal cancer* or paranasal sinus cancer* or oral cancer* or nasopharyngeal cancer* or salivary gland cancer* or lip cancer* or throat cancer* or (malignant head and neck cancer*) or (benign head and neck cancer*) or metastatic squamous neck cancer with occult primary).mp.

Concept: Trismus

4. (trismus.mp. or exp TRISMUS/)

5. exp neoplasms/ or exp jaw neoplasms/ or exp mandibular diseases/ or temporomandibular joint disorders/ or exp mandibular neoplasms/ or exp maxillary diseases/ or joint diseases/ or muscular diseases/ or musculoskeletal abnormalities/

6. (mandibular function or masseter muscle spasm* or jaw stiffness or lockjaw or temporomandibular joint cancer*).mp

Concept: Physical Therapy

7. "diseases (non mesh)"/ or physical therapy modalities/ or exercise movement techniques/ or exercise therapy/ or musculoskeletal manipulations/ or radiotherapy/ or rehabilitation/ or therapies, investigational/ or "health care (non mesh)"/

8. (physiotherap* or manual therap* or rehab*).mp.

9. (exercis* rehab* or physical therap* treatment or physical therap* technique*).mp.

CHAPTER 3: METHODS AND PROCEDURES

3.1 Overview of Study Design

STRIDE or "Stretching Therapy for Patients with Trismus using a Dynasplint® and Exercise" was a feasibility study conducted at the University of Alberta in Edmonton, Alberta, Canada from September 2018 to June 2019. Participants meeting eligibility requirements were enrolled in an eight-week trismus program including manual therapy and a Jaw Dynasplint® System.

3.2 Ethics Approval

Ethical approval was received from the Health Research Ethics Board of Alberta Cancer Committee on September 4, 2018 (Appendix A). The study was registered at www.clinicaltrials.gov (Identifier: NCT03178110). Written informed consent including the right to withdraw, confidentiality, risks, and the benefits of participating in the study was obtained from each individual with trismus taking part in the study (Appendix B). Participants were informed that they could withdraw from the study at any time point, for any reason. Study documents were maintained in a locked filing cabinet at the Cancer Rehabilitation Clinic in Corbett Hall at the University of Alberta.

3.3 Participants

Participants were identified through clinics at the Cross Cancer Institute, University of Alberta Hospital, and Institute for Reconstructive Sciences in Medicine (Misericordia Hospital). If a survivor was interested in taking part in the study, he/she was required to initiate contact with the investigators. Further information about the study was available for interested survivors via a study brochure, as seen in Appendix C. Participants contacting the research team were then screened for eligibility (Appendix D).

3.4 Inclusion Criteria

1. A diagnosis of head and neck cancer

2. Cancer treatment included surgery and/or radiation therapy
3. An oral opening of less than 35mm between the upper and lower incisors or an oral opening of less than 55mm for edentulous participants (as measured with a slide calliper).
4. Completed all treatments for cancer (no restrictions on the time post-treatment)

3.5 Exclusion Criteria

1. 17 years or younger
2. Osteoporosis, osteoradionecrosis, or active cancer in the region
3. Serious or uncontrolled co-morbid disease that would interfere with testing or treatment (for example: heart failure, uncontrolled diabetes, mental illness, depression, fibromyalgia, or other active cancers)
4. Inability to provide informed consent
5. Inability to comply with the assessment and/or treatment (i.e. unable to attend treatment sessions due to extended vacation > two weeks)

3.6 Study Design

A pre-post single group study with a single-subject analyses method was conducted.[15, 64, 65] The single-subject analysis was chosen because in addition to providing feedback to investigators about the effect of the intervention, clinical significance of the results for a specific group of patients can be derived.[64] Thus, variables that are functionally important for treatment can become evident. To determine the effectiveness of the treatment protocol, multiple baseline measures as well as repeated measures during the intervention phases were completed. The multiple baseline measures were used to increase the potential number of comparisons that can be made between within a data series, ultimately strengthening the confidence with which conclusions are made from the data (Appendix E).

3.7 Baseline and 8-Week Evaluation

On the first day of study enrollment, participants were asked to complete questionnaires (explained below) and six jaw opening measurements: three active openings (the participant

opened their jaw as wide as they could on their own) and three passive openings (the participant opened their jaw as wide as they could and the therapist applied additional pressure to open the mouth further). This series of measurements was repeated at baseline and upon completion of the study. MIO was measured by two assessors with one ensure proper positioning, and the other taking the measurement using a slide caliper. One assessor placed a popsicle stick on the upper incisors and the other popsicle stick on the lower incisors. The second assessor took the measurement using the slide caliper (Figure 1). This procedure was done as positioning of the lower mandible and measuring with the slide caliper alone was difficult. Moreover, we had concerns over safety of the caliper edges on compromised tissues, especially in those with limited mouth opening and/or were edentulous. In addition, the sticks were more comfortable for participants who were edentulous than the rigid edges of the caliper. We used popsicle sticks for each participant at each session to standardize the measurement. It was also standardized by always taking three measurements and having a single assessor measure with the caliper each time. Each measurement was recorded, and the average of the three active range of motion measurements was used to determine the active MIO range, and the average of the three passive measurements was used to determine the passive MIO range.

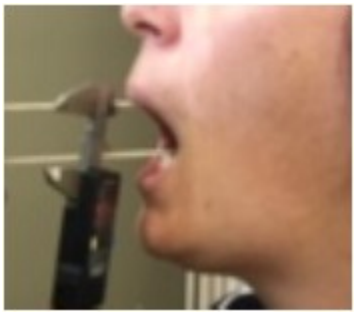


Figure 1: MIO Measurement

3.7.1 Questionnaires:

Participants were asked to complete questionnaires at the beginning and end of the STRIDE study. The first questionnaire provided information on the participant's identifying information (Appendix F). The second included three questionnaires combined into one survey package

(Appendix G): the Short-Form 36 Health Survey (SF-36) [21], a pain Visual Analogue Scale (VAS)[20, 66] and the Gothenburg Trismus Questionnaire (GTQ).[19]

Short-Form 36 Health Survey (SF-36): The SF-36 is comprised of 36 items that cover eight health domains: (1) limitations in social activities because of health problems, (2) limitations in social activities because of physical or emotional problems; (3) limitations in usual role activities because of physical health problems; (4) bodily pain, (5) general mental health, (6) limitations in usual role activities because of emotional problems, and (7) vitality, and (8) general health perceptions. The number of response choices per item range from two to six. The scores on each dimension are coded, summarized, and transformed onto a scale from 0 to 100 in which a higher score indicates better self-perceived health.[21]

Pain Visual Analogue Scale (VAS): A visual analogue linear scale was used. The VAS was labeled with the two boundaries of pain sensation: "0", meaning "no pain" at the one end and "100", meaning "worst possible pain" at the other end. The literature reported and confirmed the validity and reliability of these methods for determining pain intensity.[20, 66]

Gothenburg Trismus Questionnaire (GTQ): GTQ is a symptom-specific trismus questionnaire.[3] It contains 21 items; with 13 items divided into the three domains: jaw-related problems (six items); eating limitation (four items); and muscular tension (three items). The remaining eight items are retained as single items. The domains and single items range from 0–100, where 100 indicate maximal number of symptoms and 0 is equal to no symptoms. The questionnaire has a one-week recall period for the three domains. The GTQ is suggested to be used as a screening tool as well as an endpoint in interventions and jaw physiotherapy/rehabilitation studies.[19]

The study coordinator completed a questionnaire of each participant's medical information, which included information about their cancer diagnosis (Appendix H).

3.8 Intervention

Individuals included in the study participated in a combined physical therapy protocol comprising manual therapy and home use of a jaw-mobilizing device for eight weeks. The first two weeks of treatment included two days a week of manual therapy and education on jaw exercises to do at home (Table 1). In addition, participants were scheduled for a dental appointment for assessment of the Dynasplint® mouthpiece. Participants met at Corbett Hall and then walked to the School of Dentistry Oral Health Clinic in the Edmonton Clinic across the street. Participants met with the study dental specialist and had a mouthpiece fabricated for use with the Dynasplint®.[13] Home use of the Dynasplint® was started on week three of the protocol (Table 1).

3.8.1 Manual Therapy component:

The participants underwent a 30-60-minute treatment session of manual therapy two times per week, for an eight-week period. We followed the procedures as outlined by de-las-Penas et al (2018).[67] Treatment was adapted individually to the needs and presentation of the participant (further details on modifications are provided in Appendix I).

At the beginning and end of each session, three active MIO measurements were taken. This was done using a slide caliper and popsicle sticks, as explained above. The best score was recorded for each time point (Appendix J).

Table 1: Prescribed Dynasplint® intervention

Week	**Time per session (Minutes)**	**Dynasplint® Resistance Level**	**Modifications**
1 2	Manual therapy only		
Start of Dynasplint			
3	15	0.5	
4	20	0.5	

5	25	0.5	
6	30	0.5	
7	30	1.0	
8	30	1.5	

The manual therapy intervention for the TMJ[67-69] comprised of:

1. Cervical spine range of motion and stretching: distraction, side flexion and rotations: 5-10 minutes.[70]
2. TMJ distraction
3. TMJ distraction with anterior translation (protrusion)
4. TMJ traction in the anterior-distal direction (J stroke)
5. TMJ lateral deviations

These techniques are illustrated in Appendix K.

3.8.2 Home-based Opening Exercises

This home exercise program was introduced at the first manual therapy session. Each participant was given a written copy of the seven exercises and an explanation of how to perform them. The program sheet included a list of the exercises, a written description of how to execute the exercise, a picture of the exercise, and the amount of repetitions (6) and sets (3) they were to perform each day. Participants were also offered an electronic copy of the program through email. This online program was the exact same as the paper copy; however, the exercise pictures were substituted with videos to demonstrate the exercises. Participants were encouraged to do the program at least once a day to help them improve their MIO (home exercise program shown in Appendix L).

3.8.3 Home Exercise Component with Dynasplint®

All participants were instructed on use of the Jaw Dynasplint® System at home. The participant's initial introduction to the Dynasplint® included training on donning and doffing of the device. Verbal and written instructions were provided at the initial session and were repeated, as needed, through the duration of the study for safety, general wear and care, and tension setting goals. Participant started use of the Dynasplint® for 15 minutes, twice a day starting in week three. The duration of each treatment session was progressed, as tolerated, by five minutes each week from weeks 4-6 (Week 4: 20 minutes; Week 5: 25 minutes, Week 6: 30 minutes). The participants were asked to perform two sessions each day, every day. If the exercises were well tolerated, after week 6, the duration was held constant at 30 minutes and the intensity was increased over weeks 7-8.

Participants were given an Exercise Diary to record their daily exercise sessions. They were instructed to document the Dynasplint® duration, resistance, and number of sessions completed each day. Participants were also encouraged to report any issues with use of Dynasplint® such as inability to apply, use the device or symptoms such as jaw pain after use. They were also asked to record any benefits such as less discomfort or improved opening after sessions. Participant diaries are outlined in Appendix M.

3.9 Statistical Analysis

Demographic variables are presented in a tabulated form as median/range for interval data, and frequency/percentage for nominal data. As the primary objective of the study was to test feasibility; the recruitment rates, retention rates, and adherence rates were calculated, and the mean percentage was reported. Objective measures and self-reported questionnaires involved interval data and are presented as the median and range for the descriptive statistic.

The 2-standard deviation band method (2-SD)[71] was used to analyze the behavior of each participant on the outcome of interest before, during, and after the treatment. The 2-SD band was performed as described in the literature: the mean and the standard deviation of the baseline data

points were computed, then, bands representing 2-SD were drawn on the graph, above and below the mean of the baseline data points. A significant change was present when two or more consecutive data points in the treatment period fell outside the 2-SD bands (α=0.05).[71] The minimally important difference (MID) levels were determined to inform clinical relevance of the findings. The mean difference (md) were calculated by subtracting the mean value of the Phase 2 data points (mp2) from the mean value of the baseline data (mb) points (md = mp2 – mb).[71]

CHAPTER 4: RESULTS

A total of 10 individuals with trismus related to HNC were recruited to the study (Table 2). Participants included 4 females and 6 males, with a mean age of 62.2 years and a standard deviation of 24.

Further information on the baseline characteristics and demographics of the participants are provided in Table 2. The medical data related to the type of HNC, overall AJCC Stage, Human Papilloma Virus (HPV) status, and the type of treatment undergone are summarized in Table 3.

Table 2: Participant characteristics and demographics

N=10	**Participants**
Gender	Male: 6 Female: 4
Age (years)	Mean: 62.2 Standard deviation: 24
Marital Status	**Frequency**
Never Married	(5) 50%
Married	(4) 40%
Common Law	(1) 10%
Separated	
Widowed	
Divorced	

Education (highest level attained)	**Frequency**
Some High School	(3) 30%
Completed High School	(2) 20%
Some University/College	(2) 20%
Completed University/College	(2) 20%
Some Graduate School	
Completed Graduate School	(1) 10%
Annual Family Income	**Frequency**
<20,000	(1) 10%
Between 20-39,999	(1) 10%
Between 40-59,999	
Between 60-79,999	(4) 40%
Between 80-99,999	
>100,000	(2) 20%
N/A	(2) 20%
Current Employment Status	**Frequency**
Disability	(4) 40%
Retired	(4) 40%
Part-Time	(1) 10%
Homemaker	
Full Time	(1) 10%
Temporarily Unemployed	
Ethnic Origin or Ancestry	**Frequency**
European	(7) 70%
British/Aboriginal	(1) 10%
Canadian	(1) 10%
Other	(1) 10%

Smoking	**Frequency**
Never Smoked	(1) 10%
Ex-Smoker	(6) 60%
Occasional Smoker	(3) 30%
Regular Smoker (smoke everyday)	
Drinking	**Frequency**
Never Drank	
Ex-Drinker	(2) 20%
Occasional Drinker	(3) 30%
Social Drinker	(5) 50%
Regular Drinker (drink every day)	

Table 3: Medical data

Type	**Number (%)**
Oropharyngeal	(8) 80%
Nasal cavity and paranasal sinus	(1) 10%
Rhabdomyosarcoma	(1) 10%
Overall AJCC Stage	**Number (%)**
I	(1) 10%
II	(2) 20%
III	(3) 30%
IV	(3) 30%
Unknown	(1) 10%
HPV status	**Number (%)**
Positive	(5) 50%
Negative	(5) 50%
Treatment	**Number (%)**

Surgery alone	
Radiation Therapy alone	
Chemotherapy alone	
Surgery + Radiation Therapy	(5) 50%
Surgery + Chemotherapy	
Surgery + Radiation Therapy + Chemotherapy	(5) 50%
Date of Treatment to Start of STRIDE Study (2018)	**Number (%)**
</=36 months	(5) 50%
>36 months	(5) 50%

4.1 Primary Feasibility Outcomes

4.1.1 Feasibility of the Process:

Recruitment rate:

From December 2018 to April 2019, a total of 10 of the 12 eligible participants were enrolled in the STRIDE study for an overall recruitment rate of 83% (approximately 2 participants per month). Two individuals were referred but did not contact STRIDE coordinators to join the study. All 10 participants contacting the STRIDE study coordinators were included in the study (100%).

Mapping the steps in the study process:

Participants called the Cancer Rehabilitation Clinic to be enrolled in the study. After they were screened and deemed eligible to enter STRIDE, they were booked for their first appointment. Upon completing the initial baseline assessment session, they were scheduled for two manual therapy sessions a week for an 8-week period. In addition, they were scheduled for a dental appointment to be fitted with a Dynasplint® mouthpiece. The final assessment session was booked within 1-3 days of completion of the intervention protocol.

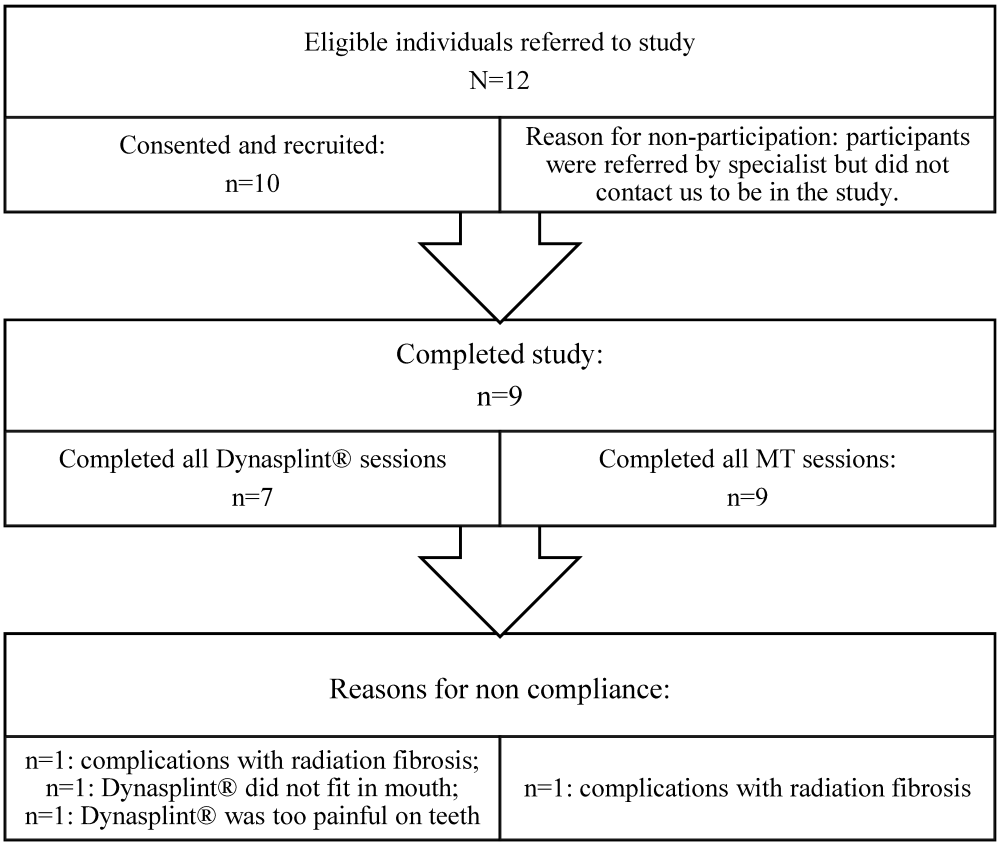


Figure 2: Study Flow

Retention rate:

Nine of 10 (90%) participants who started the STRIDE study completed the program. The individual who was unable to complete STRIDE had complications due to a radiation fibrosis syndrome flare-up.

Adherence:

All participants completed the baseline questionnaire and MIO measurements. Two participants were unable to be fitted for a mouthpiece; both due to limited mouth opening. The adherence rate for the manual therapy sessions was 98%, with one participant missing 4 sessions due to the above stated complications with radiation fibrosis syndrome prior to study withdrawal. The other nine participants were able to attend 100% of their manual therapy sessions.

Adherence rates for the Dynasplint® sessions are summarized in Table 4. Seven out of ten participants (70%) were able to use the Dynasplint®. One participant was unable to be fitted for a mouthpiece because the Dynasplint® plates were too wide to fit inside her mouth. Another participant had severe trismus (approximately 5mm of mouth opening) on study entry. She was instructed to wedge the Dynasplint® plates between her teeth to try passively opening her jaw. She used the device twice a day; however, was only able to tolerate use of the device for five minutes each time. A third participant did not adhere to the Dynasplint® protocol due to pain from the device on his upper anterior dental bridge. He was not able to tolerate the device despite modifications, and discontinued use of the device at week 7.

Six out of the seven participants who used the Dynasplint® completed and returned their daily diary. Of the six participants that provided data through the diary, a total of 482 sessions out of a possible 504 were completed (96%). Three participants were unable to reach the 1.5 intensity mark on the Dynasplint®. Reasons for not progressing in intensity included (1) infection in the region unrelated to the study causing pain (n =1), (2) onset of headache at increased intensity (n =1), and (3) dental discomfort with higher pressure (n =1). The total minutes of stretching completed by the six participants who completed their diary was 11,845 out of a possible 12,600 minutes (94%).

Table 4: Dynasplint® Adherence

	Number of Dynasplint® Sessions (Attended/Prescribed)	**Participants able to Manage Dynasplint® Intensity**	**Dynasplint® Minutes (Completed/Prescribed)**
Total (6 participants)	482/504 (96%)	3/6 (50%)	11,845/12,600 minutes (94%)

4.1.2 Assessment of Resource Needs:

Time requirements:

Participants were required to contact STRIDE investigators if they were interested in taking part in the study. When they called, they were informed of the study purpose and the expected commitment requirements. They were also asked questions regarding their eligibility. If they met the criteria, they were scheduled for their first appointment at Corbett Hall.

The first session (and the final session) took approximately 75-95 minutes. These sessions took more time than normal treatment days as they were asked to read and sign the consent form, complete the online questionnaire and physical assessment (active and passive MIO measurements), and then continue onto a normal treatment. Participants were then scheduled twice a week for manual therapy. These sessions took approximately 1 hour.

Participants were also booked for a dental appointment. On the day of the dental appointment, participants met a STRIDE investigator at Corbett Hall and together they walked across the road to the Dental Clinic. They met with the study dentist and were fitted with a mouthpiece. The session took approximately 1 hour.

Starting in the third week, participants were asked to start including the Dynasplint® into their jaw exercises twice a day at home. The sessions started with 15 minutes, twice a day, and progressively increased by 5 minutes each week. Once participants reached 30 minutes, twice a day, they increased tension instead of time. The time required to complete the study is summarized in Table 5.

Table 5: Time required for participants to complete the STRIDE study

Activity	**Frequency**	**Time**
Initial phone call (study description, screening)	-1x	~10 minutes
First day	-1x	-Consent form: ~5 minutes -Questionnaire: ~10-20 minutes -Baseline Assessment: ~10 minutes -Treatment: ~45-60 minutes -Total: ~70-95 minutes
Treatment Sessions	-2x/week for 8 weeks	~45-60 minutes
Dentist Appointment	-1x	~60-90 minutes
Dynasplint® Exercise Sessions	-2x/day for 6 weeks	30-60 minutes per day
Last day	-1x	-Questionnaire: ~10-20 minutes -Final Assessment: ~10 minutes -Treatment: ~45-60 minutes -Total: ~65-90 minutes

Cost:

The total estimated cost for rental of the Dynasplint® is $1,100 per person. Four Dynasplints® were provided on loan (in kind) for the STRIDE study from the Dynasplint® company and 2 were provided on loan from the Cancer Rehabilitation Clinic, for a total in kind cost of $11,000. Each participant had a custom mouthpiece made for them by a dentist. The cost of making the mouthpiece was approximately $400 per person; however, the mouthpieces were also provided in kind. A further breakdown of the costs associated with the STRIDE study are outlined in Table 6.

Table 6: Breakdown of study costs

Position	**Time/Type/Cost per One Participant**	**Estimated Expenses for 10 Participants**
Physical Therapist	Neck stretching, jaw mobilizations, and education on the Dynasplint®. ~$40/hour* (intervention is 8 weeks) 8x2hours/week= 16 hours 16x40= $640.00	$6400.00
Parking	$5.50/visit 2 sessions/week 5.5x2=$11/week 11x8 (weeks of study) = $88	$880.00
Dynasplint®	$550/month x 2 months= $1100/person	$11,000 For STRIDE: In Kind- Cancer Rehabilitation Clinic, Dynasplint® Company
Dynasplint® Mouthpiece	$400/person	$4,000 For Study: In Kind- University of Alberta Faculty of Dentistry
Slide Caliper	$30	$30 For Study: In Kind- Susan Olivo
Miscellaneous	Gloves, alcohol swabs, tongue depressors, photocopies, brochures	~$100.00 In Kind- Cancer Rehabilitation Clinic
Total		**$22,410.00**

*Alberta Health Services (AHS): physiotherapist average pay rate is $37.30 to $55.25 per hour.

4.1.3 Personnel and Management:

Each STRIDE session required a physiotherapist (or a specialist trained by a physiotherapist) to provide the manual therapy treatment. In addition, a specialist dentist was required to make the mouthpieces for the participants and ensure the fit was appropriate and comfortable.

4.1.4 Scientific Measures:

Safety of intervention:

Adverse events: One participant who was edentulous was unable to use the Dynasplint® because it caused pain to the gums and soft tissues. Two participants experienced an infection in their mouths (not related to the STRIDE study) that caused increased swelling in the cheeks and increased soreness when opening the jaw. The associated swelling and pain impacted their ability to follow their Dynasplint® program. As noted earlier, one participant was unable to continue the program altogether due to complications with a radiation fibrosis flare-up (i.e. increased neck and chest tightness, difficulty swallowing, jaw stiffness, and overall discomfort).

Determination of protocol feasibility – sample size: Based on the mean of 2.40 and SD 3.1 (effect size of 0.4 which is a small to medium effect size according to Cohen's d values[72]) for the change in MIO from baseline to post-intervention in favour of the combined intervention group over standard care, and a p-value of 0.05 and power of 80%, we estimate the sample size for a future efficacy study would require 52 participants per group for a total sample size of 104.[73]

Primary Objective Measure:

Findings for the primary objective measurement, MIO, are outlined in Table 7. The mean MIO of the nine participants who completed the study showed an increase of 2.4mm with a standard deviation of 3.1mm. The median score was 2.36. Six participants had a mean increase in MIO at the end of 8-weeks, three had a mean decrease in MIO, and one did not finish so her average MIO at the end of the study was not available. Individual measurements are displayed below.

Table 7: MIO measurements

Participant ID	**Pre-Treatment Avg. (active-mm)**	**Post Treatment Avg. (active-mm)**	**Difference**
S1	10.87	10.79	-0.08
S2	18.94	--	Could not finish
S3	5.19	3.20	-1.99
S4	11.58	12.06	+0.48
S5	20.04	25.34	+5.30
S6	23.49	30.91	+7.42
S7	17.38	19.74	+2.36
S8	16.30	16.13	-0.17
S9	22.04	27.09	+5.05
S10	22.60	25.85	+3.25
			Mean: 2.40 **Stand. Dev.:** 3.1 ---------- **Median:** 2.36 **Range:** -1.99 to +7.42

2 Standard Deviation Band Method

The mean and standard deviation (SD) of each participant's baseline mouth opening measurements were calculated. Once calculated, lines representing 2-SD were drawn on a graph, above and below the orange line that represented the mean of the baseline data points. The best active MIO measurement of each treatment day was plotted to determine whether a significant difference was achieved. If two consecutive points in the treatment phase fall outside the 2-SD range, this would indicate a statistically significant change.[71] Individual graphs are displayed in Figures 2-11. Six out of the nine participants who completed the study showed a significant

improvement in MIO (67%) and three saw no improvement. The one participant who did not complete the study did show a significant improvement before she withdrew from the study. One participant (S7) saw a significant decline in MIO in the middle of treatment, and then by the end had a significant improvement.

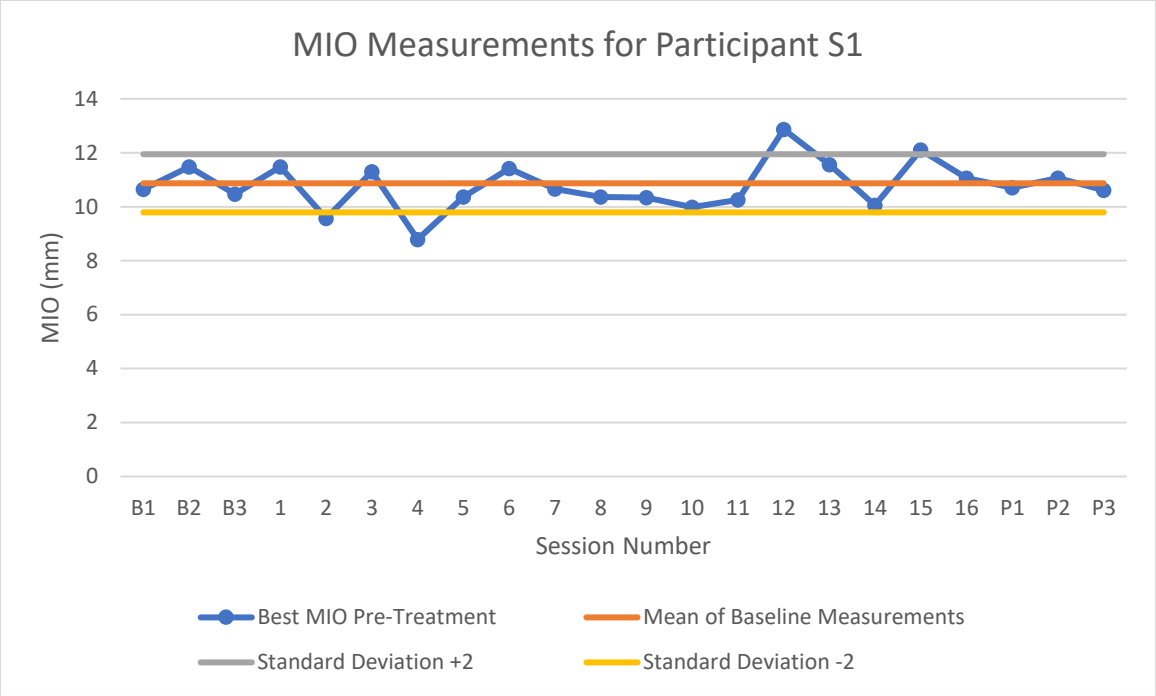


Figure 3: MIO Measurement for Participant S1

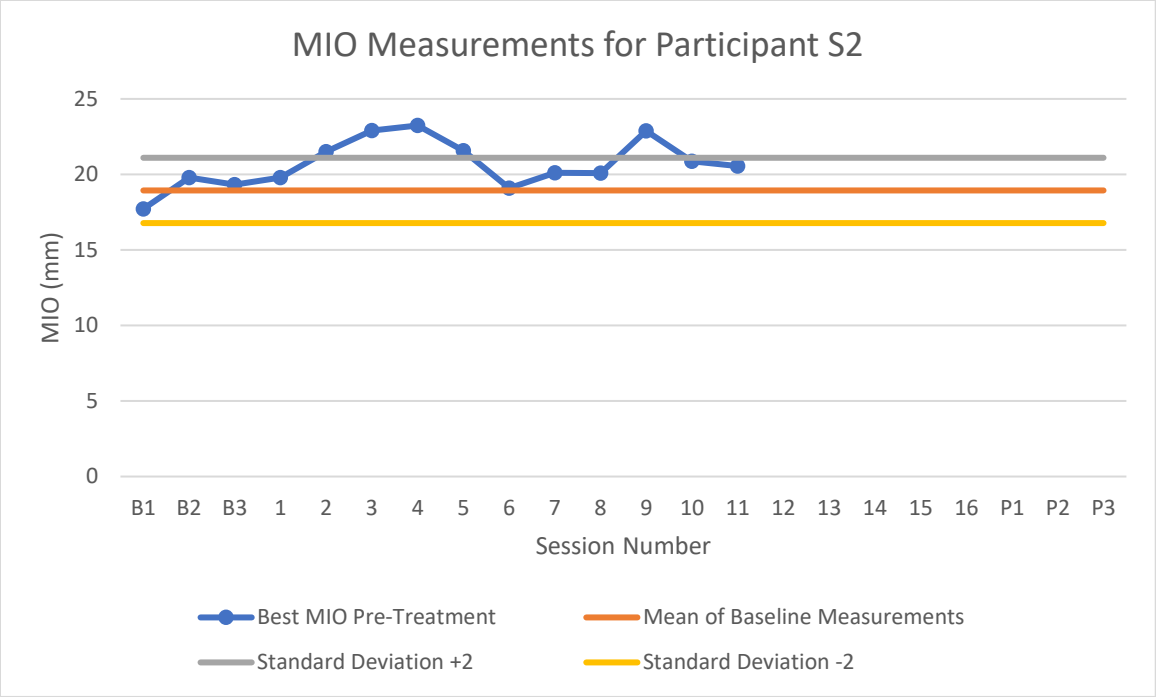


Figure 4: MIO Measurement for Participant S2

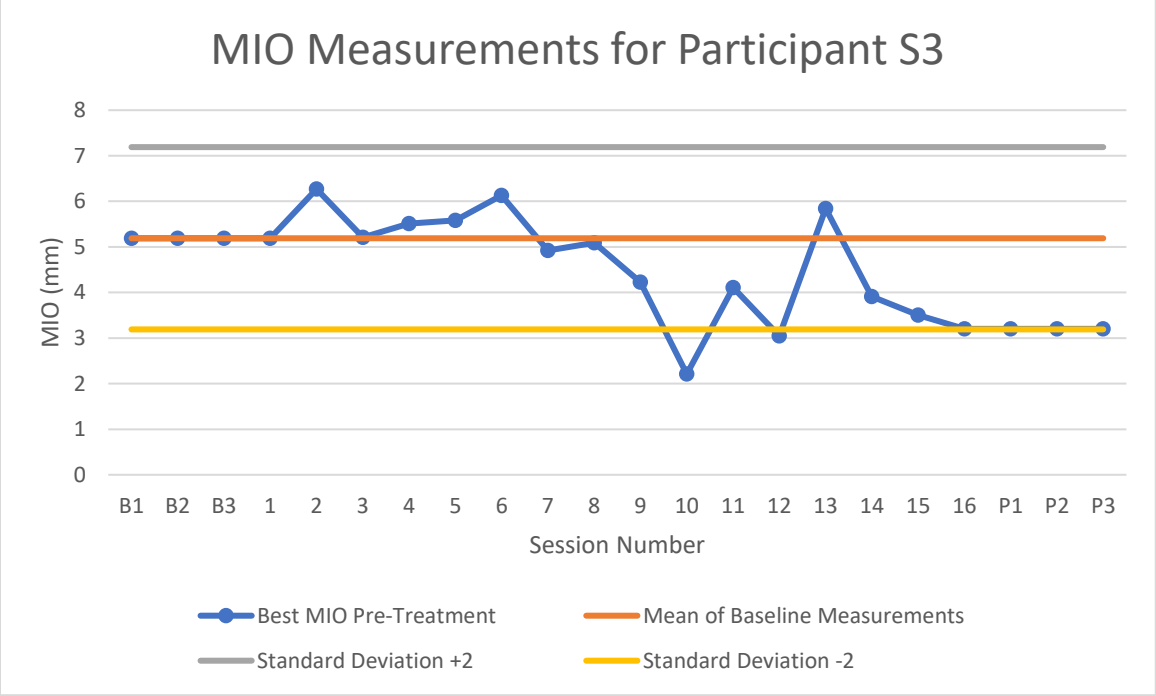


Figure 5: MIO Measurements for Participant S3

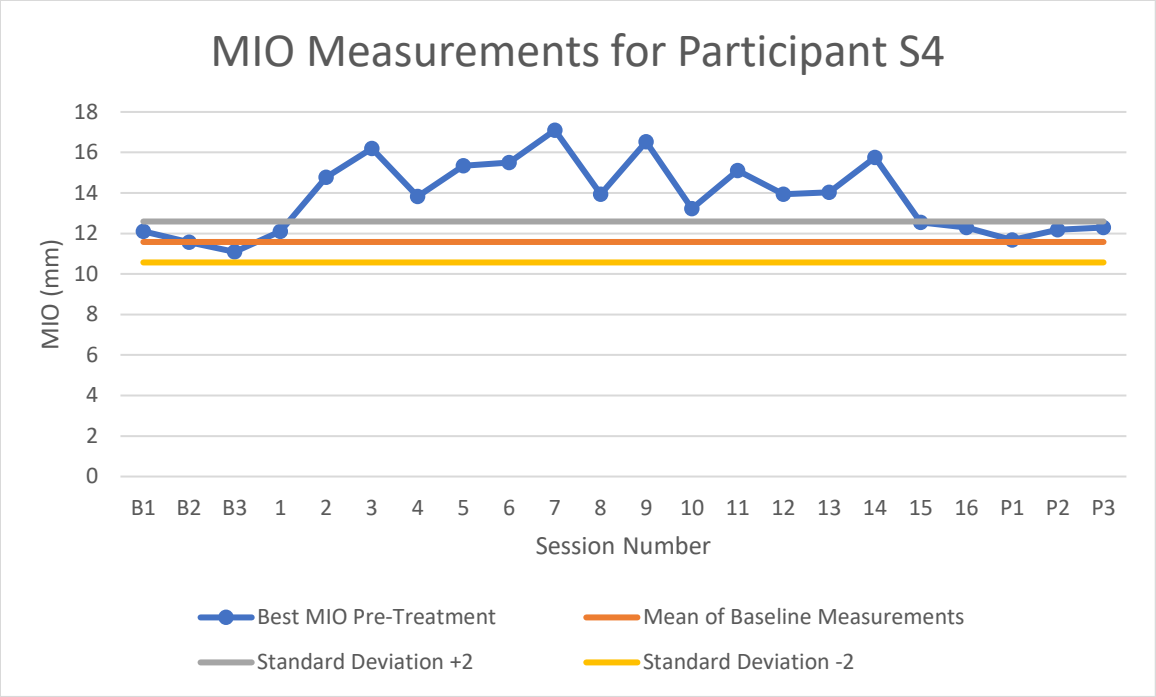


Figure 6: MIO Measurements for Participant S4

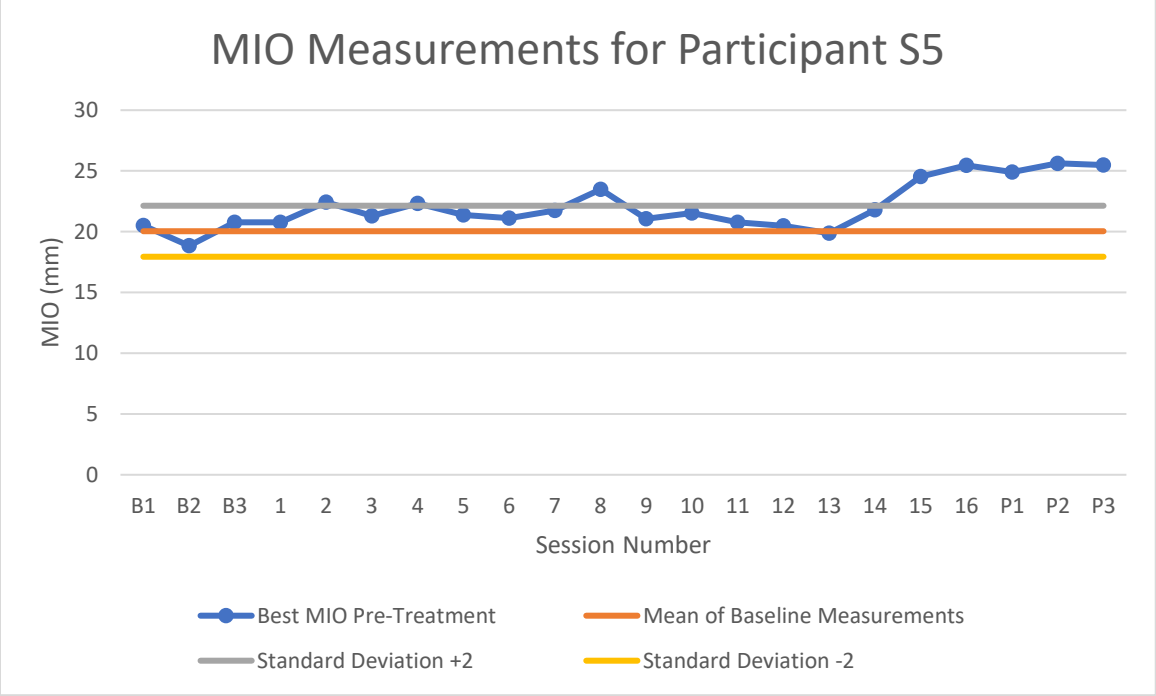


Figure 7: MIO Measurements for Participant S5

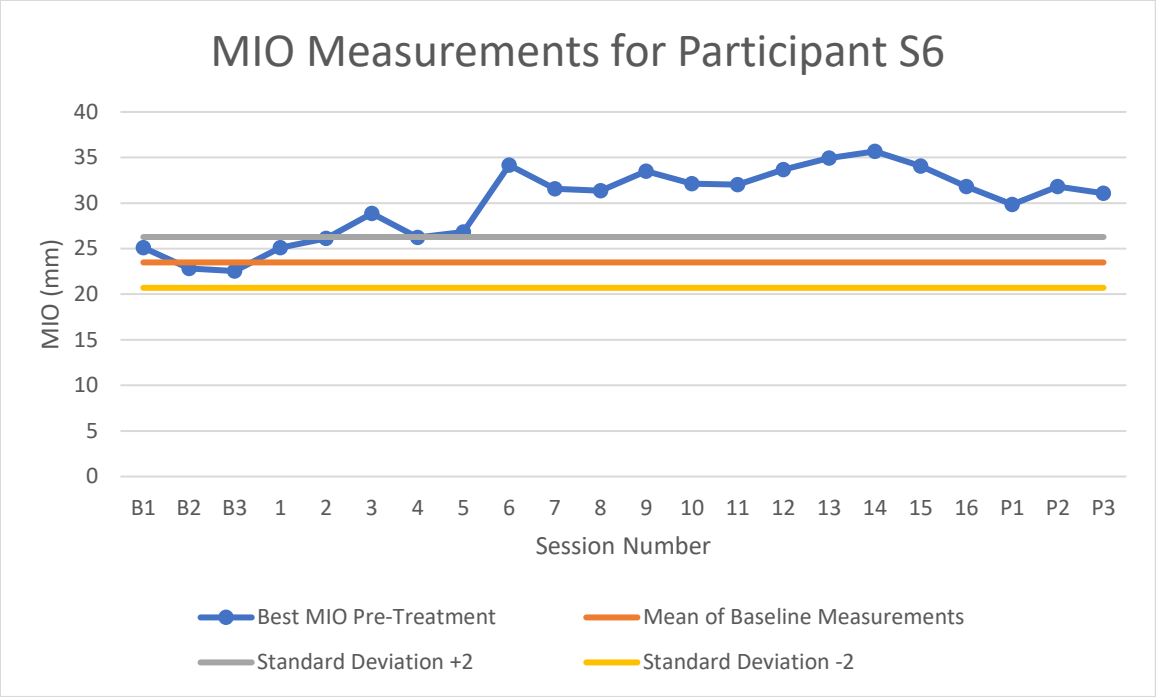


Figure 8: MIO Measurements for Participant S6

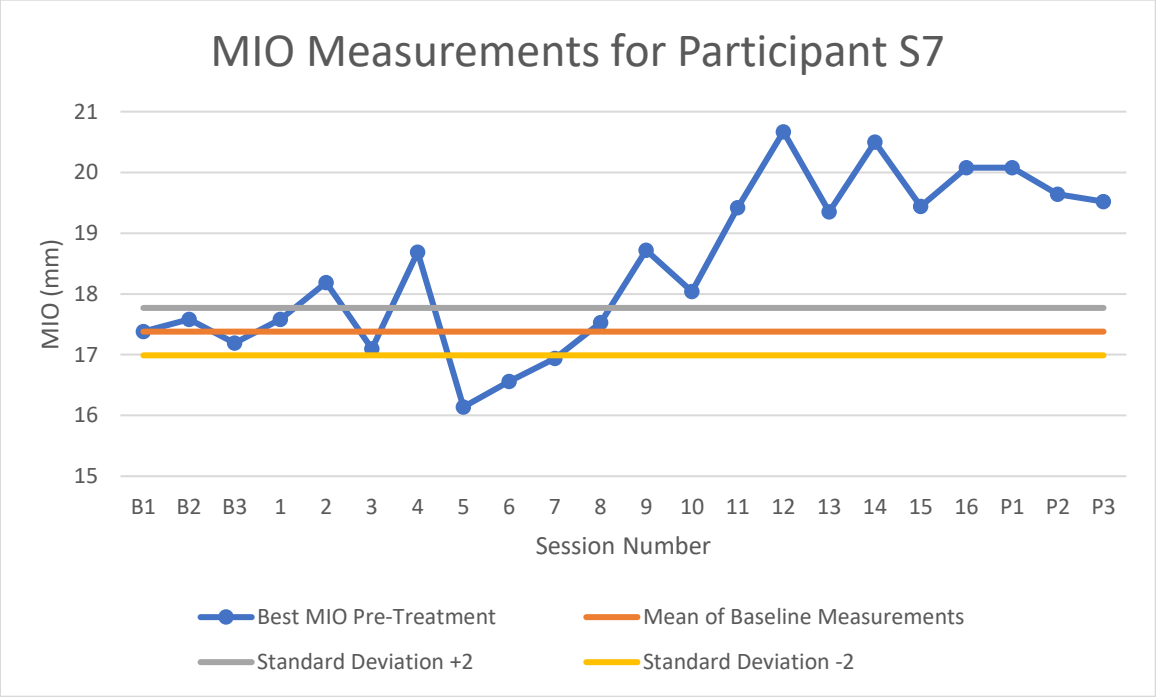


Figure 9: MIO Measurements for Participant S7

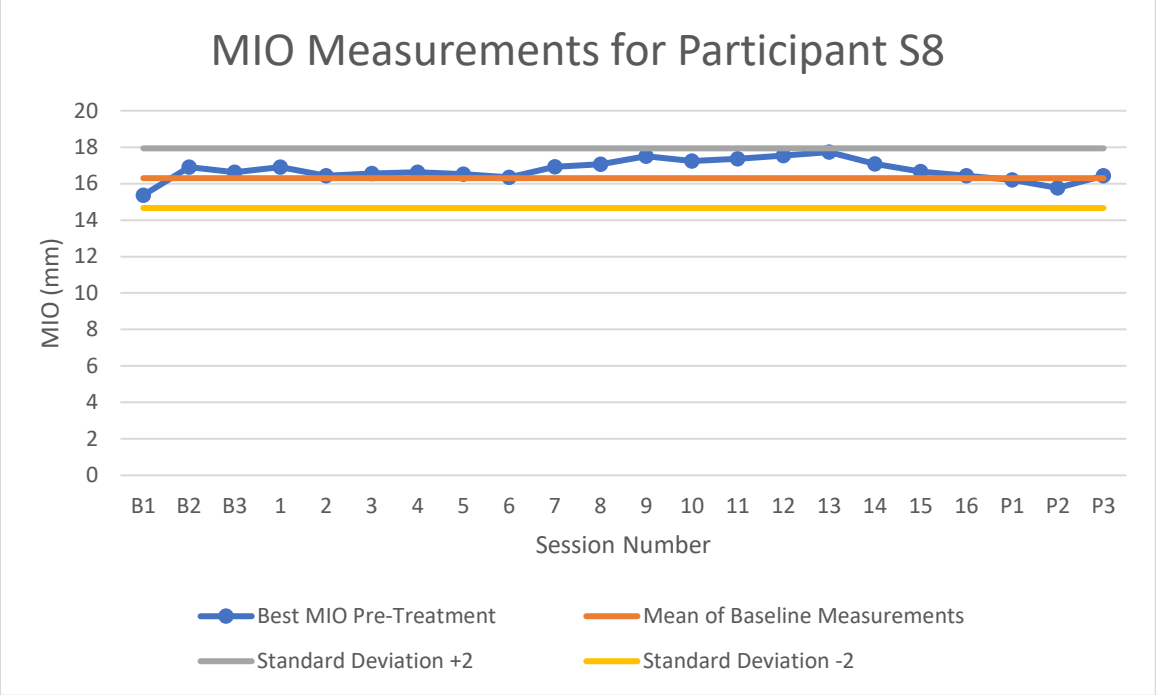


Figure 10: MIO Measurements for Participant S8

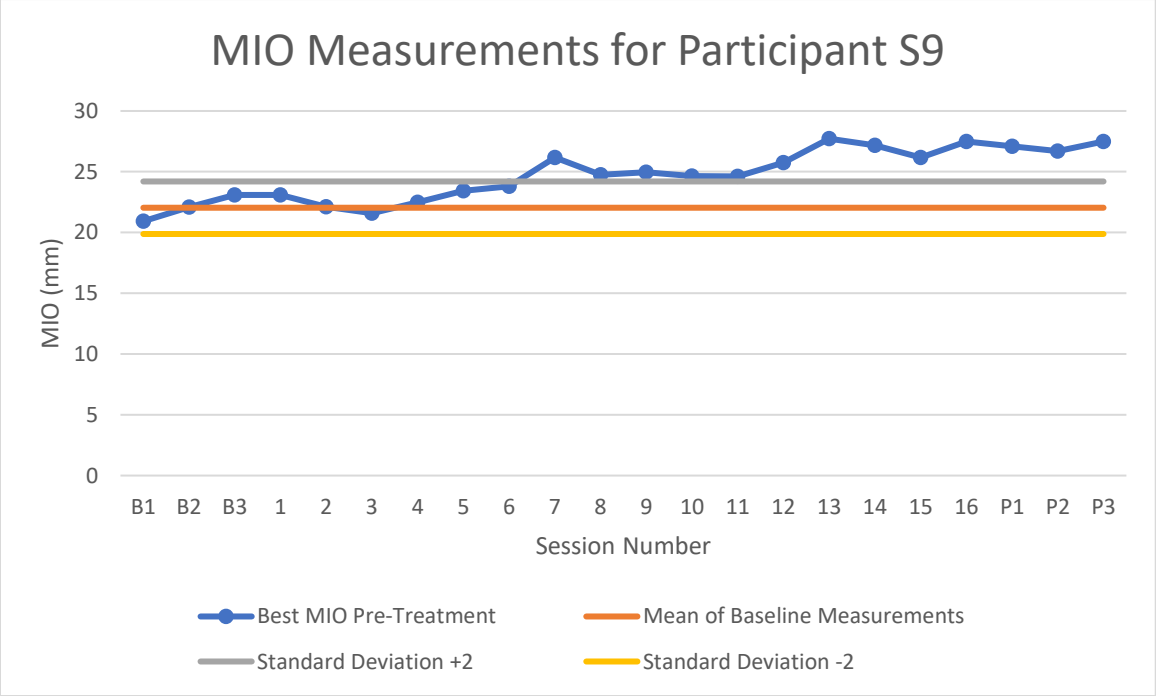


Figure 11: MIO Measurements for Participant S9

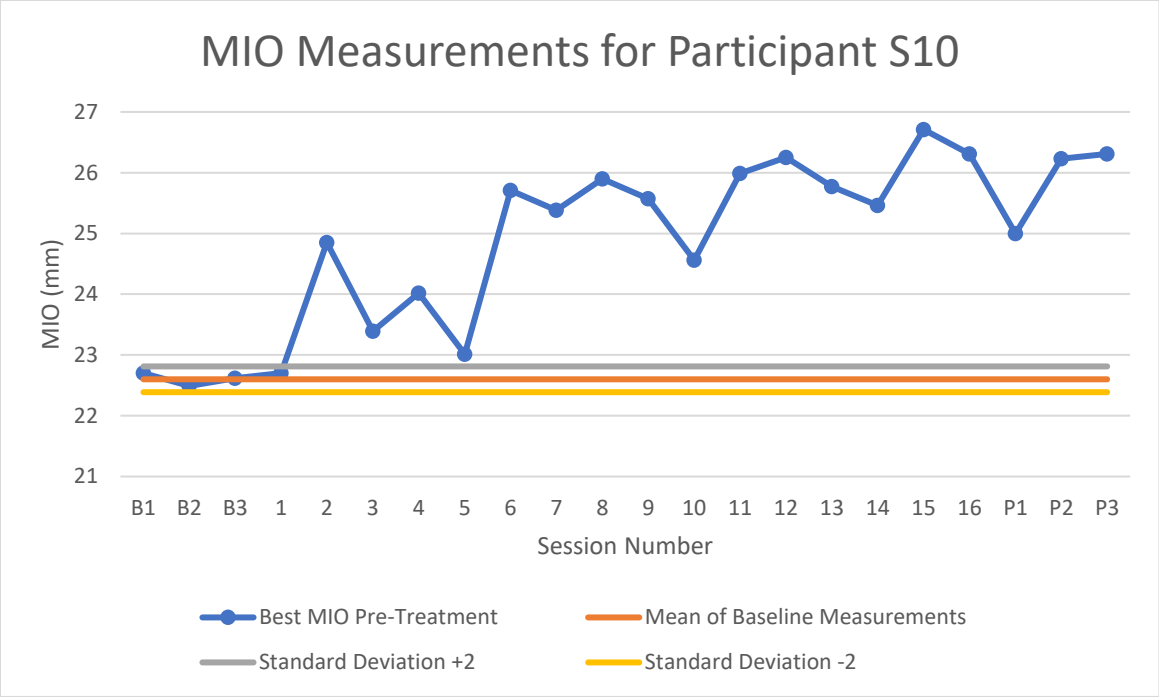


Figure 12: MIO Measurements for Participant S10

4.2 Secondary Outcomes

1. Questionnaire for trismus symptoms (Gothenburg Trismus Questionnaire)
2. Pain (Visual Analogue Scale)
3. Quality of life (Short-Form 36 Health Survey).

These outcomes were administered at baseline and the eight-week intervention period.

4.2.1 Trismus Symptoms: Gothenburg Trismus Questionnaire

The results of the GTQ are summarized in Appendix N along with individual scores in Appendix O. Symptom domains of jaw related problems, eating limitations, and muscular tension found the greatest improvements among the participants (67%, 78%, and 67% respectively). There seems to be no effect in pain levels before and after treatment as 89% of participants had no change in the single item questions asking about "facial pain now" and "worst facial pain in the last month."

4.2.2 Pain: Visual Analogue Scale

Participants were asked to rate their pain at the beginning of the study and again at the end. The scale ranged from 0 to 100. Fifty percent of participants reported an increase in pain and 30% reported a decrease. One participant (10%) had no change in pain and one participant (10%) stopped the study before completing the post intervention VAS. The results are summarized in Figure 12.

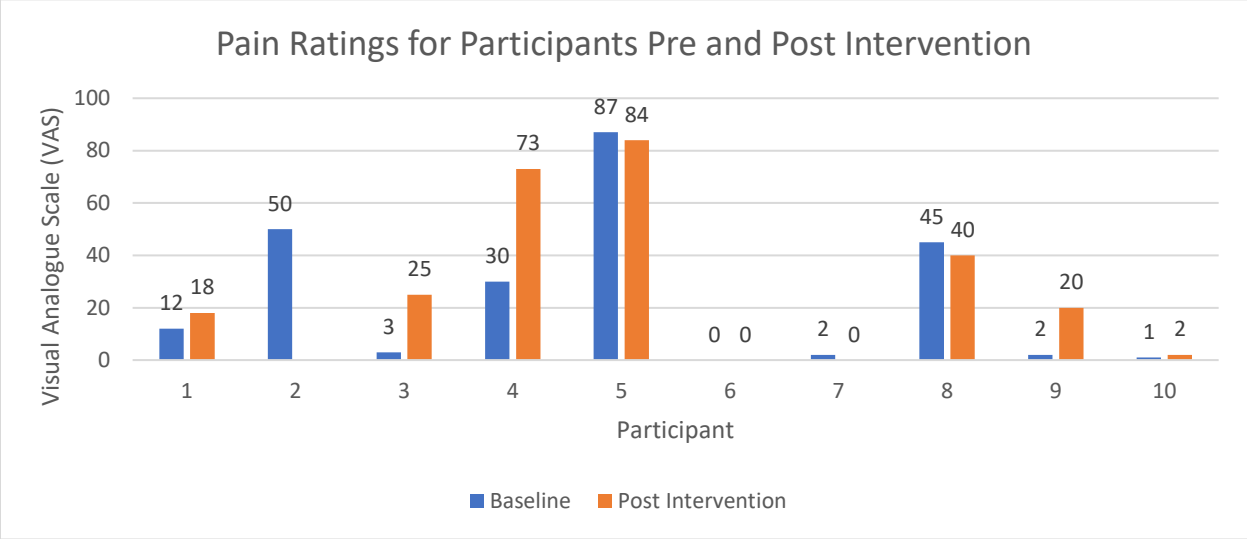


Figure 13: Visual analogue scale for pain

4.2.3 Quality of Life: Short Form-36 Health Survey

The results of the SF-36 Health Survey are summarized in Appendix P along with individual scores in Appendix Q. Nine participants completed the questionnaire at the end of the intervention. Of the nine participants, four had an improved score in physical functioning (44%), and 5 improved in emotional wellbeing (56%). Additionally, 5 participants had no change in their social functioning score (56%). Four participants worsened in their pain score (44%) and 5 in their general health score (56%).

CHAPTER 5: DISCUSSION

5.1 Researcher Positionality

As a graduate student, my interests center around helping cancer survivors recover from the side effects of treatment they are experiencing. While working with participants in the TARGET Trial (a randomized controlled trial examining a combined therapeutic and physical exercise program for head and neck cancer survivors) at the Cancer Rehabilitation Clinic in Edmonton, I encountered survivors who were also experiencing trismus and dealing with the eating and speech problems associated with it. I was intrigued to learn more about the condition and what could be done to improve the jaw stiffness and dysfunction. I then embarked on a scoping review to examine the research in the field. I was particularly interested in the interventions that survivors were receiving clinically at the Cross Cancer Institute, namely manual therapy and home programs involving use of a jaw-mobilizing devices. From this work, I came to realize that the research field related to the prevention and management of trismus related to HNC was very limited.

The findings of my scoping review demonstrated the large heterogeneity among studies in methods, the timing of the intervention and the chosen intervention protocols. I found that studies aimed at managing trismus appeared to benefit to some extent from use of a jaw-mobilizing device. In contrast, studies examining the prevention of trismus did not show benefit from use of a jaw-mobilizing device. The scoping review also revealed the need for personalized care and enhanced support for HNC survivors with trismus. There were no studies included in the review that used manual therapy to manage trismus, even though manual therapy is commonly used in physical therapy clinical settings. Some evidence was found supporting jaw-mobilizing devices; however, patient-related factors often led to poor adherence with use of a device. In speaking with clinicians, they agreed that device fit and comfort were common challenges from their experience. This led to my interest in looking at the feasibility of a combined intervention involving both manual therapy and use of a jaw-mobilizing device. I was interested to see if I could improve device fit by partnering with a specialist dentist for the mouth piece, and if the addition of manual therapy intervention might help improve jaw mobility and thus comfort with use of the device. I decided to test my intervention using a pre-post single group design with single-subject analysis methodology so that I could look more closely at the

issues at the level of the individual. My intent was to examine the feasibility of the protocol in order to propose solutions for a subsequent larger scale trial.

In this discussion, I integrate the findings of the Scoping Review with those of the STRIDE study.

5.2 Hypothesis related to feasibility

5.2.1 A combined intervention of manual therapy and the use of a Dynasplint® will be feasible and safe for survivors with head and neck cancer experiencing trismus.

The findings of the STRIDE study support the above hypothesis. The recruitment, retention, and adherence rates obtained from the 8-week STRIDE intervention support the feasibility and safety of an intervention involving manual therapy and a Dynasplint® to improve MIO in HNC survivors with trismus.

5.2.2 Feasibility of the process: Recruitment

Recruitment of participants to the STRIDE study (n = 2/ month) mirrors rates reported in other studies examining interventions for trismus. A study by Zatarain et al recruited 40 participants in a 14-month period which is approximately 3 survivors per month.[57] Likewise, the study by Kamstra et al, which had similar study parameters as STRIDE, enrolled 18 participants in a pre-post study design conducted between November 2012 and February 2014.[29] Some studies included in the scoping review did not report the number of participants recruited each month but did explain why survivors declined to enter the study.[49, 55] For example, one study reported that some HNC survivors thought the protocol was too intense or they did not feel they needed treatment, thus declined enrolment.[55] Our findings are consistent with the literature, which suggests that recruitment rates for HNC with trismus to an intervention study will generally be slow. This is due to the low incidence of HNCs as a tumour type[25] and the likely percentage of survivors at risk of developing trismus.[52] Based on our findings, we recommend planning for a recruitment rate of approximately 2-3 participants each month for future single-centre trials at a single site similar to ours.

5.2.3 Feasibility of the process: Retention and Adherence rates

Adherence rates can be divided into two components for a closer analysis of the STRIDE intervention: manual therapy treatment sessions and Dynasplint® sessions.

5.2.3.a Manual therapy adherence:

As previous studies did not include manual therapy in their trismus protocols it is not possible to compare adherence rates to past interventions.[18, 29, 40, 49-57] Although STRIDE participants had a high adherence rate (98%) to manual therapy, half of the participants reported pain or discomfort in the TMJ region after treatment, requiring protocol modification. Moreover, participants with severe trismus required specific modifications to the manual therapy protocol to improve tolerance to treatment itself. For example, feedback from these participants was needed to determine the most comfortable level of pressure, and adjustments made for hand positioning to avoid discomfort or problem teeth. We feel these subtle modifications to improve comfort helped to optimize adherence.

5.2.3.b Dynasplint® adherence:

Adherence to use of the Dynasplint® in the STRIDE study was 70%. Seven participants in the STRIDE study were able to use the device and reported high adherence to the protocol. Three participants, however, were unable to use the device at all, a finding similar to Kamstra et al where some, but not all participants were able to successfully use the device.[29] One study reported a low adherence rate with use of the Dynasplint® due to issues with fit, gagging, and fatigue.[57] Participants in another study experienced tenderness in the muscles of mastication due to stretching and jaw spasms from incorrect use of the Dynasplint®.[55] In the STRIDE study, we were able to avoid or minimize many of these issues. Customized mouthpieces likely contributed to the high adherence rates seen in the STRIDE study. A specialist dentist fabricated the mouthpieces which eliminated many of the issues associated with ill-fitting pads, and even one participant who was edentulous, was able to be fitted well and comfortably. Moreover, at each session, the therapists asked participants about any pain and discomfort, or problems with use or fit of the Dynasplint®. If there were concerns, the therapist was able to respond promptly and suggest modifications for use.

Another factor likely influencing adherence rates in the STRIDE study was the lower commitment in the length of the prescribed device intervention. In the study, we prescribed a progressive protocol with a gradual increase in stretching time from 15 to 30 minutes twice a day, and an intensity that was increased based on tolerance. Our goal was to gradually increase tissue tolerance to stretching. In contrast, other study protocols prescribed three Dynasplint® sessions per day, for 30 minutes each session, for a total of 90 minutes per day.[29, 55, 57] Two of these studies reported low completion rates, citing that participants found it difficult to comply to the prescribed schedule.[55, 57] Even with our less aggressive and shorter duration protocol, we noted improvements in mouth opening in six participants. In the future, we recommend a longer intervention duration (increasing the number of weeks of the study) to allow for continued progression of time and intensity, with close attention to intervention time burden.

5.2.4 Feasibility: Safety

No serious adverse events occurred during the STRIDE study. This finding is consistent with three systematic reviews of trismus in head and neck cancer survivors that did not include any reports of adverse events.[12, 40, 74] A systematic review of manual therapy and therapeutic exercise for temporomandibular disorders reported that only 10 out of 48 articles had any adverse events and 8 studies had no adverse events at all.[47]

Minor adverse effects, however, such as gum, tooth, and jaw pain did occur. Three participants were not able to use the Dynasplint® due to poor fit and discomfort with use. Our findings are consistent with other studies reporting minor adverse events and issues with device use.[55-57] With proper supervision and consideration given to comfort during sessions and attention to fit of the mouth piece, early evidence supports the safety of interventions for trismus.

5.2.5 Feasibility of Resource Needs

5.2.5.a Therapist Time

Therapists in the STRIDE study were able to spend one-on-one time with participants during the manual therapy sessions of the protocol. During these appointments, therapists asked questions regarding participant pain or discomfort and acknowledged any issues they were experiencing with the Dynasplint®. If there were concerns, the therapist was able to respond promptly, adapt the prescription as needed, and provide support for the participant. This may have been a

contributing factor to the high adherence and retention rates the study reported. This finding is similar to that of Wang et al[63] who found that regular telephone call follow-up was effective in improving exercise adherence rates. In the study, the therapist phoned the participant to provide encouragement and work through challenges the participant was experiencing.[63] While costs associated with this approach will be higher, providing support to survivors during the intervention period of the study may help to optimize intervention adherence.

5.2.5.b Cost of Intervention

It appears that the costs associated with treating trismus or other TMDs can be considerable for the survivor seeking treatment. The cost of renting or purchasing a jaw-mobilizing device varies and may be a barrier for head and neck cancer survivors with trismus. The Dynasplint® devices used in the STRIDE study were provided on loan, but would normally cost approximately $550.00 per month for the survivor to rent. In comparison, the Therabite® can be purchased for approximately $800 Canadian dollars[75] and the EZBite is reported at one fifth of the cost of the Therabite®.[50] In a study evaluating interventions for temporomandibular disorders (TMDs) in a non-cancer population, both jaw exercises and jaw-mobilizing devices were found to be effective for improving MIO but exercises alone were reported as much cheaper.[76] At this point in time, as no single device has shown to be more beneficial in addressing trismus, device cost is a primary consideration.[18, 40, 50]

Lee et al[49] performed a cost analysis of all points of contact with primary and secondary care services in a six-month study period comparing the Therabite® to use of tongue depressors. While the cost of the Therabite® was reported at £250 British pounds ($425 Canadian); associated healthcare service costs for both intervention groups were reported at approximately £141 per person/ month ($239 Canadian/ month). This equates to an approximate per participant cost of $1350 Canadian over the 6-month study period.[49] The true costs associated with treatment for STRIDE included a one-time fixed cost of $400 for fabrication of the mouth piece, $550 per month for rental of the Dynasplint® and $320 per month for the physiotherapy visits. Assuming a study duration of 6 months, the true cost of this combined treatment would be approximately $5220 Canadian dollars per survivor, more expensive than an intervention with the Therabite® alone. Thus, a balance between costs and effectiveness of treatment also needs to

be considered. Therefore, we recommend that future studies consider incorporation of a cost analyses to better inform clinical decision-making.

5.3 Hypothesis 2: A combined intervention of manual therapy and the use of a Dynasplint® will increase participants' MIO and positively impact their quality of life.

5.3.1 MIO: The results of the STRIDE study indicate that the average participant MIO increased following use of a combined treatment of manual therapy and a jaw-mobilizing device. Six participants exceeded the 2 SD mark for improvement in MIO, and all were able to use both the Dynasplint® and tolerate manual therapy intervention. Although no studies were found involving both manual therapy and a jaw-mobilizing device, similar findings supporting the use of a jaw-mobilizing devices to improve MIO were reported in four studies included in the scoping review.[29, 50, 54] The participants in these studies began the interventions after they had completed their cancer treatments. In one study, participants were divided into two groups based on the time between the completion of their primary tumor treatment and the start of the intervention with a Dynasplint®.[49] The group of participants who were < 36 months post treatment were found to show more benefit than those > 36 months.[49] Comparably, in the STRIDE study, three out of four participants who did not show benefit in MIO were also > 36 months since completing oncologic treatment. Research has shown that trismus can progress for many years after radiation therapy and is more difficult to treat in later stages.[30] Therefore, we recommend interventions begin as soon as possible after oncologic treatment to optimize outcomes.[30, 40]

To improve the accuracy of the STRIDE study, therapists used consistent procedures when measuring the MIO of each participant. Measurements can be influenced by the participant, the individual taking the measurement, and the type of device used, therefore, maintaining a strict measurement protocol is important to have confidence in the results.[77] A calibrated digital slide caliper was used in the STRIDE study to measure MIO to the nearest hundredth of a millimetre. In our scoping review, six different devices were used to measure MIO.[18, 29, 50, 51, 54-57] While devices differed, most studies performed the MIO measurement between the upper and lower incisors or between the alveolar ridges for edentulous participants, consistent with our methods in the STRIDE study.[18, 29, 50, 51, 56, 57] One study, however, used a Willis bite gauge to measure the

distance between the nose and the chin when the participant's mouth was open and closed.[49] Although the study did not mention why the measurement was performed in this manner, it may have been to account for jaw positioning. Clinically, we find that patients with radiation-induced trismus often present with a lack of jaw protrusion range of motion due to tight muscles of mastication. Thus, measuring this distance may better inform this limitation and the need for manual therapy. For example, in theory, a manual therapy intervention aimed at restoring protrusion range of motion of the mandible may be helpful for these individuals.[34, 36] To further account for differences, we recommend pictures of participant from the front and side view with the jaw open and closed. Repeat photographs may show subtle changes not captured by traditional MIO measurements. This method would also be helpful for participants who attend virtual or telehealth sessions, such as those who live in rural and remote locations.

5.3.2 Quality of Life:

When we examined the data from our single-subject descriptive perspective, we did not notice any apparent changes in the QOL of STRIDE participants. Similarly, many systematic reviews acknowledge that trismus impacts QOL, but do not often find that interventions have made a significant impact on QOL.[12, 39, 40] Four studies included in the scoping review examined the QOL of participants with trismus[18, 29, 49, 55] and only one study found a significant improvement.[18] This study, was a controlled trial that used the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C30).[18] The results showed a statistical significance in the functional scales (role functioning, social functioning, and global quality of life) between the study group and control group. The STRIDE study used the Short-Form 36 (SF-36) questionnaire to evaluate QOL and most participants reported no change in role limitations due to physical health and half reported that their general health seemed to worsen. In the study by Pauli et al[18], the average MIO at baseline was 32.2mm, whereas in our STRIDE study participants started with a mean MIO of 16.8mm. Furthermore, after the 8-week intervention, participants in the STRIDE study still presented with a mean MIO of less than 20mm (19.01mm). For the jaw to open beyond 20 mm, the condyle of the TMJ needs to translate over the articular eminence.[78] QOL may not be affected until opening is greater than 20mm, as functional improvements may become more apparent.[52] Participants in the study by Pauli et al[18] finished the intervention with an average mouth opening of 38.6mm, which means

many participant no longer presenting with trismus, may have accounted for the significant improvement in QOL.

The Gothenburg Trismus Questionnaire (GTQ) used in the STRIDE study was also included in other study protocols evaluating trismus.[18, 50] This trismus-specific questionnaire evaluates symptoms such as jaw related problems, eating limitations, and muscular tension.[19] Results from one study show an increase in some of the GTQ domains in the experimental group following an intervention with an EZBite.[50] However, a major limitation of the study was that the control group was made up of participants who did not comply with their assigned intervention.[50] Another study that administered the GTQ found a statistically significant improvement in most of the domains indicating a decrease in trismus-related symptoms.[18] In the study, the intervention did not show a significant difference for the pain domain, with the exception of one question asking about current facial pain.[18] Similarly, we observed minimal changes in pain among STRIDE participants. Eight participants reported no change in 'facial pain now' and 'worst facial pain in the last month.' Similarly, descriptively few STRIDE participants reported improvement in the limitations associated with pain. This could be because facial pain was less of an issue when compared to pain from radiation fibrosis or dental issues.

Limitations:

The primary limitation of the STRIDE study was the small sample size and short intervention period. Moreover, inclusion in the STRIDE study was not restricted to a time period relative to cancer treatment, thus there was large variability among study participants related to the chronicity of their trismus. The single-subject design, although important for determining feasibility, limits our ability to evaluate the efficacy of our combined intervention on MIO and QOL.

Summary and Future Directions:

Findings from the STRIDE study suggest benefit from a combined intervention of manual therapy and the Dynasplint® jaw mobilizing device for MIO. Efforts to improve comfort and fit of the Dynasplint® by involving a specialist dentist to fabricate the mouth pieces, and enhanced

attention to participant symptoms appears to be helpful in optimizing adherence and retention rates. Overall, the STRIDE study findings support feasibility and safety of the intervention. Further study to explore the benefits of manual therapy alone or in conjunction with the Dynasplint® is warranted.

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APPENDIX

A. Ethics Approval
B. Consent Form
C. Study Brochure
D. Eligibility Form
E. Baseline and 8-Week Testing
F. Identifying Information
G. Questionnaire: Baseline and 8-Week
H. Medical Record
I. Manual therapy stretches and modifications
J. Attendance/MIO
K. Manual therapy stretches of the TMJ
L. Home Exercise Program
M. Dynasplint® Adherence (diary recordings)
N. Gothenburg Trismus Questionnaire: Number of participants with a change in results from baseline to 8-week follow up
O. Gothenburg Trismus Questionnaire Results
P. Short Form-36: Number of participants with a change in results from baseline to 8-week follow-up
Q. Short Form-36 Results

Appendix A: Ethics Approval

HREBA Health Research Ethics Board of Alberta Cancer Committee

Health Research Ethics Board of Alberta
Cancer Committee
1500, 10104 - 103 Avenue NW
Edmonton, Alberta, T5J 0H8
Telephone: (780) 423-5727
Fax: (780) 429-3509
Email: cancer@hreba.ca

Certification of Ethics Approval

This is to acknowledge that the following research has been reviewed and on behalf of the Health Research Ethics Board of Alberta (HREBA) – Cancer Committee (CC) I am granting approval for your site's participation in the research.

Ethics ID:	HREBA.CC-17-0164
Principal Investigator:	Margaret McNeely
Co-Investigator(s):	Susan Armijo-Olivo Suresh Nayar
Student Co-Investigator(s):	Joni Nedeljak
Study Title:	Manual Therapy in combination with a Dynamic Splint (Dynasplint) in the Treatment of Trismus in Patients with Head and Neck Cancer: A feasibility study
Sponsor:	Internal funds

Effective: September 3, 2018 **Expires:** September 2, 2019

Research reviewed by delegated review on 03 September 2018.

The following documents have been approved:

- Study Brochure, June 26, 2018, August 30, 2018
- Consent Form CCI, August 28, 2018, August 28, 2018
- Global Rating Scale
- SF-36
- GTQ
- Study Protocol, June 26, 2018, August 30, 2018
- Budget Stride Study, August 28, 2018, August 28, 2018

This Committee is constituted and operates in accordance with the Alberta Health Information Act (HIA), the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2), Good Clinical Practice (GCP) Guidelines of the International Conference on Harmonization (ICH), Health Canada's *Food and Drug Regulations* (FDR), Part C, Division 5 and is registered with the U.S. Department of Health and Human Services (HHS), Office for Human Research Protections (OHRP), IRB # 00009687.

It is noted that the study team would like to access personal health information for the purposes of this research.

The committee has determined that consent must be obtained from participants for the disclosure of this information.

As a requirement of the HIA, if your study uses health information a copy of this certification will be sent to the Office of the Information and Privacy Commissioner (OIPC).

Members of the HREBA-CC who are named as principal investigators or co-investigators in this research do not participate in discussions related to, nor vote on, such studies when they are presented to the Committee. The membership of this Committee is listed at www.hreba.ca.

This approval is subject to the following conditions:

1. It is being granted only for the research described in this application.
2. Any modification to the approved research must be submitted to the Committee for approval prior to implementation.
3. Reportable events (SAE's, new safety information, protocol deviations, audit findings, privacy breaches, and participant complaints) are to be submitted in accordance with the Committee's reporting requirements.
4. A request to renew this ethics certification must be submitted and reviewed by the Committee in advance of the expiry date indicated above. Failure to submit a request will result in the file entering into an expired state, whereby all research must cease.
5. A closure request must be submitted to the Committee when the research is complete or has been terminated.

This approval does not guarantee that you will be able to access health records for research purposes. Other institutional or organizational requirements may be in place that you will be required to meet prior to initiating your research. These include approvals for the allocation of resources in support of your study. Inquiries regarding these additional approvals should be directed to the appropriate institutional or organizational body.

Please accept the Committee's best wishes for success in your research.

Approved on behalf of CC by,

Peter Venner , HREBA-CC

Date:

September 4, 2018

Note: This correspondence includes an electronic signature (validation and approval via an online system).

Alberta Health Services

Informed Consent Form for Participation in a Research Study

Manual Therapy in combination with a Dynamic Splint (Dynasplint®) in the Treatment of Trismus in Patients with Head and Neck Cancer: A pilot feasibility study

Stretching Therapy for Patients with Trismus using a Dynasplint® and Exercise (STriDE)

Protocol ID: *HREBA.CC-17-0164*

Principal Investigator: Dr. Margaret McNeely, PT, PhD
Department of Physical Therapy/ Department of Oncology
University of Alberta & Cross Cancer Institute
Phone: 780-248-1531

Sponsor/Funder(s):University of Alberta

Emergency Contact Number (24 hours / 7 days a week):
Cross Cancer Institute Telephone Triage Nurse: 780-432-8919 or 1-877-707-4848 (toll free)

You are being invited to participate in a research study because you have stiffness in your jaw as a result of head and neck cancer treatment.
This consent form provides detailed information about the study to assist you with making an informed decision. Please read this document carefully and ask any questions you may have. All questions should be answered to your satisfaction before you decide whether to participate.

The study staff will tell you about timelines for making your decision. You may find it helpful to discuss the study with family and friends so that you can make the best possible decision within the given timelines.

Taking part in this study is voluntary. You may choose not to take part or, if you choose to participate, you may leave the study at any time without giving a reason. Deciding not to take part or deciding to leave the study will not result in any penalty or any loss of medical or health related benefits to which you are entitled.

The principal investigator, who is one of the researchers, will discuss this study with you and will answer any questions you may have. If you do consent to participate in this study, you will need to sign and date this consent form. You will receive a copy of the signed form.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Trismus, or jaw stiffness, is a known complication of treatments for head and neck cancer. Jaw stiffness may result from surgery and/ or radiation therapy. With trismus, you will have difficulty opening your mouth. The jaw stiffness may occur immediately following surgery, during radiation therapy or may start months after finishing cancer treatment. Trismus will limit your ability to chew, swallow and talk. If you cannot open your mouth wide enough, you may find it difficult to brush your teeth or have dental work done.

Physical therapy treatment has been shown to help reduce the jaw stiffness. Treatment usually involves active jaw opening exercises and manual therapy (physical therapy to improve jaw joint movement and to stretch the tissues around your jaw). Unfortunately, to improve trismus often requires 6 months or more of regular physical therapy treatment. For this reason, jaw opening devices such as the Jaw Dynasplint® System are recommended to patients for home use, as a way for patients to self-manage the condition. The Dynasplint® provides low-intensity, prolonged-duration stretch to the stiff tissues to help increase jaw movement. To date, there is limited evidence supporting the benefit of the Dynasplint®, and the device is very expensive to rent or purchase. Therefore, we do not know whether there is any additional benefit from using the device at home, and whether we should recommend patients pay for a device. This study is being done because we want to see if adding home use of the Dynasplint®, is helpful to patients with trismus. The Dynasplint® device used in this study has been approved by Health Canada.

The Health Research Ethics Board of Alberta – Cancer Committee (HREBA-CC), which oversees the ethical acceptability of research involving humans, has reviewed and granted ethics approval for this study.

WHY IS THIS STUDY BEING DONE?

There is limited research evidence on the effectiveness of physical therapy and jaw opening devices for trismus. We are interested evaluating a combined treatment program involving manual therapy, exercises and home-use of the Dynasplint® device. The main objective of this study is to see if patients are willing and able to complete the treatment and to see if it is helpful in reducing jaw stiffness.

WHAT ARE OTHER OPTIONS IF I DECIDE NOT TO PARTICIPATE IN THIS STUDY?

You do not have to take part in this study, in order to receive continued medical care. Your physiotherapist will discuss with you other treatment options. Right now the, the usual treatment at the Cross Cancer Institute is to receive manual therapy and home exercises for trismus.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

A minimum of 10 people with trismus will take part in this study.

WHAT WILL HAPPEN DURING THIS STUDY?

STUDY INTERVENTION

If you agree to take part in this study, you will undergo testing to determine the extent of stiffness in your jaw and take part in a treatment protocol involving manual therapy, active exercises, and use of the Dynasplint® device at home. You will receive physical therapy treatment twice a week for eight weeks. Each session will take between 30 minutes to one hour. The physical therapy treatment will involve manual therapy and active jaw opening exercises. For the first two weeks of the study, you will receive the physical therapy treatment only. During this time period, an appointment will be arranged for you to be fitted for a mouth piece for the Dynasplint® device by a dentist in the Temporomandibular Joint Dysfunction Clinic at the University of Alberta. Once your mouth piece is made, you will be instructed in use of the Dynasplint® device by the physical therapist. You will use the device at home daily from weeks 3 to 8 of the study. You will start by using the device for a 10-15 minute period per day (up to 3x per day as tolerated) and will progress to 30 minutes per day over the study period. You will be asked to bring the Dynasplint® to one physical therapy session each week and will perform one supervised session with the device to ensure proper progression and technique, and to monitor symptoms.

This study is using a single-subject design, which means that we are looking at the effect of the treatment for each person rather than the average effect of the group. This information will give us a better idea of who may benefit or not from the treatment, and why.

STUDY PROCEDURES

Established Procedures

The following established procedures will be done as part of this study. Some of these procedures may be done as part of your standard care, in which case the results may be used. Some may be done more frequently than if you were not taking part in this study. Some of these procedures may be done solely for the purpose of the study. If the results show that you are not able to continue participating in the study, the principal investigator will let you know.

- Maximal Interincisal Opening (MIO)- we will measure the maximal distance you can open your mouth from the upper teeth to the lower teeth. This measurements will be taken at the beginning of the study, at each physical therapy session and at the end of the study.

Questionnaires

You will be asked to complete a series of study questionnaires (electronic or paper copy) before starting this study, and again at 8weeks. The purpose of the questionnaires is to understand how the treatment impacts your jaw function and overall quality of life. The questionnaires include:

- Gothenburg Trismus Questionnaire (GTQ): This questionnaire asks about your jaw stiffness, jaw problems including ability to eat, and symptoms such as pain. The questionnaire has 21 questions and will take 5-10 minutes to complete.
- Health-related Quality of Life – This questionnaire asks about your health- related quality of life the Rand Short Form-36 (SF-36). It involves 36 questions about your mental health, physical health, social health, function, pain, vitality/energy, health perceptions. It is will take 8-10 minutes to complete.
- Pain Visual Analogue Scale (VAS): You will be asked to rate your pain on a 10 cm visual analogue scale (line). The line will be labeled with “no pain”, at the one end and “worst pain imaginable” at the other end. The scale will take 1 minute to complete.

The information you provide is for research purposes only and will remain strictly confidential. Some of the questions are personal; you may choose not to answer them.

Even though you may have provided information on a questionnaire, these responses will not be reviewed by individuals not involved in this study, e.g., your health care practitioner/team. If you would like them to know this information, please bring to their attention.

Participant Diaries

You will be asked to keep a diary of your home exercise and Dynasplint® use. You will be instructed to document the Dynasplint® duration, resistance, and number of sessions completed each day. You will also be asked to report issues with use of the Dynasplint® such as the ability to use the device or jaw pain/relief after use. This information will help us better understand the benefits and challenges of using the device. You will be asked to return the diary after 8 weeks to the Cancer Rehabilitation Clinic in Corbett Hall, University of Alberta or to submit an electronic copy to the researchers.

WHAT ARE THE POTENTIAL SIDE EFFECTS FROM PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be side effects that are not expected. You should discuss these with the principal investigator. The risks and side-effects of the standard or usual treatment will be explained to you as part of your standard care. These risks are not included in this consent form.

The main side effects that you may experience are dental pain and jaw soreness or stiffness. These symptoms will be carefully monitored and generally improve as you progress with the treatment. Also, your program will be personalized based on the amount of stiffness and symptoms you are experiencing. We will modify your program as needed if you have increased pain or excessive muscle soreness.

If you experience any side effects, you should call the study investigator immediately.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

Participation in this study may or may not be of personal benefit to you. The expected benefit from taking part in this study include improved mouth opening (reduced jaw stiffness) and improved quality of life but there is no guarantee that the intervention may be of direct benefit to you. However, based on the results of this study, it is hoped that in the long-term, patient care can be improved.

WHAT ARE MY RESPONSIBILITIES AS A STUDY PARTICIPANT?

If you choose to participate in this study, you will be expected to:

- Tell the study investigator about your current medical conditions;
- Tell the study investigator about all prescription and non-prescription medications and supplements, including vitamins and herbals, that you may be taking and check with the study doctor before starting, stopping or changing any of these. This is for your safety as these may interact with the intervention you receive on this study;
- Tell the study investigator if you are thinking about participating on another research study;
- Attend all scheduled study visits and undergo all of the procedures described above and complete the questionnaires;
- Return any diaries taken home to complete;
- Tell the study investigator of any injuries, side effects or health problems that you may be experiencing

HOW LONG WILL I BE PARTICIPATING IN THIS STUDY?

The study program will last for about 8 weeks.

WILL THERE BE ANY LONG-TERM FOLLOW-UP INVOLVED WITH THIS STUDY?

No long-term follow-up required after the study period.

In the event it is necessary to further evaluate the feasibility and efficacy of the intervention program, it may be necessary to have access to additional information about your health status. The study team may attempt to obtain study-related information about your health from you or from other private sources, including your care physician. This may include

contacting you again by phone or letter, but only if you have not withdrawn your consent for future contact. However, contacting you, your care physician or using other private sources of information, is optional, please indicate your decision using the check boxes below.

You give permission to the study doctor or member of the study team to attempt to obtain study related information about your health status to further evaluate the feasibility and efficacy of the intervention program. This may include contacting your care physician, or by contacting you by phone or letter (i.e., future contact).

☐ Yes ☐ No Participant's Initials: _____

Name/phone number of care physician: _____

CAN I CHOOSE TO LEAVE THIS STUDY EARLY?

You can choose to end your participation in this research (called early withdrawal) at any time without having to provide a reason. If you choose to withdraw early from the study without finishing the intervention, procedure or follow-up, you are encouraged to contact the principal investigator or study staff. You may be asked questions about your experience with the study intervention.

You may withdraw your permission to use information that was collected about you for this study at any time by letting the principal investigator know. However, this would also mean that you withdraw from the study. Information that was recorded before you withdrew will be used by the researchers for the purposes of the study, but no additional information will be collected or sent to the sponsor after you withdraw your permission.

CAN MY PARTICIPATION IN THIS STUDY END EARLY?

The principal investigator may stop your participation in the study early, and without your consent, for reasons such as:

- You are unable to tolerate the exercise;
- You sustain an injury as a result of participation.
- You experience an adverse effect during or after exercising;
- You are unable to complete all required study procedures;
- Your doctor no longer feels this is the best treatment for you;
- The sponsor decides to stop the study;
- A regulatory authority (for example, Health Canada) or the research ethics board withdraws permission for the study to continue.

If this happens, it may mean that you would not receive the study intervention for the full period described in this consent form. If you are removed from the study, the principal investigator will

discuss the reasons with you and plans will be made for your continued care outside of the study.

HOW WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the principal investigator and study staff will only collect the information they need for this study.

Records identifying you, including information collect from your medical files/records, such as your Electronic Medical Records (EMR), Netcare, charts, etc., will be kept confidential to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your identifiable medical/clinical study records at the site where these records are held for quality assurance purposes and/or to verify that the information collected for the study is correct and follows proper laws and guidelines:

- Members of the Regulatory/Audit team at at the Cross Cancer Institute, for quality assurance purposes
- The Health Research Ethics Board of Alberta – Cancer Committee, which oversees the ethical conduct of this study

Authorized representatives of the above organizations may **receive** information related to the study from your medical/clinical study records that will be kept confidential in a secure location and may be used in current or future relevant health research. Your name or other information that may identify you will not be provided (i.e., the information will be de-identified). The records received by these organizations will be coded with a number. The key that indicates what number you have been assigned will be kept secure by the researchers directly involved with your study and will not be released. To protect your identity, the information that will be on your assessment forms and questionnaires will be limited to your study ID and initials.

Any disclosure of your identifiable health information will be done in accordance with federal and provincial laws including the Alberta Health Information Act (HIA). The organizations listed above are required to have organizational policies and procedures to protect the information they see or receive about you, except where disclosure may be required by law. The principal investigator will ensure that any personal health information collected for this study is kept in a secure and confidential location AHS facility as also required by law.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during the study will be used in analyses and will be published and/or presented to the scientific community at meetings and in journals, but your identity will remain confidential. This information may also be used as part of a submission to regulatory authorities around the world to support the approval of this intervention.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated. Every effort will be made to keep your identifiable information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information.

Data collected will be entered into the secure REDCap server held at the University of Alberta and data will only be used for research purposes.

Studies involving humans sometimes collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

WILL MY HEALTHCARE PROVIDER(S) BE INFORMED OF MY PARTICIPATION IN THIS STUDY?

Your family doctor/health care provider will be informed that you are taking part in a study so that you can be provided with appropriate medical care. If you do not want your family doctor/health care provider to be informed, please discuss with your study team to find out your options.

WILL THERE BE ANY COSTS INVOLVED WITH PARTICIPATING IN THIS STUDY?

You will not have to pay for the Dynasplint® or the home exercise program you receive in this study. We will provide a parking pass to cover your parking costs at the University of Alberta when you come for any exercise sessions, tests, or procedures associated with the study. There may be additional costs to you for taking part in this study such as:

Taking part in this study may result in added costs to you. For example:

- transportation,
- snacks/meals during the study;
- babysitting, etc.

Possible Costs After the Study is Complete

You may not be able to receive the study intervention after your participation in the study is completed. There are several possible reasons for this, some of which are:

- Your caregivers may not feel it is the best option for you;
- You may decide it is too expensive and insurance coverage may not be available;

The principal investigator will discuss these options with you.

WILL I BE COMPENSATED FOR PARTICIPATING IN THIS STUDY?

You will not be paid for taking part in this study. However, in the case of research-related side effects or injury, as a direct result of participating in this research, you will receive all medical treatments or services recommended by your doctors.

Although no funds have been set aside to compensate you in the event of injury or illness related to the study treatment or procedures, you do not give up any of your legal rights for compensation by signing this form.

WHAT ARE MY RIGHTS AS A PARTICIPANT IN THIS STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study. You have the right to be informed of the results of this study once the entire study is complete. If you would like to be informed of these results, please contact the principal investigator.

The results of this study will be available on a clinical registry; refer to the section titled “Where can I find online information about this study?”. Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form, you do not give up any of your legal rights against the hospital, investigators, sponsor, involved institutions for compensation or their agents, nor does this form relieve these parties from their legal and professional responsibilities.

IS THERE CONFLICT OF INTEREST RELATED TO THIS STUDY?

There are no conflicts of interest declared between the principal investigator and sponsor of this study.

WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT ME AS A RESEARCH PARTICIPANT?

During the study, the researchers may learn something about you that they didn’t expect. For example, the researchers may find out that you have another medical condition.

If any clinically important information about your health is obtained as a result of your participation in this study, you will be given the opportunity at that time to decide whether you wish to be made aware of that information.

WHERE CAN I FIND ONLINE INFORMATION ABOUT THIS STUDY?

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

The study registration number to use this website is: NCT03178110

WHO DO I CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you should talk to the project coordinatior or principal investigator. These person(s) are :

Dr. Margaret McNeely, PT,PhD	780-432-8716 or 780-248-1531
Name	Telephone

Dr. Margaret McNeely can also be paged through the Cross Cancer Institute Switchboard at 780-432-8771

If you have questions about your rights as a participant or about ethical issues related to this study and you would like to talk to someone who is not involved in the conduct of the study, please contact the Office of the Health Research Ethics Board of Alberta – Cancer Committee at:
Telephone: 780-423-5727 Toll Free: 1-877-423-5727

SIGNATURES

Part 1 - to be completed by the potential participant.

	Yes	**No**
Do you understand that you have been asked to take part in a research study?	☐	☐
	☐	☐
Do you understand the potential benefits of taking part in this study?	☐	☐
Do you understand why this study is being done?	☐	☐
Do you understand what you will be asked to do should you decide to take part in this study?	☐	☐
Do you understand the alternatives to participating in this study?	☐	☐

Do you understand that you are free to leave the study at any time, without out having to give reason and without affecting your future health care?	☐	☐
Do you understand who will see your records, including health information that identifies you?	☐	☐
Do you understand that by signing this consent form you are giving us permission to access your health information if applicable?	☐	☐
Do you understand that by signing this consent form that you do not give up any of your legal rights?	☐	☐
Do you understand that your family doctor/health care provider will/may be informed of your participation in this study?	☐	☐
Do you understand the risks of taking part in this study?	☐	☐
Have you had enough opportunity to ask questions and discuss this study?	☐	☐

By signing this form I agree, or *allow the person I am responsible for*, to participate in this study.

Signature of Participant /*Substitute Decision-Maker*	PRINTED NAME	Date

(As a Substitute Decision-Maker, you are being asked to provide informed consent on behalf of a person who is unable to provide consent for him/herself. If the participant gains the capacity to consent for him/herself, your consent for them will end.)

Part 2 - to be completed by the principal investigator or designee who conducted the informed consent discussion. Only compete this section if the potential participant has **agreed** to participate.

I believe that the person signing this form understands what is involved in the study and has freely decided to participate.

Signature of Person Conducting the Consent Discussion	PRINTED NAME	Date

Version date of this form: *28 August 2018*

Part 3 - to be completed only if the participant is unable to read or requires assistance of an oral translator/interpreter.

- The informed consent form was accurately explained to, and apparently understood by the participant*/substitute decision maker.*
- Informed consent was freely given by *or on behalf of* the participant.

Signature of Impartial Witness/Interpreter	PRINTED NAME	Date

You will be given a copy of this signed and dated consent form prior to participating in this study.

Contact Us!

If you are interested in joining the STRIDE study or have any other questions, please contact:

Joni Nedeljak:
Phone: 780-492-6007
Email: jnedelja@ualberta.ca

Margaret McNeely:
Phone: 780-492-6007
Email: mmcneely@ualberta.ca

Cancer Rehabilitation Clinic:
Phone: 492-6007
Email: frmace@ualberta.ca

"The Health Research Ethics Board of Alberta– Cancer Committee, which oversees the ethical conduct of research involving humans, has reviewed and accepted this study."

HREBA.CC-17-0164
HREBA Contact Information:
780-423-5727
Toll Free: 1-877-423-5727
08-30-2018

Q & A:

How many participants will take part in the study?

- At least 10 people with trismus will participate in the study.

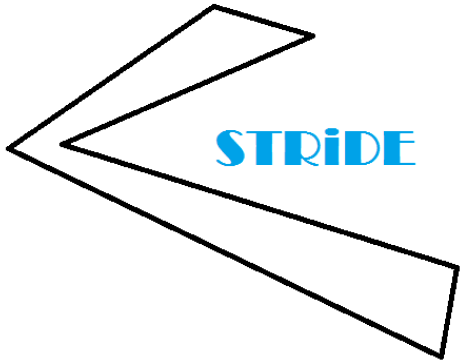
How long will each session take?

- The sessions will take approximately 1 hour

Will I get to take the Dynasplint home?

- Yes. The Dynasplint can be taken home for weeks 3-8. Dynasplint devices are provided on loan and will need to be returned at the end of the 8 weeks.

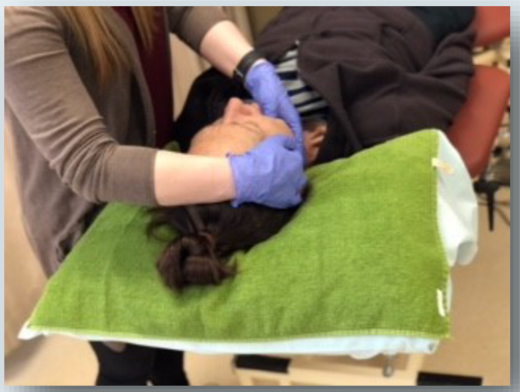
Stretching Therapy for patients with trismus using a Dynasplint and Exercise



Study Investigators:
Joni Nedeljak– Graduate Student
Susan Olivo– PT, PhD
Suresh Nayar MDS, DPhil
Margaret McNeely– PT, PhD
Dr. Hadi Seikaly, MD

What is Trismus?

Trismus, or restricted mouth opening, is one of the symptoms you may experience after your head and neck cancer treatment. Early intervention is important as trismus can impact your ability to eat, chew, and perform dental care. Interventions can include treatments such as exercise, stretching, and the use of jaw opening devices, such as a Dynasplint.



Why are we doing this study?

This study will be looking at the feasibility of developing guidelines for jaw stretching therapy and the effective use of a Dynasplint device.

Who is eligible for the study?

- 18 years of age or older
- Been diagnosed with head and neck cancer
- Currently not on Chemotherapy or Radiation Therapy
- Has not been diagnosed with:
  - -Bone Metastasis
  - -Osteoporosis
  - -Osteoradionecrosis
- Mouth opening less than 35 mm

What is involved in this study?

- **Where is this study taking place?**

The study will take place at Corbett Hall, located at the University of Alberta (8205 114 St NW, Edmonton, AB)

- **What are my responsibilities?**

- STRIDE participants will attend 2 appointments of manual therapy a week for 8 weeks.

- Baseline and post-session questionnaires on health and wellbeing (physical and emotional)

- Participant will also be taught how to use a Dynasplint device at home from weeks 3-8. Dynasplint mouthpieces will be fitted to each participant's jaw.

Eligibility Form

Please complete the survey below.

Thank you!

1)	Is the participant 18 years or older?	◯ Yes ◯ No
2)	Has the participant gone through surgery and/or radiation therapy?	◯ Yes ◯ No
3)	Is the participant finished cancer treatment?	◯ Yes ◯ No
4)	Has the participant been cleared of the following: -Bone metastasis -Osteoporosis -Osteoradionecrosis	◯ Yes ◯ No
5)	Is the potential participant's mouth opening less than 35 mm or less than 55mm if they are edentulous?	◯ Yes ◯ No
6)	Is the participant eligible for the study?	◯ Yes ◯ No

Testing

Please complete the survey below.

Thank you!

1) MIO Measurement (1) Active (Pre session) _____

2) MIO Measurement (2) Active (Pre session) _____

3) MIO Measurement (3) Active (Pre session) _____

4) MIO Measurement (1) Passive (Pre session) _____

5) MIO Measurement (2) Passive (Pre session) _____

6) MIO Measurement (3) Passive (Pre session) _____

7) Pre-Session Active Measurement Average _____

8) Pre-session Passive Measurement Average _____

Identifying Information

We appreciate you taking the time to complete this survey.

It should take about 10 minutes of your time. You are allowed to stop the survey at any time and return to it later. In order to save your answers and to continue where you left off, you must scroll down to the end of the page and click the "Save and Return Later" button.

If you do not complete the questionnaire, an email will automatically be sent to you. When you are ready to return, please open the email and click on the link provided to you. You will be ask to answer a personnal question to access your questionnaire.

We would like to remind you that your informations will not be disclosed or made publicly available, except as described in the consent document.

For any questions or concerns, please contact us:

Email: frmace@ualberta.ca

Phone: 780-492-6007

Thank you!

Baseline Demographic

First Name

_____

Last Name

_____

Date of birth

_____
(yyyy-mm-dd)

Gender

◯ Female
◯ Male

Personal Health Care Number

_____
(11111-1111)

Alberta Cancer ID

_____
(E111111)

Email

_____

Marital Status

◯ Never Married
◯ Married
◯ Common Law
◯ Separated
◯ Widowed
◯ Divorced

Education (check highest level attained)	◯ Some High School ◯ Completed High School ◯ Some University/College ◯ Completed University/College ◯ Some Graduate School ◯ Completed Graduate School
Annual Family Income:	◯ < $20 000 ◯ Between $20 000-$39 999 ◯ Between $40 000-$59 999 ◯ Between $60 000-$79 999 ◯ Between $80 000-$99 999 ◯ >$100 000
Current Employment Status:	◯ Disability ◯ Retired ◯ Part Time ◯ Homemaker ◯ Full Time ◯ Temporarily Unemployed
Ethnic origin or Ancestry? (Select ALL that apply. If you are not sure please check "other" and let us know the city, country or region your ancestors originated)	☐ British ☐ Western European ☐ Eastern European ☐ Northern European ☐ Southern European ☐ Aboriginal ☐ East and Southern Asia ☐ Southern Asia ☐ Western Asia ☐ Pacific Islands ☐ Arab ☐ Latin/Central and South America ☐ Caribbean ☐ African ☐ Other
If other, please specify	_____
Smoking Status:	◯ Never Smoked ◯ Ex-Smoker ◯ Occasional Smoker ◯ Regular Smoker (Smoke every day)
Drinking Status:	◯ Never Drank ◯ Ex-Drinker ◯ Occasional Drinker ◯ Social Drinker ◯ Regular Drinker (drink every day)
Phone number	_____ (###-###-####)
Street Address	_____
City	_____

Postal Code

_____
(A1A 1A1)

Name of Family Physician

_____

Name of Oncologist

_____

Name of other treating physician.
Please indicate the doctor's specialty (e.g., cardiologist, neurologist, etc.)

_____

Emergency Contact Information

Name of Emergency Contact

_____

Relationship

_____

Mobile Phone

_____
(###-###-####)

Home Phone

_____
(###-###-####)

Questionnaire

We appreciate you taking the time to complete this survey.

It should take about 10 minutes of your time. You are allowed to stop the survey at any time and return to it later. In order to save your answers and to continue where you left off, you must scroll down to the end of the page and click the "Save and Return Later" button.

If you do not complete the questionnaire, an email will automatically be sent to you. When you are ready to return, please open the email and click on the link provided to you. You will be ask to answer a personnal question to access your questionnaire.

We would like to remind you that your informations will not be disclosed or made publicly available, except as described in the consent document.

For any questions or concerns, please contact us:

Email: frmace@ualberta.ca

Phone: 780-492-6007

Thank you!

Health Questionnaire

1) In general, would you say your health is:

- ◯ Excellent
- ◯ Very good
- ◯ Good
- ◯ Fair
- ◯ Poor

2) Compared to one year ago, how would you rate your health in general now?

- ◯ Much better now than one year ago
- ◯ Somewhat better now than one year ago
- ◯ About the same as one year ago
- ◯ Somewhat worse than one year ago
- ◯ Much worse than one year ago

3) Please rate your pain: 0 — 100

(Place a mark on the scale above)

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

		Limited a lot	Limited a little	Not Limited at all
4)	Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	◯	◯	◯
5)	Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	◯	◯	◯
6)	Lifting or carrying groceries	◯	◯	◯
7)				

	Climbing several flights of stairs	◯	◯	◯
8)	Climbing one flight of stairs	◯	◯	◯
9)	Bending, kneeling or stooping	◯	◯	◯
10)	Walking more than a mile	◯	◯	◯
11)	Walking several blocks	◯	◯	◯
12)	Walking one block	◯	◯	◯

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

		Yes	No
13)	Cut down on the amount of time you spent on work or other activites	◯	◯
14)	Accomplished less than you would like	◯	◯
15)	Were limited in the kind of work or other activities	◯	◯
16)	Had difficulty performing the work or other activities (for example, it took extra effort)	◯	◯

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

		Yes	No
17)	Cut down the amount of time you spent on work or other activities	◯	◯
18)	Accomplished less than you would like	◯	◯
19)	Didnt do work or other activities as carefully as usual	◯	◯

20) During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors or groups?

- ◯ Not at all
- ◯ Slightly
- ◯ Moderately
- ◯ Quite a bit
- ◯ Extremely

21) How much bodily pain have you had during the past 4 weeks

- ◯ None.
- ◯ Very mild.
- ◯ Mild.
- ◯ Moderate.
- ◯ Severe.
- ◯ Very severe.

22) During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

- ◯ Not at all
- ◯ A little bit
- ◯ Moderately
- ◯ Quite a bit
- ◯ Extremely

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks

		All of the time	Most of the time	A good bit of the time	Some of the time	A Little of the time	None of the time
23)	Did you feel full of pep?	◯	◯	◯	◯	◯	◯
24)	Have you been a very nervous person?	◯	◯	◯	◯	◯	◯
25)	Have you felt so down in the dumps that nothing could cheer you up?	◯	◯	◯	◯	◯	◯
26)	Have you felt calm and peaceful?	◯	◯	◯	◯	◯	◯
27)	Did you have a lot of energy?	◯	◯	◯	◯	◯	◯
28)	Have you felt downhearted and blue?	◯	◯	◯	◯	◯	◯
29)	Did you feel worn out?	◯	◯	◯	◯	◯	◯
30)	Have you been a happy person?	◯	◯	◯	◯	◯	◯
31)	Did you feel tired?	◯	◯	◯	◯	◯	◯

32) During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

- ◯ All of the time
- ◯ Most of the time
- ◯ Some of the time
- ◯ A little of the time
- ◯ None of the time

How TRUE or FALSE is each of the following statements for you?

		Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33)	I seem to get sick a little easier than other people	◯	◯	◯	◯	◯
34)	I am as healthy as anybody I know	◯	◯	◯	◯	◯
35)	I expect my health to get worse	◯	◯	◯	◯	◯
36)	My health is excellent	◯	◯	◯	◯	◯

Trismus Questionnaire

Symptom Domains

During the last week, have you had:

		Not at all	Mild	Moderate	Severe	Very Severe
37)	Fatigue/stiffness in your jaw	◯	◯	◯	◯	◯
38)	Aches or pain in your face or your jaw	◯	◯	◯	◯	◯
39)	Pain moving your jaw, opening mouth/chewing	◯	◯	◯	◯	◯

40)

	Problems when opening your mouth wide or taking a big bite	○	○	○	○	○
41)	Pain or soreness in your jaw muscles	○	○	○	○	○
42)	Problem yawning	○	○	○	○	○

Due to your jaw problems, to what extend are you limited or incapable to:

		Not at all	Mild	Moderate	Severe	Very Severe
43)	Eat solid food	○	○	○	○	○
44)	Put food in your mouth	○	○	○	○	○
45)	Eat soft food	○	○	○	○	○
46)	Bite food	○	○	○	○	○

Muscular Tension

Do you usually:

		Not at all	Mild	Moderate	Severe	Very severe
47)	Clench your teeth	○	○	○	○	○
48)	Press with your tongue	○	○	○	○	○
49)	Hear noises from your jaw	○	○	○	○	○

Facial pain

		None	Mild	Moderate	Severe	Very severe	Unbearable
50)	How much facial pain do you have right now?	○	○	○	○	○	○
51)	How strong wast the worst pain you have had in the last month?	○	○	○	○	○	○
52)	On average, how strong has your pain been in the last month?	○	○	○	○	○	○

Facial Pain Impact

		Not at all	A little	Moderately	Quite a bit	very much	Have not had any facial pain
53)	How much has your facial pain interfered with your social, leisure and family activities during the last month?	○	○	○	○	○	○
54)	How much as your facial pain affected your ability to work including both gainful employment and household duties during the last month?	○	○	○	○	○	○

Jaw Limitation

55) How limited are you in your ability to open your mouth right now?

- ◯ Not at all
- ◯ A little
- ◯ Moderately
- ◯ Quite a bit
- ◯ Very

Jaw Limitation Impact

	Not at all	A little	Moderately	Quite a bit	Very much	Have not been limited to open
56) How much has your limitation to open your mouth interfered with your social, leisure and family activities during the last month?	◯	◯	◯	◯	◯	◯
57) How much has your limitation to open your mouth changed your ability to work including both gainful employment and household duties during the last month?	◯	◯	◯	◯	◯	◯

Medical Record

Please complete the survey below.

Thank you!

Cancer Diagnosis

Primary Cancer Diagnosis	☐ Laryngeal ☐ Hypopharyngeal ☐ Oral ☐ Salivary Gland ☐ Oropharyngeal ☐ Nasal cavity and paranasal sinus ☐ Other (Check all that apply.)
Other Cancer.	_____
Date of diagnosis	_____
Overall AJCC Stage	◯ 0 ◯ I ◯ II ◯ III ◯ IV
Primary Tumor	◯ TX ◯ T0 ◯ Tis ◯ T1 ◯ T2 ◯ T3 ◯ T4
Regional Lymph Nodes	◯ NX ◯ N0 ◯ N1 ◯ N2 ◯ N3
Distant metastasis	◯ M0 ◯ M1
Cancer Treatment(s)	☐ Surgery ☐ Chemotherapy ☐ Radiation ☐ Biological Agent ☐ Hormone Therapy (Check all that apply.)

Cancer Recurrence or Progression

Did patient have a recurrence?	◯ Yes ◯ No
Was patient treated for recurrence?	◯ Yes ◯ No
What treatment(s) did the patient receive?	☐ Surgery ☐ Chemotherapy ☐ Radiation ☐ Biological Agent ☐ Hormone Therapy (Check all that apply.)
Did patient have a progression?	◯ Yes ◯ No
Was patient treated for progression?	◯ Yes ◯ No
What treatment(s) did the patient receive?	☐ Surgery ☐ Chemotherapy ☐ Radiation ☐ Biological Agent ☐ Hormone Therapy (Check all that apply.)

Appendix I: Manual therapy stretches and modifications

Participant	Manual therapy stretches				Comments
	1) Distraction	2) Protrusion	3) J Stroke	4) Lateral Deviation	
S1	✓	✓	✓	✓	Performed all stretches.
S2	✓	☒	☒	☒	Very gentle distractions; she had limited mouth opening and had very sensitive gums and oral tissues due to radiation fibrosis.
S3	✓	☒	☒	☒	Needed 2 people due to very limited MIO; one to push down on bottom teeth and the other person tried to get their thumb as far back on the participant's tooth to provide distractions.
S4	✓	☒	☒	☒	Only did distractions as he reported a pinching sensation on his right side with protrusions. Developed an infection which limited his mouth opening and increased pain.
S5	✓	✓	☒	☒	Participant had sore teeth (right side: 3 mandibular molars and one pre-molar; left side: maxillary canine) so had to watch contact on teeth and had to gently perform stretches.
S6	✓	✓	✓	✓	Performed all stretches.
S7	✓	✓	☒	☒	Right side (affected side) more stiff than left.
S8	✓	☒	☒	☒	Painful gums due to dental bridge- could only tolerate light pressure on tissues.
S9	✓	✓	✓	✓	Performed all stretches.
S10	✓	✓	✓	✓	Edentulous but able to tolerate all stretches.

Attendance/MIO

Record ID	_____
Attendance Week 1: Session 1	◯ Yes ◯ No
MIO best of 3_session 1pre	_____
MIO best of 3_session_1post?	_____
Attendance Week 1_Session 2	◯ Yes ◯ No
MIO best of 3_session_2pre	_____
MIO session 2 post	_____
Dynasplint Session Week 1?	◯ Yes ◯ No
Dynasplint Notes Week 1	_____
Attendance Session 3: Week 2	◯ Yes ◯ No
MIO best session 3 pre	_____
MIO best session 3 post	_____
Attendance Session 4: Week 2	◯ Yes ◯ No
MIO best session 4 pre	_____
MIO best session 4 post	_____
Dynasplint Session Week 2?	◯ Yes ◯ No
Dynasplint Notes Week 2	_____

Attendance Session 5_ Week 3	◯ Yes ◯ No
MIO best session 5 pre	_____
MIO best session 5 post	_____
Attendance Session 6_Week 3	◯ Yes ◯ No
MIO best session 6 pre	_____
MIO best session 6 post	_____
Dynasplint Session Week 3?	◯ Yes ◯ No
Dynasplint Notes Week 3	_____
Attendance Session 7_Week 4	◯ Yes ◯ No
MIO best session 7 pre	_____
MIO best session 7 post	_____
Attendance Session 8_Week 4	◯ Yes ◯ No
MIO best session 8 pre	_____
MIO best session 8 post	_____
Dynasplint Session Week 4?	◯ Yes ◯ No
Dynasplint Notes Week 4	_____
Attendance Session 9_Week 5	◯ Yes ◯ No
MIO best session 9 pre	_____

MIO best session 9 post

_____

Attendance Session 10_Week 5

◯ Yes
◯ No

MIO best session 10 pre

_____

MIO best session 10 post

_____

Dynasplint Session Week 5?

◯ Yes
◯ No

Dynasplint Notes Week 5

_____

Attendance Session 11_Week 6

◯ Yes
◯ No

MIO best session 11 pre

_____

MIO best session 11 post

_____

Attendance Session 12_Week 6

◯ Yes
◯ No

MIO best session 12 pre

_____

MIO best session 12 post

_____

Dynasplint Session Week 6?

◯ Yes
◯ No

Dynasplint Notes Week 6

_____

Attendance Session 13_Week 7

◯ Yes
◯ No

MIO best session 13 pre

_____

MIO best session 13 post

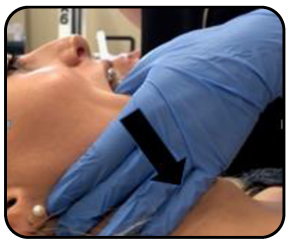
_____

Attendance Session 14_Week 7

◯ Yes
◯ No

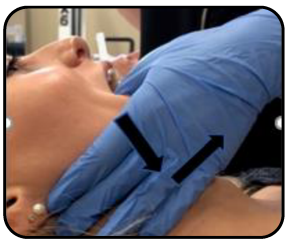
MIO best session 14 pre	_____
MIO best session 14 post	_____
Dynasplint Session Week 7?	◯ Yes ◯ No
Dynasplint Notes Week 7	_____
Attendance Session 15_Week 8	◯ Yes ◯ No
MIO best session 15 pre	_____
MIO best session 15 post	_____
Attendance Session 16_Week 8	◯ Yes ◯ No
MIO best session 16 pre	_____
MIO best session 16 post	_____
Dynasplint Session Week 8?	◯ Yes ◯ No
Dynasplint Notes Week 8	_____

Manual Therapy Stretches of the TMJ



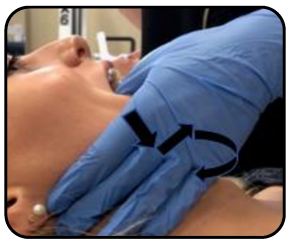
Distraction

-30 repetitions each side



Protrusion (TMJ distraction with anterior translation)

-30 repetitions each side



J Stroke

-30 repetitions each side

Lateral Deviation

-10 repetitions each side

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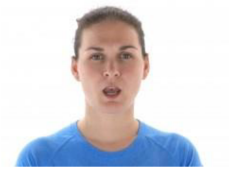
Notes:

1- Mouth opening- Sets:6 / Repetition:3



With your tongue resting on the roof of your mouth, let your jaw drop partially, then lower your tongue and let your jaw drop completely down and back.

2- Active jaw opening with finger

Place one finger between your upper and lower teeth.
Remove your finger but try to maintain your mouth open one finger-width.
Close your mouth.
To progress, repeat by placing two fingers between your upper and lower teeth.

3- Isometric jaw opening

Place your thumbs under your chin.
Apply gentle pressure onto your chin in an upward direction but resist any actual movement of the jaw by contracting your muscles.
Relax your chin.

4- Lateral glide

Move your jaw to one side, then straight down, then to the other side.
Relax your jaw.

5- Left Isometric lateral glide

Place two fingers on the left side of your lower jaw.
Apply gentle horizontal pressure onto the lower jaw towards the right, but resist any actual movement of the jaw by contracting your muscles.
Relax your jaw.

6- Right isometric lateral glide

Place two fingers on the right side of your jaw.
Apply gentle horizontal pressure onto the jaw towards the left, but resist any actual movement of the jaw by contracting your muscles.
Relax your jaw.

7- Isometric jaw protraction

Place two fingers on your chin.
Apply gentle pressure onto your chin in a backward direction but resist any actual movement of the jaw by contracting your muscles.
Relax your chin.

Sets:6 / Repetition:3

Exercise 1 : Mouth opening

Exercise 2 : Active jaw opening with finger

Exercise 3 : Isometric jaw opening

Exercise 4 : Lateral glide

Exercise 5 : Left Isometric lateral glide

Exercise 6 : Right isometric lateral glide

Exercise 7 : Isometric jaw protraction

Dynasplint® Adherence (Diary Entries)

Participant	Week	Number of DTS Sessions (Attended/ Prescribed)	DTS Intensity (Completed/ Prescribed)	DTS Minutes (Completed/ Prescribed)	Comments
S1	3	14/14	0.5/0.5	210/210	-Pins + needles left jaw lower front 2 teeth + lip sensitive low pain
	4	14/14	0.5/0.5	280/280	n/a
	5	11/14	0.5/0.5	275/350	-Sometimes do 2 sessions at night close together because of time increase -Tearing sensation upper ridge right side (flap side); started a few days ago
	6	14/14	0.5/0.5	420/420	n/a
	7	14/14	0.8/1.0	420/420	-Headaches so decreased tension
	8	14/14	0.8/1.5	420/420	n/a
	Total	81/84	53%	2025/2100	
S2	Did not complete a diary as she was unable to use the DTS due to limited mouth opening. She was given a children's TB device to try. She attempted to use it 3x/day and would try more if her mouth cooperated. The prescription for the TB was 7 reps, 7x/day, hold for 10 seconds.				
S3	Did not complete a diary as she was unable to use the DTS due to limited mouth opening. At home she would use popsicle sticks or the plates of the DTS to wedge in between her teeth.				
S4	3	10/14	0.5/0.5	150/210	-felt good; little tight on right side -unable to use device-jaw won't open enough (swelling + redness- mostly on right side, some on left side around cheeks) -right side of jaw a little sore -didn't use device due to a meltdown day
	4	14/14	0.5/0.5	280/280	-little tight on right side of jaw after use ½ hour later -no problems -jaw a little stiff had to stretch it first to get device in -jaw stiff today mostly due to cold weather
	5	14/14	0.5/0.5	350/350	-no problems -jaw a little tight had to stretch first to get device in -woke up jaw stiff, couldn't open mouth very wide. Could use device after
	6	13/14	0.5/0.5	390/420	-jaw sore on right side, face a little swollen -missed one session due to travelling -sore on right side
	7	4/14	0.5/1.0	95/420	-did not use at all-sick all day, face and jaw swollen, jaw very tight

					-woke up unable to open mouth, face swollen. Went to the hospital. -infection in throat -jaw a little sore had to stretch jaw first before I used device
	8	14/14	0.5/1.5	420/420	-jaw a little sore after use -sore jaw about an hour after use. -jaw getting better, not as sore -removed counterweight from device-jaw not as sore.
	Total	69/84	33%	1685/2100	
S5	Did not complete diary. Did report verbally that he was using the Dynasplint, even with sore teeth (right side: had to avoid 3 mandibular molars and one pre-molar; left side: had to avoid left maxillary canine). Started hyperbaric chamber in week 6 of study for upcoming tooth extraction surgery.				
S6	3	12/14	0.5/0.5	180/210	-none
	4	14/14	0.5/0.5	255/280	-none -Participant continued doing 15 minutes for 6 sessions and went over by 5 minutes on one session
	5	14/14	0.5/0.5	350/350	-none -feel it working muscles
	6	14/14	0.5/0.5	420/420	-none -feel muscles work and a little more tension on muscles -no pain -took a small break in the middle
	7	14/14	0.5-1.0/1.0	285/420	-none -working muscles -more tension on muscle -feel discomfort -don't feel muscle working -Participant had some discomfort so he was instructed to decrease resistance to 0.5
	8	14/14	0.5/1.5	420/420	-none -Participant had discomfort in previous week so we kept tension at 0.5
	Total	82/84	33%	1910/2100	
S7	3	14/14	0.5/0.5	210/210	-fine -OK
	4	14/14	0.5/0.5	280/280	-no pain -Ok -fine
	5	14/14	0.5/0.5	350/350	-Ok -fine
	6	14/14	0.5/0.5	350/420	-no pain
	7	14/14	1.0/1.0	420/420	-no pain
	8	14/14	1.5/1.5	420/420	-no pain
	Total	84/84	100%	2030/2100	
S8	Participant did not complete a diary. The DTS was hurting his teeth.				

S9	3	14/14	0.5/0.5	210/210	-O.K.
	4	14/14	0.5/0.5	280/280	-O.K.
	5	14/14	0.5/0.5	350/350	-O.K.
	6	14/14	0.5/0.5	420/420	-O.K.
	7	14/14	1.0/1.0	420/420	-O.K.
	8	14/14	1.5/1.5	420/420	-O.K.
	Total	84/84	100%	2100/2100	
S10	3	14/14	0.5/0.5	222/210	-lower jaw slips if I'm not sitting straight -stopped at 11 min to wipe mouthpiece -lower brace wiggles -mouth a little dry when done
	4	14/14	0.5/0.5	276/280	n/a
	5	14/14	0.5/0.5	363/350	n/a
	6	14/14	0.5/0.5	437/420	n/a
	7	12/14	1.0/1.0	379/420	n/a
	8	14/14	1.5/1.5	418/420	-Harder to get DTS in and out of my mouth at this tension
	Total	82/84	100%	2095/2100	

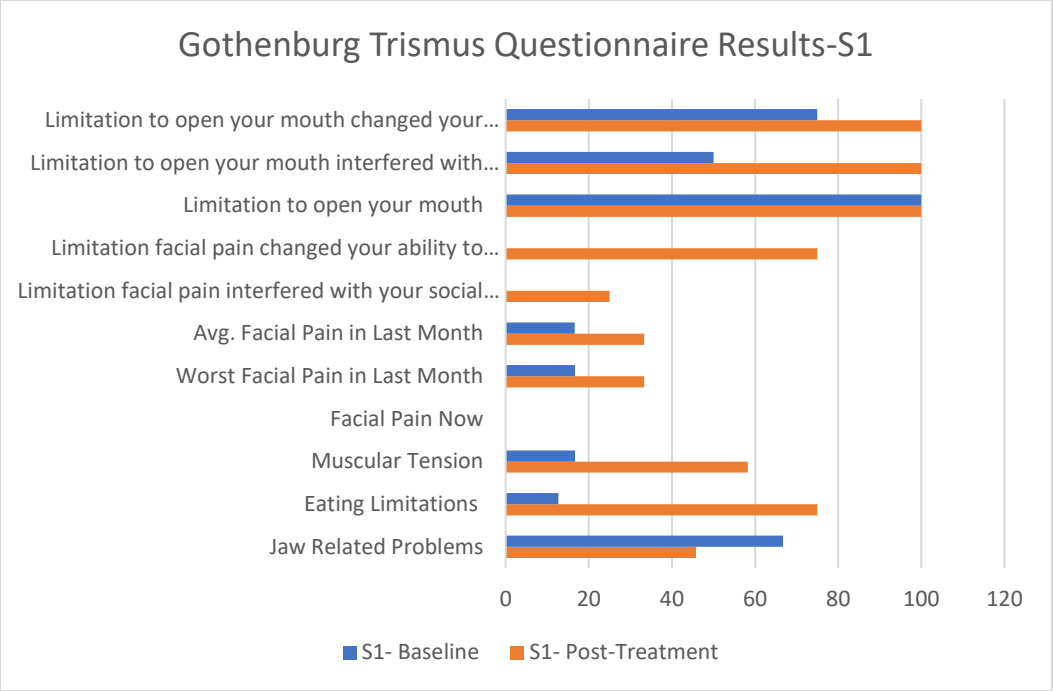
Appendix N: Gothenburg Trismus Questionnaire: Number of participants with a change in results from baseline to 8-week follow up

Gothenburg Trismus Questionnaire: number of participants with a change in result from baseline to 8-week follow up

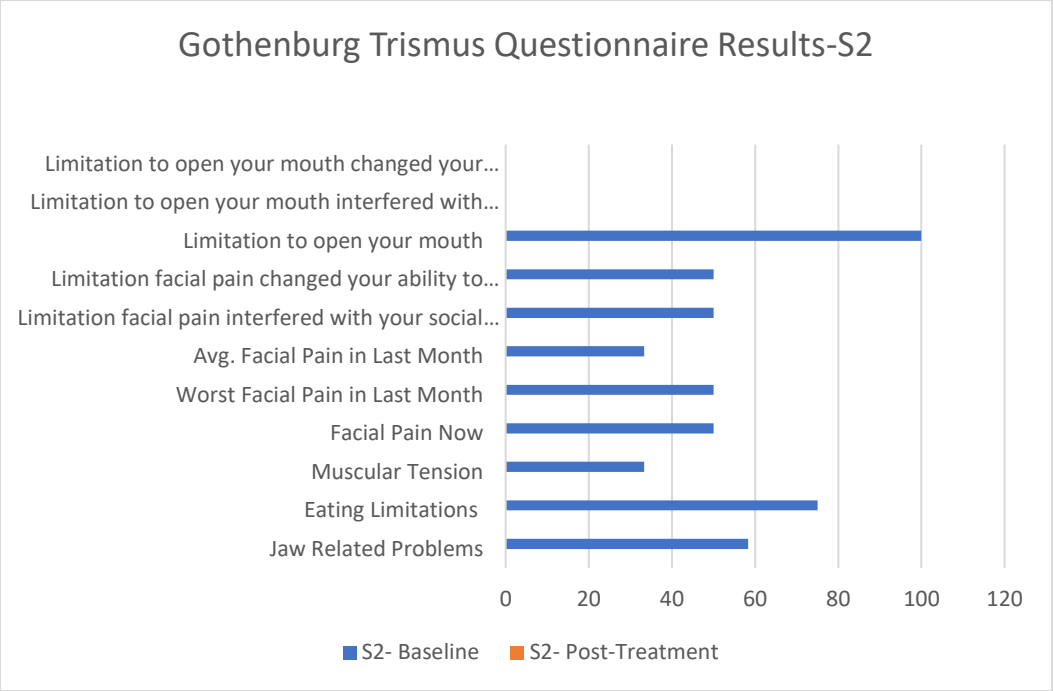
Domain	Improvement	Worsen	No change
Jaw related problems	6	2	1
Eating limitations	7	2	0
Muscular tension	6	2	1
Facial pain now	1	0	8
Worst facial pain in last month	0	1	8
Average facial pain in last month	2	3	4
Lim. Facial pain interfere social	1	3	5
Lim. Facial pain change ability to work	0	4	5
Lim. to open mouth	3	1	5
Lim. Open mouth interfere w social	1	2	6
Lim. Open mouth changed ability to work	1	5	3

Appendix O: Gothenburg Trismus Questionnaire Results

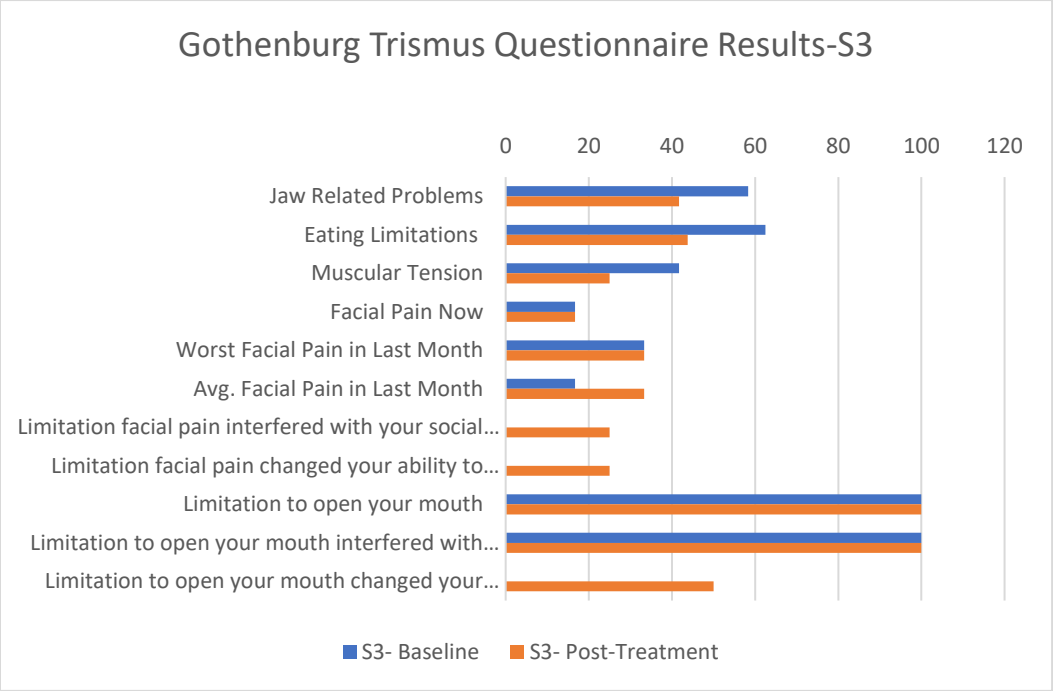
GTQ Results for Participant S1



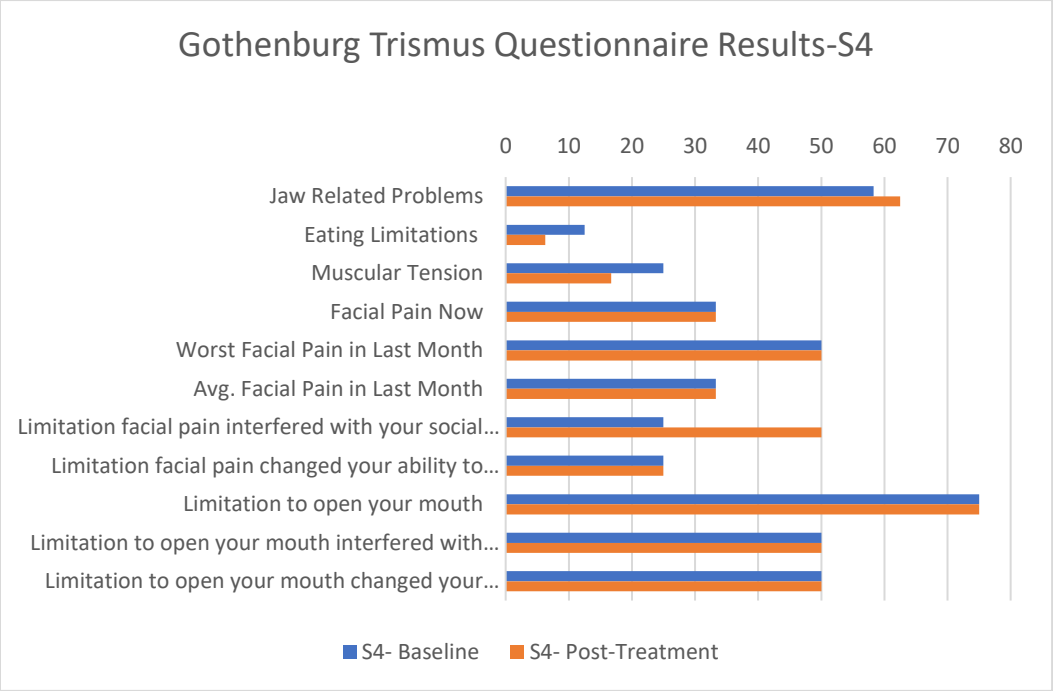
GTQ Results for Participant S2



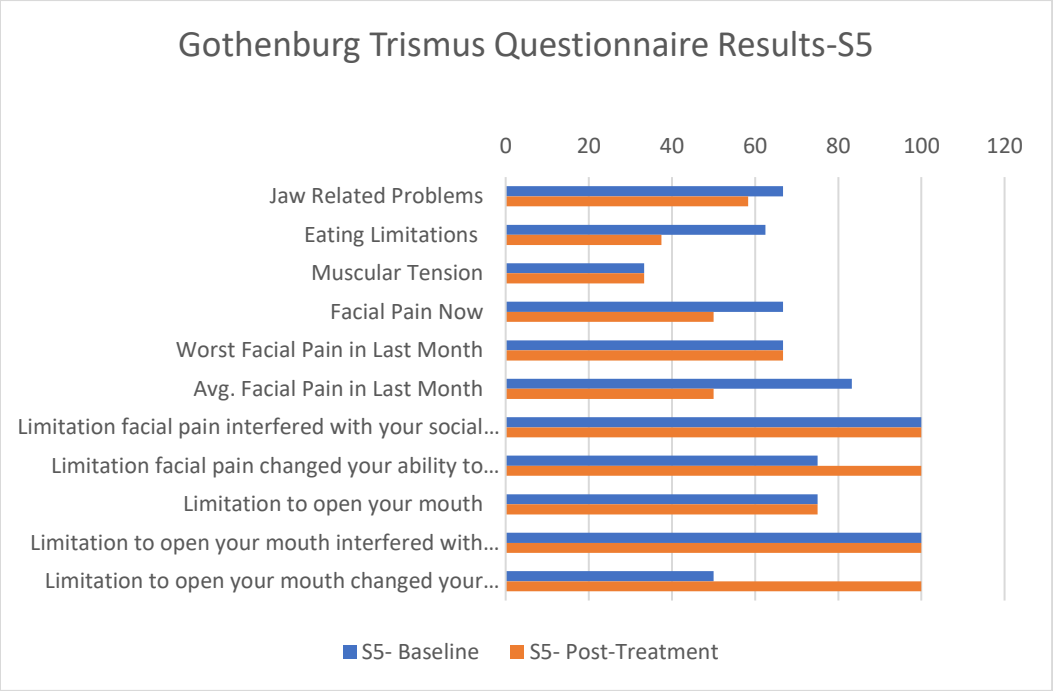
GTQ Results for Participant S3



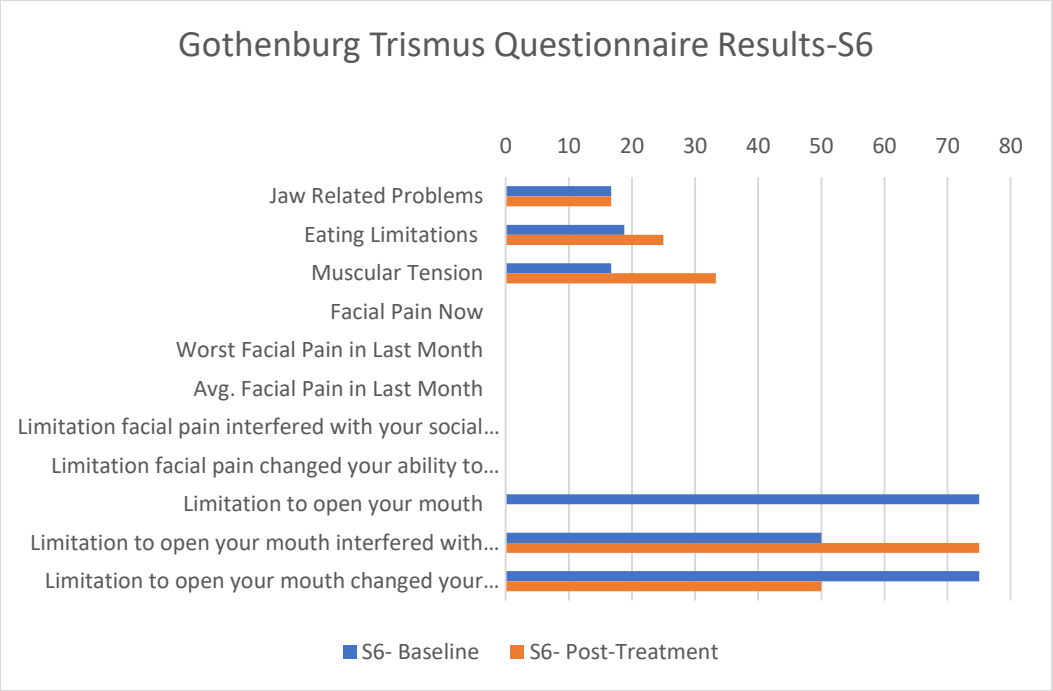
GTQ Results for Participant S4



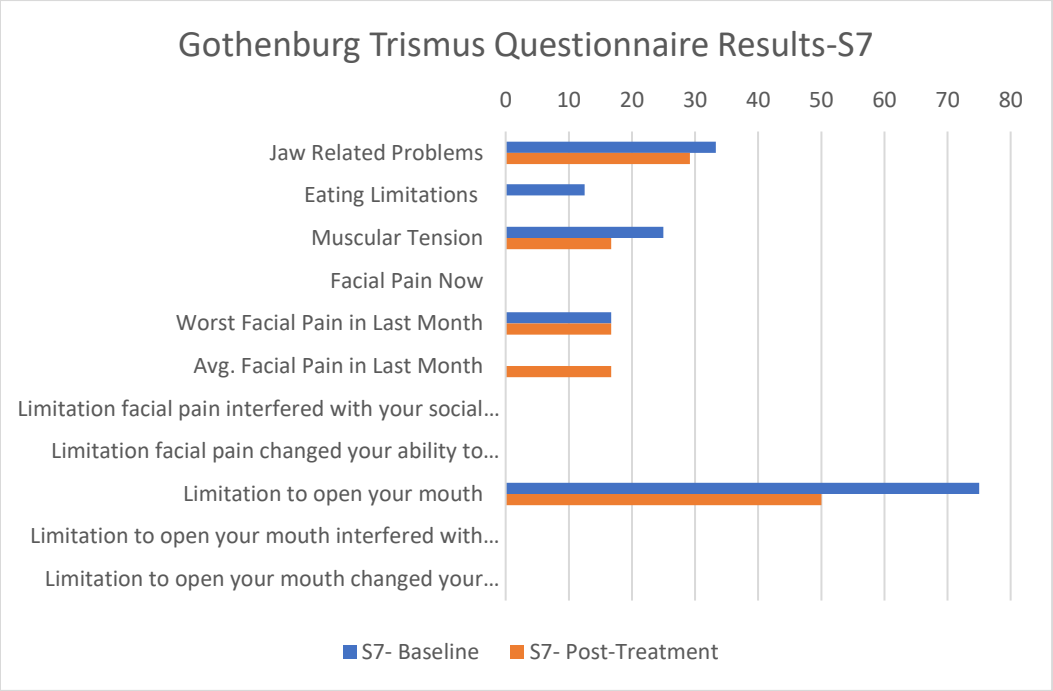
GTQ Results for Participant S5



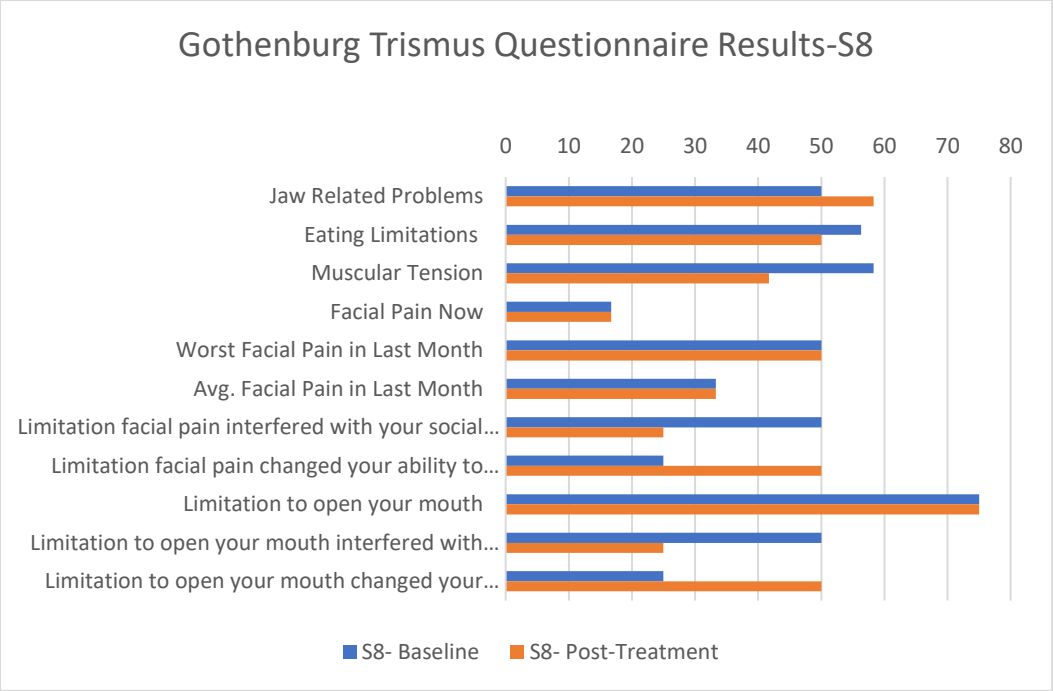
GTQ Results for Participant S6



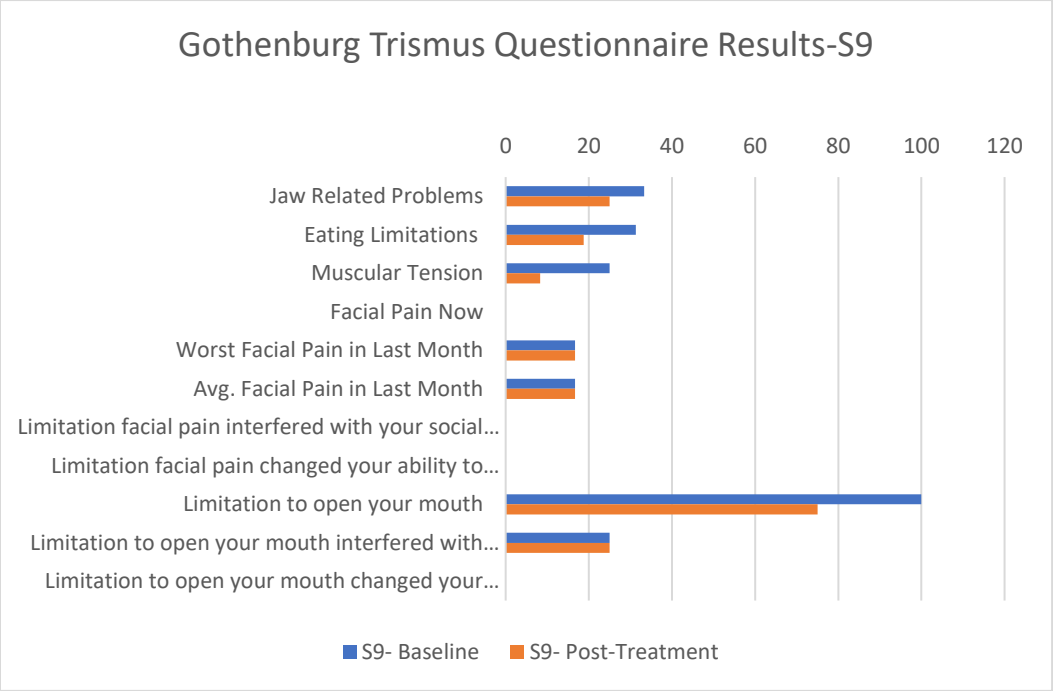
GTQ Results for Participant S7



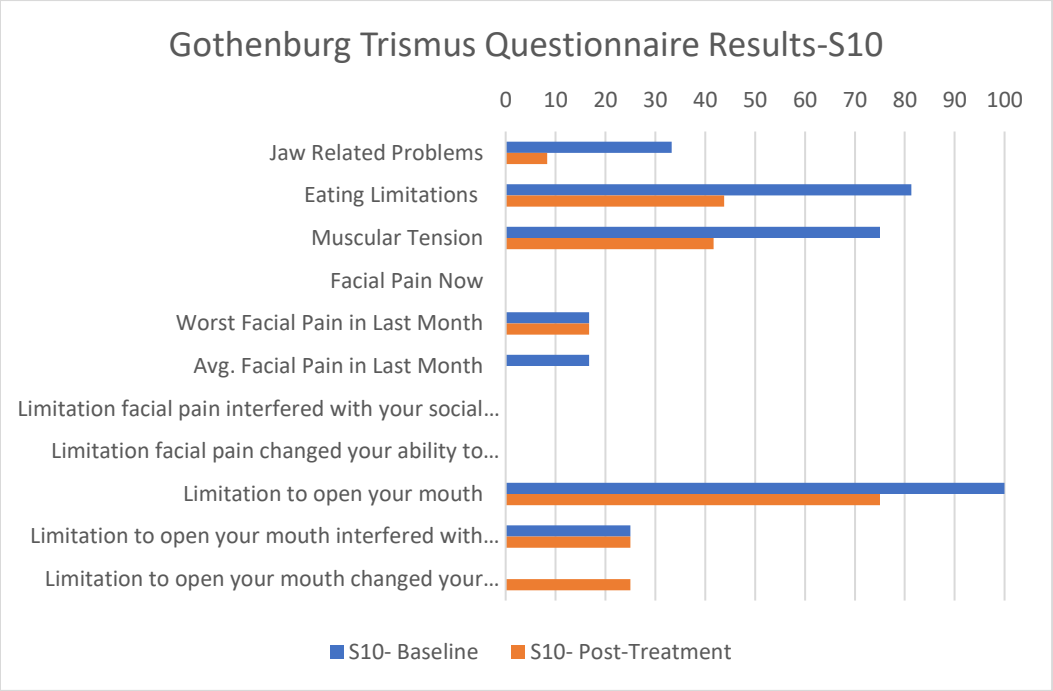
GTQ Results for Participant S8



GTQ Results for Participant S9



GTQ Results for Participant S10



Appendix P: Short Form-36: Number of participants with a change in results from baseline to 8-week follow-up

Short Form-36: number of participants with a change in results from baseline to 8-week follow up

Domain	Improvement	Worsen	No change
Physical Functioning	4	3	2
Role lim. due to physical health	2	1	6
Role limitations due to emotional problems	2	3	4
Energy/Fatigue	4	3	2
Emotional Wellbeing	5	3	1
Social Functioning	3	1	5
Pain	2	4	3
General Health	2	5	2

Short Form-36 Results

ID	Time	Physical Functioning	Role Limitations due to Physical Health	Role Limitations due to Emotional Problems	Energy/ Fatigue	Emotional Well-Being	Social Functioning	Pain	General Health
	Baseline	80	100	100	60	80	50	80	65
	8-Weeks	75	50	33.3	70	80	62.5	45	60
S1	Change	-5	-50	-66.7	+10	0	-12.5	-35	-5
	Baseline	65	0	33.3	55	60	50	45	70
	8-Weeks	-	-	-	-	-	-	-	-
S2	Change	-	-	-	-	-	-	-	-
	Baseline	95	25	66.7	55	60	12.5	57.5	75
	8-Weeks	90	25	0	30	64	25	57.5	60
S3	Change	-5	0	-66.7	-25	+4	+12.5	0	-15
	Baseline	50	0	100	50	56	50	20	50
	8-Weeks	75	0	66.7	55	72	50	45	45
S4	Change	+25	0	-33.3	+5	+16	0	+25	-5
	Baseline	25	0	0	20	16	0	22.5	50
	8-Weeks	20	0	0	15	12	0	22.5	35
S5	Change	-5	0	0	-5	-4	0	0	-15
	Baseline	65	25	33.3	60	64	37.5	100	90
	8-Weeks	85	25	66.7	55	60	50	87.5	65
S6	Change	+20	0	+33.4	-5	-4	+12.5	-12.5	-25
	Baseline	90	100	100	75	88	100	100	75
	8-Weeks	90	100	100	80	96	100	90	75
S7	Change	0	0	0	+5	+8	0	-10	0
	Baseline	40	0	0	45	72	25	45	60
	8-Weeks	55	0	100	55	80	75	55	60
S8	Change	+15	0	+100	+10	+8	+50	+10	0
	Baseline	65	25	100	60	88	75	77.5	70
	8-Weeks	70	75	100	60	92	75	57.5	75
S9	Change	+5	+50	0	0	+4	0	-20	+5
S10	Baseline	55	75	100	70	96	100	90	50

	8-Weeks	55	100	100	70	88	100	90	60
	Change	0	+25	0	0	-8	0	0	+10