Temporomandibular Disorders and Headaches

Two Pains, One Face

Hedwig A. van der Meer

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Faculteit der Tandheelkunde

"If nothing ever changed, there would be no such things as butterflies"
Wendy Mass, The Candymakers

Table of contents


1

Chapter 1

General Introduction

General Introduction

Femke, a 37-year old woman, experiences pain in her face and headache. She is unsure what is going on. When she goes to see her dentist for her annual check-up, she tells her dentist about her complaints, as she thinks it may be her teeth bothering her. The dentist concludes that her complaints are caused by her jaw muscles, which may cause her headaches too. The dentist has a close working relationship with a specialized physical therapist and suggests Femke to make an appointment with that physical therapist. She asks the dentist what a physical therapist can do for her. The dentist tells her that she can perform an additional examination of the jaw and neck, followed by giving exercises suited for her complaints. He explains that he diagnosed a 'temporomandibular disorder' and has good experiences that the physical therapist can be helpful to reduce her complaints.

When Femke made an appointment with the physical therapist, the therapist told her that she needs to have a clear understanding of the complaints, how the jaw and headache complaints are related, and what factors influence Femke's complaints. Based on the information from Femke and a diagnostic examination she will make decisions how to help Femke best.

In this dissertation our studies are presented, which we performed to further improve physical therapy care for patients like Femke.

Temporomandibular Disorders

In the general population, approximately 10 to 15% of the adults report to have a temporomandibular disorder (TMD).[1] TMDs are defined as complaints of the masticatory system involving the temporomandibular joint, the masticatory muscles and associated structures (Figure 1.1).[2] The temporomandibular joint (TMJ) is a bilateral joint with a disc between the two articular facets of the TMJ. The joint can make several movements: opening and closing of the mouth, lateral deviation, protrusion and retraction. These movements are executed by the masseter and temporal muscles, as well as the pterygoid muscles.

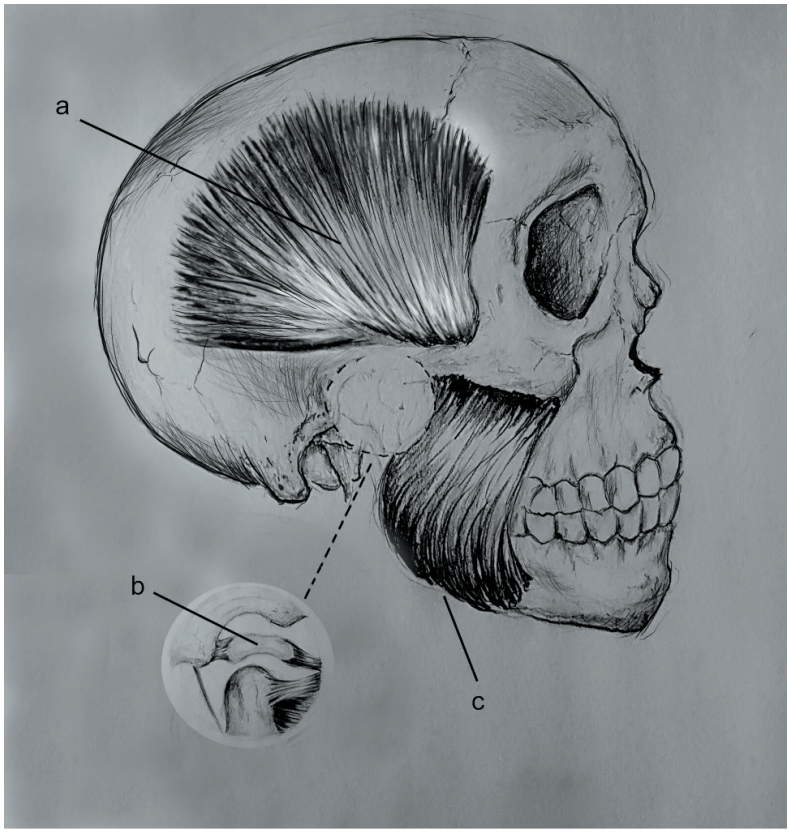

Figure 1.1: Superficial view of the temporomandibular joint (TMJ) anatomy. (a) temporalis muscle, (b) temporomandibular disc, and (c) masseter muscle. Drawing by J.P. Trujillo.

TMDs can be classified into disorders of the TMJ and painful TMD conditions (e.g. myalgia, arthralgia).[4] Disorders of the TMJ are disc displacement (with or without reduction), subluxation and degenerative joint disease.[4] Disc displacement and subluxation may cause clicking of the joint, which is reported in 56% of patients with TMD and 36% of healthy controls.[5] Pain is, however, the main reason for patients to seek care for their TMD pain complaints,[6] with a myalgia of the masticatory muscles as the most common subclassification of TMD (45 to 80%).[7,8] Myalgia may lead to referred pain to the head or face,[4] which can make accurate diagnosis of the complaints challenging. In addition, myalgia of the temporal muscles may be experienced as a headache by the patient. Given the fact that there are more than 85 types of headache, the presence of headache complaints in TMD patients may further complicate accurate diagnosis.

Headaches

Up to 77% of the adults in Europe experience headache at least once in their life and up to 50% have experienced headaches in the last year.[9] The most prevalent headache (62.6%) is tension-type headache (TTH), followed by migraine (14.7%).[9] As described by the International Classification of Headache Disorders (ICHD-3), both TTH and migraine, for example, are primary headaches.[10] For primary headaches, the headaches are disorders by themselves that are caused by independent pathological mechanisms and not by other disorders. In contrast, secondary headaches are defined as headaches which are a symptom of an underlying disorder, such as a cervicogenic headache and a headache attributed to TMD.[10]

TTH is a bilateral headache, with a pressing pain around the head and temple areas of mild to moderate severity.[10] Even though the exact etiology of TTH is unclear, it is known that several muscles of the neck are contributing to the perceived complaints.[11] Migraine is more considered a neurovascular disorder and is usually unilateral with a pulsating pain of moderate to severe intensity.[10,12,13] Headache attributed to TMD may be bilateral or unilateral, depending on where the TMD complaints are located, but always in the temple area.[14]

TMD and Headaches

Patients with a painful TMD are up to 8.8 times more likely to have a headache, compared to healthy controls.[15] Up to 88% of patients with TMD experience headaches, which is higher than the prevalence of headache in the general population.[9,16–19] Where TTH is most common in the general population, in patients with TMD migraine is more prevalent. [16,17,19] When comparing patients with TMD to healthy controls, the odds ratio (OR)* of having migraine is 2.8 and 2.5 for TTH.[17] This shows not only a high co-occurrence of the complaints, but also a strong association between TMD and the primary headaches migraine and TTH. The secondary headache attributed to TMD has not been studied as thoroughly as the primary headaches. The prevalence of headache attributed to TMD is 5% in patients with TMD.[18] In a group of patients with TMD and headache in the temple area, the prevalence of headache attributed to TMD increases to 45.6%.[14]

Etiology of TMD and headache

The etiology of TMD is considered to be multifactorial.[20] Based on a large study in the United States of America (the Orofacial Pain Prospective Evaluation and Risk Assessment, or OPPERA), a model has been developed discussing risk factors that may contribute to the onset and persistence of TMD, specifically TMD-pain.[21] According to this model, aside from genetics and environmental contributions, two phenotypes (psychological distress and pain amplification) are described as risk factors for TMD. High psychological distress can come from mood swings, anxiety, depression, stress response, or somatization.[21]

* Odds ratio is the ratio between the odds of variable A (e.g. headache) in the presence of variable B (e.g. TMD) and the odds of variable A in the absence of variable B or vice versa. In case of an OR of 1 in our example, the odds of the presence of headache is the same for those with or without a TMD. If the OR is higher than one, the two variables are correlated which means the presence of TMD increases the odds of having headache.[56]

These psychosocial factors are risk factors in the development and chronification of TMD-pain. Pain amplification, a general construct that includes phenomena like hyperalgesia, allodynia and central sensitization, also plays an important role in the onset and persistence of TMD pain.[21]

Interestingly, some (chronic) headache types like TTH and migraine have the same phenotypical risk factors.[22–26] This may explain why there is a high co-occurrence of TMD and headache complaints.[27] For example, both TMD and headache are more frequent in women compared to men and it is suggested that psychosocial factors like stress and somatization contribute to the complaints.[27–29] This raises the question whether TMD and headaches are directly associated, or rather through the presence of confounders. The latter option is supported by a study where the association between TMD and episodic TTH was corrected by gender, depression and somatization.[19] This study showed that the initial association between TMD and episodic TTH was lost after correction.[19] Further understanding of how TMD, headaches and shared risk factors are interrelated is still needed.

The Physical Therapeutic diagnostics and intervention process

Due to the musculoskeletal origin of TMD, physical therapists can use their expertise on musculoskeletal disorders in the care of patients with TMD. The aim of physical therapy as described by the Royal Dutch Society for Physical Therapy (KNGF) is: "*Physical therapists offer treatment aimed at recovery, optimization, and maintenance of movements. They use a clinical reasoning process to arrive at a specific physical therapy diagnosis, which is then used to design and implement a program of therapeutic and/or preventive interventions*".[30] Physical therapists work by using the Evidence Based Practice (EBP) principles, in which their expertise combined with knowledge from the literature and input from the patients are combined to optimize care.[31] Through the entire clinical reasoning process, the EBP principles are applied through the following steps: 1) identify gaps in knowledge of the physical therapist regarding the patient case or complaints; 2) formulate clinically relevant questions; 3) conduct an efficient literature search; 4) apply rules of evidence; and 5) apply the literature findings appropriately to the patient problem.[31] These steps can be applied throughout the entire clinical reasoning process, from formulating an initial hypothesis when the patient first comes to the clinic to apply treatment tailored to the patient.

To further support clinical reasoning, physical therapists use the International Classification of Functioning, Disability and Health (ICF; Figure 1.2).[32,33] By using the ICF framework, physical therapists can work from the history of the patient to the clinical tests needed to confirm or reject hypotheses and then use the findings for an optimal treatment plan. The ICF framework depicts outcomes of interactions between health conditions (diseases, disorders and injuries) and contextual factors. The contextual factors

are shown as environmental factors (e.g. social attitudes, legal and social structures) and internal personal factors (e.g. gender, age, coping styles).[32] There are three levels of human functioning within the ICF framework: functioning at the level of body or body part (body functions and structure), at the level of the whole person (activities) and the whole person in social context (participation).[32] After physical therapists have better insight of the interaction between different factors within the ICF framework, they formulate a hypothesis, which can be tested through additional diagnostics or therapy.

Femke indicated she suffers from moderate orofacial pain, rated 5/10, (*body function*) and it gets worse while she is chewing, rated 7/10 (*activities*). She is scared she might hurt something and make her complaints worse, so she is avoiding chewing tough foods (*personal factors*). Because of this, she cancelled two dinner parties in the last two months (*participation*).

Hypothesis 1: Femke is limited in chewing food due to orofacial pain combined with catastrophizing thoughts.

Hypothesis 2: Femke is restricted in participating in social activities due to pain in her jaw, which gets aggravated with chewing.

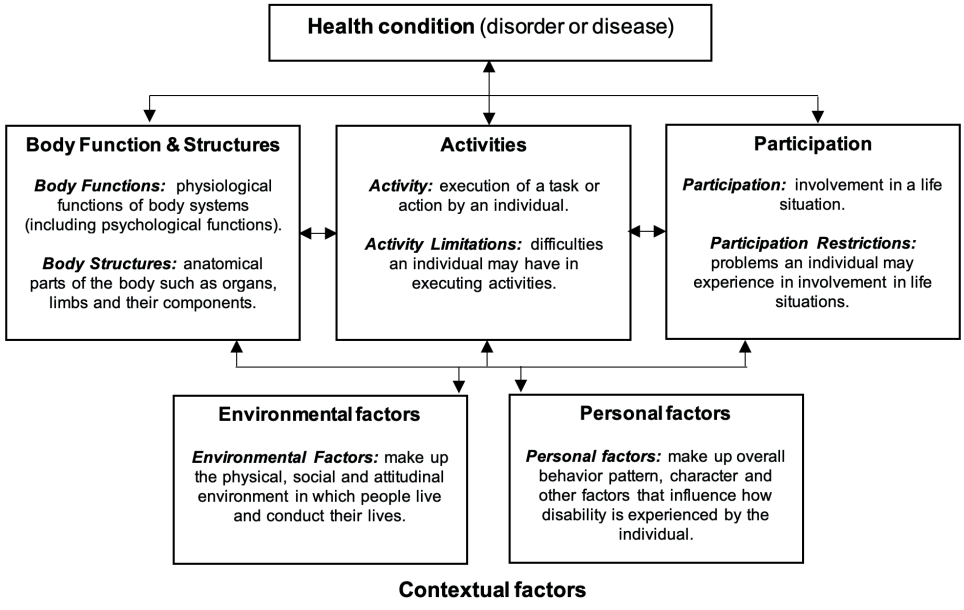

Figure 1.2: Overview of the International Classification of Functioning, Disability and Health.[32]

The role of the Physical Therapist in TMD and headache care

For the diagnosis of a TMD, the Diagnostic Criteria for TMD is the internationally accepted model.[4] The DC/TMD distinguishes between two components of a diagnosis: the physical diagnosis and the psychological components.[4] The physical diagnosis would be considered the 'health condition' within the ICF framework. The information needed for the physical diagnosis (e.g. pain location, mouth opening) as well as the psychological components are part of the other domains of the ICF. The ICHD-3 is used to diagnose headache disorders.[10] The diagnosis is also considered the 'health condition' when applying the ICF framework, and some information from the ICHD-3 criteria can be assigned to the other ICF domains (e.g. pain type and severity).

Physical therapists can use the health conditions as diagnosed by the dental or medical specialist as a starting point to ask further specific questions or perform additional tests to gather information based on the ICF domains. This way, not a medical diagnosis but a physical therapeutic diagnosis is formulated.[34] In the Netherlands, specialized orofacial physical therapists are educated to examine and treat patients with complaints in the head, neck and face area including TMD and headaches.[35] They are therefore especially equipped to work together with other care providers, such as dentists and neurologists, to provide the optimal care for patients with TMD and headaches. Within the diagnostic process of a physical therapist, they use general measurement instruments like the numeric pain rating scale, as well as specialized measurement instruments like the mandibular function questionnaire for TMD or cranio-cervical flexion test for head- and neck problems. These findings can be linked to problems in activities or participation problems, which result in hypotheses.

Based on findings from the diagnostic process and hypotheses formulated from the ICF framework, a physical therapeutic treatment plan can be developed. Patients with TMD are best treated in a multidisciplinary setting, where dentists specialized in orofacial pain and orofacial physical therapists work together.[36,37] Conservative, noninvasive treatment including physical therapeutic modalities and splint therapy are advised for patients with TMD.[36,38] A splint is a removable appliance that covers the occlusal and incisal surfaces of the teeth of the lower or upper jaw, with the aim of protecting the teeth during bruxing (e.g. clenching or grinding) and to reduce loading of the TMJ.[39] Within the field of physical therapy, interventions are often labelled as hands on or hands off, though when it comes to pain complaints it may be best to combine the two.[40] Often used hands-on therapies include massage therapy, myofascial release and manual therapies like mobilization and manipulation of joints.[38,41] Due to limited number of high-quality studies, there is a low to moderate level of evidence for these hands on therapies for patients with TMD.[38,41] This is similar for the different hands-off therapies like jaw exercises, cognitive behavioral therapy and biofeedback. Jaw exercises for mobilization, muscle strengthening, coordination

and posture are all considered to be effective for the management of painful TMDs.[42,43] Cognitive behavioral therapy and biofeedback are both considered effective interventions to decrease pain and depression in patients with orofacial pain, such as painful TMDs.[44]

Patients with headache should preferably also be treated in a multidisciplinary setting, where neurologists and physical therapists work together.[37,45] This is because each discipline has their own specialty and focus within the headache care process. Neurologists focus on diagnosing the patient and finding the right medication for the patient, whereas physical therapists often focus more on the prevention of headache episodes.[45] There are indications that hands-on treatment for migraine could be as effective as prophylactic (medical) treatment for the reduction of migraine frequency and pain intensity.[46] Also for TTH hands-on therapies can reduce pain intensity, but not duration or frequency of the headache.[47] Because most studies use different hands-on techniques, it is difficult to interpret the results and apply the findings in clinical practice.[46–48] For hands-off treatments, exercise seems to be effective for both TTH and migraine, but different types of exercises are required.[49] For TTH, strengthening exercises for the neck and shoulders are indicated as these muscles appear to be involved in the etiology of TTH,[11,49,50] whereas patients with migraine benefit from aerobic exercises which has an effect on more centrally regulated systems and the neurovascular system.[47,51,52] Furthermore, patient education and other behavioral therapies are also important and effective treatment strategies to decrease migraine headache frequency and disability.[53,54] Patients with TTH may also benefit from behavioral therapies and education.[55]

Even though there is evidence for both hands-on and hands-off therapies for patients with TMD and headaches, few studies have looked at the effectiveness of these therapies when patients have both TMD and headache. If these disorders are closely related and share the same risk factors, some of the therapies could affect both disorders simultaneously. More insight in the response to treatment by both disorders can increase the knowledge of the association between TMD and headache.

For Femke a hypothesis was formulated at the beginning of her physiotherapeutic treatment session. She received the hands-off therapies *counseling* by an orofacial physical therapist to increase her knowledge on her own complaints, followed by *exercises* she could perform at home to relax her masticatory muscles and herself. One of these home-exercises was hands-on massage therapy of the masseter muscle.

After successful treatment, Femke experiences no more jaw pain (rating 0/10). The previously described hypothesis should be tested: did Femke still experience difficulty in chewing and if so, was it because of her pain and/or catastrophizing thoughts? During evaluation, Femke stated she could eat everything (rating 0/10) and had just gone to

dinner with her friends. She also indicated that after her treatment, she experienced fewer headache complaints.

No a-priori hypotheses were described regarding the headache possibly being attributed to TMD, but afterwards her headache complaints seemed to be related to her TMD complaints. In order to improve the patient care of the next patient with comparable complaints, more information about the interrelation between the two disorders is needed. This way we can predict if the next person with TMD and headaches will also improve. after physical therapy.

Aim and outline of this dissertation

From the introduction it can be seen there is evidence for TMD and physical therapy on one hand, evidence for headache and physical therapy on the other hand, as well as evidence for a strong association between TMD and headaches, but there is information missing on the role of physical therapy in patients with both TMD and headaches. Therefore, the general aim of this dissertation is to establish evidence for the different steps in the physical therapeutic process for patients with TMD and headache. With the results of this dissertation we want to streamline the future physical therapeutic process for patients with TMD and headache. The aim of the dissertation relates to three main questions:

1. What do we know about the association between TMD and headaches and which factors influence this association?
2. What are the measurement instruments that can be used to identify headaches?
3. What effective intervention possibilities are present for patients with TMD and concomitant headache and how are these interventions perceived by this target group?

The three questions are the fundaments of the three parts of this dissertation. Each part consists of two or more chapters, described below.

Association between TMD and headache

Chapter 2 described the association between TMD and headache, specifically migraine and TTH. The confounding factors for this association are described, as well as the prevalence of headache attributed to TMD. **Chapter 3** looks more in detail at how the presence of psychosocial factors influence headache pain intensity and pain-related disability in TMD patients with migraine, TTH or headache attributed to TMD. In **chapter 4**, a cohort of TMD patients with headache is followed while receiving usual care for TMD. In this study, the development of TMD complaints is compared to that of the concomitant headache complaints. In this chapter a distinction is made between migraine, TTH and headache attributed to TMD.

Measurement instruments for headache

In **chapter 5**, the development and validation of a headache screening questionnaire to screen for the presence of migraine and TTH is described. In **chapter 6**, a systematic review and meta-analysis is presented that describes the diagnostic accuracy of measurement instruments for different headache types.

Physical Therapy for TMD and headache

In **chapter 7**, the effectiveness of physical therapeutic TMD-treatment on concomitant headache complaints in TMD patients is described in a systematic review. **Chapter 8** describes the perception of physical therapists and patients with TMD on TMD-treatment and the value of physical therapy in the health care process. Additionally, the barriers and facilitators for the use of e-Health during TMD-treatment are identified. In **chapter 9**, patients who have received physical therapy combined with e-Health for their TMD complaints were asked about their experiences with the e-Health, based on the facilitators and barriers described in chapter 8.

After answering the three main research questions, **chapter 10** will summarize the main findings of this dissertation and discuss strengths, limitations, clinical relevance and recommendations for future research. A summary in English and Dutch concludes this dissertation.

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PART I

PATIENT INFORMATION


2

Chapter 2

The association between headaches and temporomandibular disorders is confounded by bruxism and somatic complaints

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Objectives:
The objective of this observational study was to establish the possible presence of confounders on the association between temporomandibular disorders (TMD) and headaches in a patient population from a TMD and Orofacial Pain Clinic.

Methods:
Several subtypes of headaches were diagnosed: self-reported headache, (probable) migraine, (probable) tension-type headache (TTH), and secondary headache attributed to TMD. The presence of TMD was subdivided into two subtypes: painful TMD and function-related TMD. The associations between the subtypes of TMD and headaches were evaluated by single regression models. Subsequently, to study the influence of possible confounding factors on this association, the regression models were extended with age, gender, bruxism, stress, depression, and somatic complaints.

Results:
Of the included patients (n=203), 67.5% experienced headaches. In the subsample of patients with a painful TMD (n=58), the prevalence of self-reported headaches increased to 82.8%. The associations found between self-reported headache and 1) painful TMD and 2) function-related TMD, were confounded by the presence of somatic complaints. For probable migraine, both somatic complaints and bruxism confounded the initial association found with painful TMD.

Discussion:
The findings of this study imply there is a central working mechanism overlapping TMD and headache. Healthcare providers should not look at these disorders separately, but rather at the bigger picture to appreciate the complex nature of the diagnostic and therapeutic process.

Introduction

Headaches are common among the general population. Estimations for the lifetime prevalence of headache for adults range from 77%[1] to 91.3% [2], and for the point prevalence (current headache) from 47%[3] to 53%[1]. The most common headache is tension-type headache (TTH) (mean point prevalence 62.6%), followed by migraine (mean point prevalence 14.7%).[1] Headache is positively associated with several musculoskeletal disorders.[4] For example, most patients with TTH and/or migraine also suffer from neck pain (85.7%).[5] Temporomandibular disorders (TMDs) are also rather common (58%) in patients with these types of headaches.[6]

TMDs are conditions involving the structures of the temporomandibular joint, the masticatory muscles and associated structures.[7] Symptoms include orofacial pain, limited mandibular movements, and joint sounds.[7] Of the Dutch population, 3.1% seek medical attention for their TMD.[8] In line with the aforementioned association between headache and TMD, a high point-prevalence of headache in TMD patients is also reported (78% - 85.5%).[9–11] Interestingly, in these studies, migraine was more prevalent than TTH.[9–11] Within a population of patients with TMD, another type of headache that could be expected to be common is the so-called 'secondary headache attributed to TMD'.[12,13] This headache typically originates simultaneously with the TMD, is localized in the temporal region, and may be provoked or initiated with movement of the temporomandibular system. However, to our knowledge, prevalence data for this type of headache have not yet been published.

A few studies reported a significant association between TMD and headaches such as self-reported headache, chronic daily headache, migraine and TTH. [9–11,14] This association, however, is not well understood. It is plausible that there are several factors influencing the association between TMD and headaches. For example, it is known that both TMD and headaches are more common in women,[15,16] within the age range of 20 – 50 years,[1,17] and are associated with bruxism[10,14,18] and psychological variables such as stress, depression, and other somatic complaints.[19,20] Given this knowledge, it could be hypothesized that the previously reported associations between headaches and TMD are (in part) the result of shared risk factors. Until now, it is unknown which variables are possibly confounding the association between headaches and TMD. Understanding the role of possible confounders could improve current knowledge of the etiology of these complaints and provide new insights to improve tailored treatment strategies.

Therefore, the aim of this study was to assess the presence of possible confounders on the association between TMD and different types of headache.

Materials and Methods

Study design and participants

The study design is a retrospective medical file study from patients referred to the Clinic for TMD and Orofacial Pain of the Academic Centre for Dentistry Amsterdam (ACTA). The referred population consists of patients with orofacial pain complaints, function-related complaints, and restorative dentistry. All adult patients (>18 years) who came to the clinic in the period from January 2013 until September 2013, with complete patient file data on the presence of TMD and headache, were included. As this is a retrospective medical file study, the Medical Research Involving Human Subjects Act (WMO) does not apply.

Measurement instruments

Preceding the first visit to ACTA, patients returned a standardized questionnaire, which included the necessary self-reported information for the recognition of RDC-based TMD and the various headaches, supplemented with questions about bruxism, stress, depression and somatic complaints (for details, see below).

At the intake visit, all patients underwent a standardized physical examination, according to the description of the Research Diagnostic Criteria (RDC) for TMD (for details, see below). The physical examination was performed by dentists who performed the clinical tests according to the protocol as described in the RDC/TMD.[21] These dentists were trained by dentists, who are calibrated with the RDC/TMD protocol.[22]

TMD diagnosis

Based on the physical examination and the information derived from the questionnaire, the RDC/TMD diagnoses were determined. The RDC/TMD consist of eight sub-diagnoses (eg. myofascial pain, arthralgia and disc dislocation).[21] For this study, the subtypes 'myofascial pain with and without limited opening' (Ia, Ib), 'arthralgia' (IIIa) and 'osteoarthritis' (IIIb) were aggregated to classify patients as suffering from a painful TMD, while the subtypes 'disc displacement' (IIa, IIb, IIc) and 'osteoarthrosis' (IIIc) were aggregated to classify patients as suffering from a function-related TMD. In case both a pain and a function-related diagnosis were present, the patient was classified positive for both diagnoses.

The questionnaire included questions from the RDC/TMD, such as "*Have you had pain in the face, jaw, temple, in front of the ear or in the ear in the past month?*" and "*Have you ever had your jaw lock or catch so that it won't open all the way?*". Based on the outcomes of these questions and a clinical examination, various subtypes of TMD can be classified. Clinical examination included measuring opening of the mouth, palpation of the muscles and joints of the masticatory system and registering any joint sounds, according to the RDC/TMD examination protocol.[21]

Headache diagnosis

Patients were asked if they had experienced headaches in the last year (self-reported headache). To screen for migraine and TTH, the so-called Headache Screening Questionnaire – Dutch Version (HSQ-DV) was developed (for the English version, see appendix 5.1). This questionnaire consists of 11 questions which cover the criteria needed for an International Classification of Headache Disorder 3rd edition (ICHD-3) diagnosis of migraine or TTH.[12] Patients were classified with migraine when they fulfilled the criteria for migraine without aura, as described in the ICHD-3.[12] Patients were classified with TTH when they fulfilled the criteria for either infrequent, frequent, or chronic TTH, as described in the ICHD-3.[12] If all but one criterion for migraine or TTH were met, according to the ICHD-3 protocol, the headache was classified as a 'probable' headache.[12] Within this study, the group with a probable migraine diagnosis are those who fulfill ≥3/4 migraine criteria; in other words the probable migraine group includes the patients who fulfill all migraine criteria as well. For TTH, the same principles were applied to classify TTH as being probable (≥3/4 TTH criteria) or fulfilling all (4/4) criteria. When fewer than 3 criteria were met, they could not be classified as having that specific headache type.

Patients were diagnosed with a secondary headache attributed to TMD when they fulfilled the criteria described by Schiffman et al.[13], including a TMD-pain diagnosis based on the RDC/TMD. The criteria for secondary headache attributed to TMD have been proven to be valid with a sensitivity of 89% and a specificity of 87%.[13]

Possible confounding variables

In case of an association between TMD and headache, the influence of possible confounders on this association was analyzed. Possible confounders of the association between headache and TMD were determined based on available literature. These variables are: age (in years), gender (male vs. female)[15,16], bruxism,[10,14] depression, stress, and somatic complaints.[19,20]. For all variables, it was hypothesized that they could influence the initial association between TMD and headache.

Bruxism is defined as "*a repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible*".[23] This was measured with the self-reported oral parafunction questionnaire, using the subscale bruxism.[24] This subscale consisted of four questions about bruxism, where the frequency at which the patient performs bruxism was asked for both wake and sleep bruxism. The items of the questionnaire were rated on a 5-point scale, ranging from never (0) to always (5). The total score for the bruxism questions was used for analysis, where a higher score meant a higher frequency of bruxism.

Stress was measured with a series of seven questions, which address the amount of stress experienced by the patient.[25] The questions can all be answered on a 5-point scale ranging from none (0) to very much (4). The total stress score is the mean of these seven items and was used for analysis, where a higher score meant a higher amount of stress experienced.[25]

Depression and somatic complaints were measured with subscales of the Dutch version of the Symptom Checklist – 90 (SCL-90).[26] This is a modified version of the original English-language instrument and includes 90 items, including depression (16 items) and somatic complaints (12 items). Each item is rated on a 5-point scale, measuring distress in a range from 1 (not at all) to 5 (very much). The Dutch version of the SCL-90 has been shown to be reliable (internal consistency of dimensions = .77-.97; test-retest reliability = .68-.91).[27] Several studies concluded that there is high construct validity.[27–29] For all SCL-90 dimensions, higher scores relate to higher levels of psychosocial distress.[27]

Statistical analysis

Descriptive statistics were used to characterize the participants. For all variables, the number of missing values is shown. In case of more than 5% missing data for confounders, multiple imputation was used to retain a high number of cases which could be used for logistic regression analysis.[30] The outcomes were stratified by painful TMD, function-related TMD, and headache subtypes. For age, headache pain and possible confounders' scores (bruxism, stress, depression, somatic complaints), the mean and standard deviation are given. For gender, TMD group and headache subtype, the number and percentages are given.

Single logistic regression analyses were used to evaluate the associations between TMD (painful TMD: yes vs. no, or function-related TMD: yes vs. no) and headache (self-reported headache, (probable) migraine, (probable) TTH: yes vs. no). The regression analyses with TMD pain as the dependent variable were performed irrespective of the patients' function-related TMD diagnosis, and vice versa. As having a painful TMD diagnosis is a necessary requirement for the diagnosis of a secondary headache attributed to TMD, this association was not included in the logistic regression analyses. In other words, 10 single regression analyzes were performed in order to study the association between TMD and headache. In case of a significant association between TMD and headache (model 1), a multiple logistic regression model was built, which included the possible confounders using a forward stepwise approach. With this approach, it was possible to analyze the influence of each individual possible confounder on the association between headache and TMD. Therefore, the following models were evaluated:

Model 1 – single regression analysis between headache and TMD;
Model 2 – multiple regression analysis including model 1 + age;
Model 3 – multiple regression analyses including model 2 + gender;

Model 4 – multiple regression analysis including model 3 + bruxism;
Model 5 - multiple regression analysis including model 4 + stress;
Model 6 - multiple regression analysis including model 5 + depression;
Model 7 - multiple regression analysis including model 6 + somatic complaints.

Confounding of the association between TMD and headache was considered present when the regression coefficient of TMD changed with more than 10% as compared to its value in the previous model (without that confounding variable).[31] All variables were put into a correlation matrix to check if the confounding variable in the multiple regression analysis indeed has a correlation with both headache and TMD. Furthermore, to check for possible effect modification, interactions between TMD and each possible confounder were checked. In case of a significant interaction effect, this interaction term was retained in the model. Only significant interactions will be reported. Also, to check for multicollinearity, all possible confounders were entered in a correlation matrix. In case the correlation coefficient between 2 confounders exceeds 0.7, multicollinearity is regarded present, which may disrupt the regressionmodel.[32] In that case, only 1 of the 2 confounders will be chosen to enter the regression model.

Analysis of the data was performed using the *Statistical Package for the Social Sciences* (IBM SPSS) version 22.0 (SPSS Corp, Chicago, Ill, USA). Findings were considered significant when the p-value < 0.05.

Results

Description of study population

In the study period, a total of 251 eligible patients visited ACTA, of whom 16 did not provide consent for their data to be included in scientific research projects and for 30 patients, we could not provide a RDC/TMD diagnosis due to missing data. Two patients failed to report their headache status. These 48 patients were excluded from this study. Of the 203 included patients, most were female (73.4%). Function-related TMD was present in 91 patients (44.8%), painful TMD in 58 patients (28.6%) and 26 patients (12.8%) had both a function-related as a painful TMD.

Self-reported headache was present in 137 patients, of whom 22 patients had migraine, 44 patients fulfilled the criteria for TTH, and 11 patients were classified with a secondary headache attributed to TMD (Table 2.1). Two patients suffered from both a migraine and a secondary headache attributed to TMD diagnosis, and three patients shared a TTH and a secondary headache attributed to TMD diagnosis (Figure 2.1a). When for migraine and TTH the criteria for a probable headache were applied, the number of patients with migraine increased from 22 to 48 with a probable migraine, and the number of patients

with TTH increased from 44 to 78 with a probable TTH (Figure 2.1b). Patients with a secondary headache attributed to TMD diagnosis had an overlap with probable migraine (n=5) and probable TTH (n=6).

Within the painful TMD group, TTH was most prevalent (n= 13; 22.0%), followed by secondary headache attributed to TMD (n= 11; 18.6%), and then by migraine (n= 10; 17.2%). Table 2.2 provides a summary of the study population characteristics by headache subtype. correlation matrix of the possible confounders showed all correlation coefficients to be lower than 0.6 and therefore multicollinearity is not distorting the regression models.[32]

Table 2.1: Patients characteristics in the temporomandibular disorder (TMD) groups.

	Total population (N=203)	Painful TMD		Function-related TMD	
		Yes (n=58)	*No (n=145)*	*Yes (n=91)*	*No (n=112)*
Age, years					
Mean (SD)	43.1 (14.1)	41.2 (15.0)	44.0 (13.7)	41.8 (14.5)	44.1 (13.8)
Min, max	18, 82	18, 71	20, 82	20, 78	18, 82
Gender, n(%)					
Men	54 (26.6)	10 (17.2)	44 (30.3)	22 (24.2)	32 (28.6)
Women	149 (73.4)	48 (82.8)	101 (69.7)	69 (75.8)	80 (71.4)
Headache, n(%)					
Yes	137 (67.5)	48 (82.8)	89 (61.4)	54 (59.3)	83 (74.1)
No	66 (32.5)	10 (17.2)	56 (38.6)	37 (40.7)	29 (25.9)
Migraine, n(%)					
Yes	22 (10.8)	10 (17.2)	12 (8.4)	8 (8.9)	14 (12.6)
No	179 (88.2)	48 (82.8)	131 (91.6)	82 (91.1)	97 (87.4)
Missing	2	0	2	1	1
Probable Migraine, n(%)					
Yes	48 (23.6)	20 (34.5)	28 (19.6)	19 (21.1)	29 (26.1)
No	153 (75.4)	38 (6535)	115 (80.4)	71 (78.9)	82 (73.9)
Missing	2	0	2	1	1
TTH, n(%)					
Yes	44 (21.7)	13 (22.4)	31 (21.7)	19 (21.1)	25 (22.5)
No	157 (77.3)	45 (77.6)	112 (78.3)	71 (78.9)	86 (77.5)
Missing	2	0	2	1	1
Probably TTH, n(%)					
Yes	78 (38.4)	27 (46.6)	51 (35.7)	35 (38.9)	43 (38.7)
No	123 (60.6)	31 (53.4)	92 (63.3)	55 (61.1)	68 (61.3)
Missing	2	0	2	1	1
Secondary headache, n(%)					
Yes	11 (5.4)	11 (22.9)	0 (0.0)	5 (5.7)	6 (5.7)
No	183 (90.1)	37 (77.1)	145 (100.0)	82 (94.3)	100 (94.3)
Missing	10	10	0	4	6
Bruxism scores					
Mean (SD)	3.7 (3.5)	4.9 (4.0)	3.2 (3.1)	3.5 (3.2)	3.8 (3.7)
Min, max	0, 16	0, 16	0, 14	0, 16	0, 15
Missing	2	0	2	0	2
Stress scores					
Mean (SD)	5.4 (4.1)	5.5 (4.6)	5.3 (3.9)	5.2 (4.5)	5.6 (3.7)
Min, Max	0, 24	0, 24	0, 18	0, 24	0, 19
Missing	10	1	9	3	7

Table 2.1: Continued.

	Total population (N=203)	Painful TMD		Function-related TMD	
		Yes (n=58)	*No (n=145)*	*Yes (n=91)*	*No (n=112)*
Depression					
Mean (SD)	22.8 (7.2)	24.1 (7.7)	22.2 (7.0)	22.0 (7.1)	23.3 (7.3)
Min, max	16, 48	16, 48	16, 47	16, 48	16, 47
Missing	10	1	9	3	7
Somatic complaints					
Mean (SD)	19.0 (6.3)	21.7 (6.3)	17.8 (5.9)	18.8 (6.8)	19.1 (5.9)
Min, max	12, 43	13, 38	12, 43	12, 39	12, 43
Missing	10	1	9	3	7

n: number of participants; SD: Standard Deviation; TTH: Tension-Type Headache. Patients may have both a Painful TMD and a function-related TMD diagnosis.

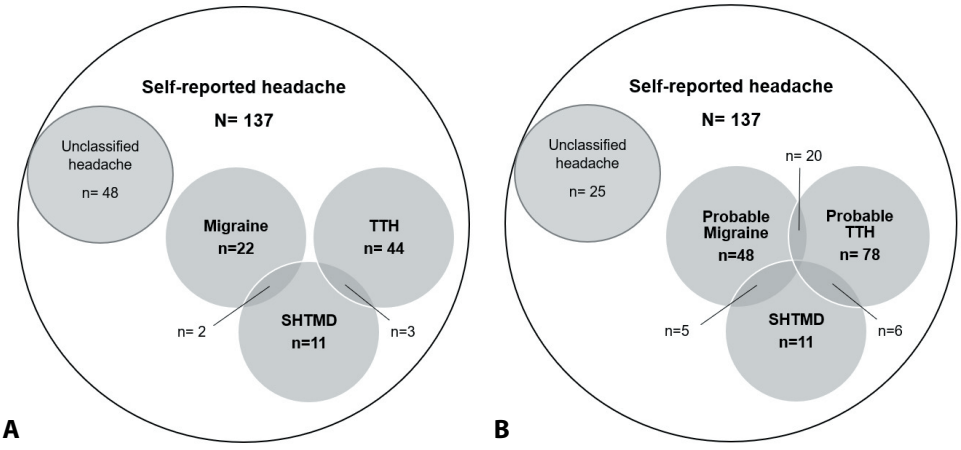

Figure 2.1: Distribution of headache diagnoses based on 4/4 (a) and ≥3/4 (b) criteria on the HSQ. HSQ: Headache Screening Questionnaire; TTH: Tension-Type Headache; SHTMD: Secondary Headache attributed to Temporomandibular Disorders; n: number of patients.

Association between painful TMD and headache

The results from the single regression analyses (Table 2.3) showed significant associations between painful TMD and self-reported headache (OR 3.0; 95%CI 1.4-6.4), and between painful TMD and probable migraine (OR 2.2; 95%CI 1.1-4.3). No other significant associations were found.

The multiple regression analysis of self-reported headache and painful TMD showed a stable association, even after a stepwise inclusion of the possible confounding variables. The only variable that appears to be a confounder is 'somatic complaints': adding this variable does not only decrease the regression coefficient (b= 1.075 → b= 0.693; 36% difference) but also neutralizes the initial association between self-reported headache and painful TMD (OR 2.0; 95%CI 0.8-4.9) (Table 2.3).

Table 2.2: Patients characteristics by headache diagnosis (N=203).

Self-reported Headache	Age; Years	Gender, n(%)		Painful TMD, n(%)		Headache; NPRS	Bruxism	Stress	Depression	Somatic Complaints
		Male	Female	Yes	No	*Missing: 2*	*Missing: 2*	*Missing: 10*	*Missing: 10*	*Missing: 10*
No (n=66)	43.7 (15.2) 20, 82	24 (36.4)	42 (63.6)	10 (15.2)	56 (84.8)	n/a	2.9 (3.1) 0, 14	4.2 (3.7) 0, 18	21.9 (7.4) 16, 44	15.3 (4.4) 12, 37
Yes (n=137)	42.9 (13.7) 18, 78	30 (21.9)	107(78.1)	48 (35.0)	89 (65.0)	6.2 (2.3) 1, 10	4.1 (3.6) 0, 16	5.9 (4.2) 0, 24	23.1 (7.2) 16, 48	20.6 (6.3) 12, 43
Migraine (n=22)	40.8 (12.3) 24, 71	2 (9.1)	20 (90.9)	10 (45.5)	12 (54.5)	8.0 (1.5) 5, 10	6.8 (4.4) 0, 16	5.9 (3.1) 0, 11	25.1 (9.0) 16, 48	25.1 (9.0) 16, 48
Probable Migraine (n=48)	41.1 (13.8) 20, 71	10 (20.8)	38 (79.2)	20 (41.7)	28 (58.3)	7.3 (2.1) 2, 10	5.3 (4.2) 0, 16	5.9 (3.8) 0, 19	23.7 (7.8) 16, 48	22.4 (7.0) 12, 43
TTH (n=44)	46.0 (13.9) 21, 78	13 (29.5)	31 (70.5)	12 (29.5)	31 (70.5)	5.1 (2.2) 1, 9	2.8 (2.6) 0, 9	5.7 (4.3) 0, 24	21.7 (5.7) 16, 45	18.5 (5.0) 12, 36
Probable TTH (n=78)	45.3 (14.3) 20, 78	20 (25.6)	58 (74.4)	27 (34.6)	51 (65.4)	5.7 (2.4) 1, 10	3.1 (2.8) 0, 13	5.6 (4.3) 0, 24	22.2 (6.6) 16, 46	19.4 (5.8) 12, 36
SHTMD (n=11)	36.4 (14.0) 18, 57	1 (9.1)	10 (90.9)	11 (100)	0 (0.0)	6.9 (2.3) 3, 10	7.2 (5.2) 0, 16	5.3 (2.1) 2, 9	25.4 (8.1) 17, 41	23.2 (4.1) 15, 30

Mean, standard deviations, minimum and maximum are given in all variables except gender and painful TMD. TTH: Tension-Type Headache; SHTMD: Secondary headache attributed to TMD. NPRS: numeric pain rating scale. Patients may have multiple headache diagnoses.

Table 2.3: Regression models for associations between different types of headaches and TMD.

	Model 1 Single regression		**Model 2** Model 1 adjusted for age		**Model 3** Model 2 adjusted for gender		**Model 4** Model 3 adjusted for bruxism		**Model 5** Model 4 adjusted for stress		**Model 6** Model 5 adjusted for depression		**Model 7** Model 6 adjusted for somatic complaints	
	b	OR	b	OR	b	OR	b	OR	b	OR	b	OR	b	OR
Painful TMD:														
Self-reported Headache (n = 203)	1.105	3.0* (1.4-6.5)	1.102	3.0* (1.4-6.4)	1.034	2.8* (1.3-6.1)	0.946	2.6* (1.6-4.0)	1.035	2.8* (1.3-6.3)	1.086	3.0* (1.3-6.6)	**0.616**	1.8 (0.7-4.6)
Probable Migraine (n= 201)	0.771	2.2* (1.1-4.3)	0.742	2.1* (1.1-4.2)	0.706	2.0* (1.0-4.0)	**0.505**	1.7 (0.8-3.4)	0.510	1.7 (0.8-3.4)	0.535	1.7 (0.8-3.5)	**0.264**	1.3 (0.6-2.8)
Function-related TMD:														
Self-reported Headache (n = 203)	-0.673	0.5* (0.3-0.9)	-0.688	0.5* (0.3-0.9)	-0.739	0.5* (0.3-0.9)	-0.711	0.5* (0.3-0.9)	-0.683	0.5* (0.3-0.9)	-0.696	0.5* (0.3-0.9)	**-0.877**	0.4* (0.2-0.9)

Imputated data used for analysis. n: number of participants in analysis. b: regression coefficient; OR: Odds Ratio; CI: Confidence Interval. Bold regression coefficients (b) indicate the newest variable in the model is a confounding factor. * *p*-value <.05.

Further confirmation of somatic complaints being a confounder of this association was found in the correlation matrix, which showed a correlation between somatic complaints and self-reported headache (r =.47; p=.000) and between somatic complaints and painful TMD (r=.31; p=.000).

The multiple regression analysis of probable migraine and painful TMD shows that besides somatic complaints, bruxism is a confounding variable as well (b=0.706 → b=0.502; 29% difference). The significant association between probable migraine and painful TMD from the single regression analysis is lost after adding these confounders (OR 1.3; 95%CI 0.6-2.8). The correlation matrix showed significant correlations between all these variables (range r=.16 -.32; p<.05), confirming bruxism to be a confounder of the association between probable migraine and TMD.

Association of function-related TMD and headache

The results from the single regression analyses (Table 2.3) showed significant, negative association between functional-related TMD and self-reported headache (OR 0.5; 95%CI 0.3-0.9). For the other headaches (migraine, probable migraine, TTH, and probable TTH), no associations with function-related TMD were found (p-values: 0.40 – 0.98).

The multiple regression analysis showed that the association between self-reported headache and function-related TMD was significant through all models, but is confounded by somatic complaints (b=-.690 → b= -.807; 17% difference). Further confirmation of somatic complaints being a confounder of this association was found in the correlation matrix, which shows a correlation between somatic complaints and self-reported headache and between somatic complaints and function-related TMD (r=.16; p=.025).

Discussion

This study found that the association between headaches and TMD is confounded by bruxism and somatic complaints. In line with earlier reports on the prevalence of TMD complaints, female gender was predominant in this study population.[33,34]

TMD and self-reported headache

A positive association between the presence of a painful TMD and self-reported headache was confirmed, however, this association ceased to exist when 'somatic complaints' was added to the regression model. In other words, both self-reported headache and painful TMD are associated with having (multiple) somatic complaints, and the presence of such general complaints is largely responsible for the reported association between TMD and self-reported headache.

Surprisingly, a negative association between function-related TMD and self-reported headache was found. Although the association was weak, it suggests that having a function-related TMD, like a disc displacement with reduction, decreases the odds of experiencing headache. Also here, somatic complaints were found to be a confounder of this association, although even after correction for somatic complaints the negative association between function-related TMD and self-reported headache remained significant. At this moment, there is no explanation for this finding. Replication of these findings is however needed before suggestions for possible etiology are further explored.

TMD and TTH

TTH was the most prevalent headache in this study. However, no associations were found between (probable) TTH and TMDs (either pain or functional disturbances). This contrasts the results of several earlier studies which reported a positive association between TTH and painful TMD.[9,10] Also in a study from Goncalves et al.[11], initially an association between TTH and painful TMD was reported. However, this association disappeared when the association was corrected for other variables, including depression and somatization.[11] Taken altogether, at this moment there is only weak evidence for an association between TMD and TTH. This association is also not corroborated by the findings from the present paper.

TMD and migraine

There was no association found between the presence of migraine and TMD (either pain or function-related complaints). When analyzing patients with probable migraine, initially an association with the presence of a painful TMD was found. Both probable migraine and painful TMD are, however, associated with bruxism, which confounded the association between probable migraine and painful TMD. Besides bruxism, the presence of other somatic complaints also confounds the association between probable migraine and painful TMD.

Other studies confirmed this three-way association between migraine, painful TMD, and bruxism.[10,14] For example, the risk of having (chronic) migraine in patients with painful TMD increased when they also reported sleep bruxism.[10] These interrelationships may be explained by sensitization. One of the theories of migraine pathology is that the pain system is dysregulated.[35] The presence of local overloading and nociceptive input in the trigeminal system could be triggered by parafunctions, which are linked to both migraine and TMD.[10,14,35–38]. It is known that long-term nociceptive input can lead to central sensitization (CS), which also plays an important role in the pathology of both TMD and migraine.[39–41] Patients with CS often experience widespread pain and other somatic complaints, which consequently increases the risk of TMD and migraine.[40] Therefore, it is no surprise that 'somatic complaints' was also a confounding variable in the association

between probable migraine and painful TMD. New insights state that chronic pain may itself be a disease, and the location on the body where the pain arises may not be as relevant as an individual's pain sensitivity.[42] Although we know there is an association between several pain disorders and CS,[41,42] we do not know if having CS makes one more susceptible to develop other pain disorders.

TMD and secondary headache attributed to TMD

This study showed that in one in five patients (18.6%) with painful TMD and headache, a secondary headache could be attributed to TMD. There are only a few articles about secondary headaches attributed to a TMD. In a study where the diagnostic accuracy of the diagnostic criteria for secondary headache attributed to TMD was tested within a population of headache patients with TMD, it was reported that almost half (45%) of the patients had a secondary headache attributed to the TMD.[13] In the present study, where the prevalence of secondary headache attributed to TMD was determined in all TMD patients (not only those with a headache), the estimated prevalence was 18.6%. If about 10% of the population experiences TMD (muscle) pain,[33] this finding would indicate a prevalence of 2% of secondary headache attributed to a TMD in the general population. Given the scarce literature on this type of headache, it is likely that this headache is not being diagnosed and treated as often as it should. These patients need to be seen by specialized health care providers (specialized dentists and/or specialized physical therapists) for proper diagnostics and treatment. It is possible that secondary headache attributed to TMD is currently diagnosed as TTH, as they share the same characteristics in location and intensity.[12,13] This is shown in the current study, where a 25-50% overlap between patients with both (probable) TTH and secondary headache attributed to TMD was present. This indicates that there is a possible overestimation of TTH in the literature and in the clinical practice.

Limitations

A limitation of this study was the retrospective design and missing data which caused us to exclude 30 patients from the study. As not all patients entered the clinic with orofacial pain symptoms, but also with, for example, questions related to tooth grinding, not all patients received a full TMD examination as described in the RDC/TMD protocol. This explains a part of the missing data. Additionally, the question of whether or not the clinical examination provoked or initiated the headache is crucial for the diagnosis of secondary headache attributed to TMD, and this question was not always asked by the dentist. Since this question was only applicable to patients with headache, only patients with headache are omitted from analysis. This may have led to an underestimation of the prevalence of secondary headache attributed to TMD.

All headaches except the secondary headache attributed to TMD were diagnosed with the ICHD-3. At the time of including patients for this study, the diagnostic criteria for secondary headache attributed to TMD were only validated by Schiffman et al.[13] Furthermore, it is important to note that patients who do not fulfill all criteria for the headaches included in this study, their headache complaints may origin from another source, such as medication overuse headache.[43,44] Therefore, it is advisable that all patients who are positively screened for headache are referred to a headache specialist for further diagnostics and possible treatment.

Even though polysomnography is considered the gold standard for assessing the presence of bruxism, this procedure is costly and time-consuming.[24] Therefore, for large-scale studies usually a questionnaire is used. Within this study, no differentiation was made between sleep- and wake-time bruxism. That is, because within this study the time the overload takes place (sleep- or wake-time) was regarded less important than the overload being present.

Clinical implications

The present results have several implications for clinical practice. In patients with (probable) migraine and painful TMD, who also engage in bruxism, treating the bruxism might be favorable to both the headache and the TMD. This is in line with the suggestion of Woolf[41] that treatment should not focus merely on local problems. This was illustrated by a study of Goncalves et al.[45] in patients with both TMD and migraine, which showed that the efficacy of a treatment that targeted only one of the disorders was comparable to that of a placebo treatment. Only when both disorders were treated at the same time, treatment outcome was favorable as compared to treatment targeting only one disorder. In line with this finding, and the fact that CS plays an important role in patients with multiple somatic complaints,[46] it is proposed that health care providers will look for the presence of CS in their patients with headaches and TMD. For this purpose, pain pressure thresholds (PPT) can be measured as patients with CS have a generalized decrease in their PPT.[47]

In conclusion, the associations between self-reported headache and TMD (both painful and function-related) are confounded by somatic complaints. The association between probable migraine and painful TMD is confounded by bruxism and somatic complaints.

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3

Chapter 3

Psychosocial factors that are associated with pain outcomes in patients with painful temporomandibular disorders and headaches

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Psychosocial factors that are associated with pain outcomes in patients with painful temporomandibular disorders and headaches.

Abstract

The objective was to explore the influence of psychosocial factors on pain intensity and pain-related disability in patients with painful temporomandibular disorders (TMD) and migraine, tension-type headache (TTH), or headache attributed to TMD. A retrospective study was conducted at an orofacial pain and dysfunction clinic. Inclusion criteria were painful TMD, with either migraine, TTH, or headache attributed to TMD. Outcome measures were headache pain intensity and pain-related disability. Psychosocial factors were anxiety, somatization, depression and optimism. Linear regressions were performed to assess the influence of psychosocial variables on pain intensity and on pain-related disability, stratified per headache type. The regression models were corrected for bruxism and the presence of multiple headache types. A total of 323 patients (61% female; mean age 42.9 ± 14.4) were included. Pain intensity was weakly associated with optimism in TMD-pain patients with migraine (R^2= 0.143), and with somatization in TMD-pain patients with TTH (R^2=0.117). Headache pain intensity was associated with all psychosocial variables in TMD-pain patients with headache attributed to TMD, with anxiety showing the strongest relation (R^2=0.222). Pain-related disability was associated with depression in TMD-pain patients with migraine (R^2= 0.103) or TTH (R^2=0.195), and with somatization in patients with headache attributed to TMD (R^2=0.162).

Introduction

Temporomandibular disorders (TMD) are complaints related to muscular and joint problems in the masticatory system, which occur in 5 to 12% of the general population.[1–4] Patients with a painful TMD according to the Diagnostic Criteria for TMD (DC/TMD)[2] experience headaches more frequently than the general population, with a prevalence of 76% to 82%[5,6] compared to 50%, respectively.[7] Most common headache types in patients with a painful TMD are the primary headaches 'migraine' and 'tension-type headache' (TTH)[5,6,8,9] One in five patients with a painful TMD and headache experience a headache attributed to TMD, which is considered a secondary headache.[2,6,9,10]

A recent review has emphasized common neuronal pathways and central sensitization processes as being mainly responsible for the association between TMD and headache.[11] Another hypothesis for this co-morbidity is the presence of shared risk factors, such as 'bruxism'. This is a repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible.[12] Bruxism is associated with TMD, migraine, and headache attributed to TMD, though it is not correlated with TTH.[5,6] Also psychosocial factors, like 'depression', 'anxiety', and 'somatic complaints', are reported as risk factors for painful TMD as well as headache.[13–15] These psychosocial factors are reported to influence the perceived pain intensity and pain-related disability in patients with various types of pain.[16–18] Individuals with TMD pain, with and without headache, who also experience depression or anxiety, usually report a higher pain intensity and more pain-related disability than those who do not experience depression or anxiety.[19,20] A similar association between psychosocial factors and pain intensity is found in studies focusing on patients with headache, and in studies focusing on subjects who report bruxism.[21–23]

Although previous research demonstrated that pain intensity and pain-related disability in individuals with a painful TMD or headache are associated with psychosocial factors, and that bruxism may influence these associations, no study has yet been performed in which all three conditions are taken into account. We hypothesize that psychosocial factors are differently associated with the various types of headache within the TMD population. To study these association, correction for bruxism is necessary to account for a possible confounding effect.[6] Therefore, the objective of this study was to assess the association between psychosocial factors (in terms of anxiety, somatization, depression, and optimism) and pain (in terms of headache pain intensity and pain-related disability), in patients with a painful TMD and one of the following headache types: migraine, TTH, or headache attributed to TMD, corrected for the influence of bruxism.

Methods

This manuscript is written according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[24]

Study design and patients

This retrospective medical file study was conducted at the specialized clinic for orofacial pain and dysfunction (OPD) of the Academic Centre for Dentistry Amsterdam (ACTA Reasons for referral to this clinic are orofacial pain complaints (including TMD and headache), bruxism, tooth wear, and/or obstructive sleep apnea. Prior to the first visit to the clinic, all patients complete a digital questionnaire, including questions on TMD complaints, headache, pain-intensity, pain-related disability, bruxism, and psychosocial factors. During the intake, a standardized examination is performed by a trained dentist following the DC/TMD protocol.[2] For this study, medical records of 2,493 patients, who visited the clinic between January 2014 and January 2019, were reviewed by one of the researchers (CT). All data in these files was retrieved as part of the usual care diagnostic procedure of the OPD clinic. The researcher checked whether the patient fulfilled the in- and exclusion criteria. Inclusion criteria were: 1) age of at least 18 years, 2) a TMD-pain diagnosis according to the criteria of the DC/TMD (i.e., myalgia or arthralgia), and 3) one of the following headache types: migraine, TTH, or headache attributed to TMD. In case of missing data relevant for this study, patients were excluded. The information from the included patients was anonymized and transferred into a separate data file for the analyses of the current study.

This study was considered by the medical ethics committee of the ACTA not to fall under the provisions of the Medical Research Involving Human Subjects Act, and to comply with the ethical research code of conduct of the ACTA (reference number 2018038). Data was collected only from patients who had given consent to the anonymous use of their information for research purposes, as part of the initial intake questionnaire.

Headache diagnosis

To screen for the presence of migraine or TTH, the Headache Screening Questionnaire Dutch Version (HSQ-DV) was used. The HSQ-DV is a validated self-report questionnaire consisting of 11 questions, and based on the criteria of the ICHD-3.[25] The HSQ provides two scores: 0-8 points for migraine (equal to 0 – 100% of the ICHD-3 criteria), and 0-8 points for TTH (equal to 0 – 100% of the ICHD-3 criteria).[25] Based on these scores, the outcome of the questionnaire are: no migraine or TTH, probable migraine or TTH (≥6 points, which equals ≥75% of the criteria of the ICHD-3), or definite migraine or TTH (8 points, which equals all of the criteria of the ICHD-3). In the current study, the cut-off of ≥6 points was applied to classify the presence of headache. In other words, all who fulfilled at least 75% of the ICHD-3 criteria for migraine or TTH were classified as patients with a probable migraine

or TTH, respectively. Double classifications were allowed. For probable migraine, the sensitivity and specificity are 0.89 and 0.54, respectively.[25] For the recognition of probable TTH the sensitivity is 0.92 and the specificity 0.48.[25]No differentiation was made between episodic or chronic headaches diagnoses, all were included under the same classification.

Headache attributed to TMD was classified by means of the DC/TMD, which is a validated classification system to diagnose the various subtypes of TMD.[2,26] The DC/TMD criteria for headache attributed to TMD have a sensitivity of 0.89 and specificity of 0.87.[26]

When a patient fulfilled the criteria for more than one headache type (e.g., both migraine and headache attributed to TMD), the recommendations of the International Headache Society were followed. The subsequent hierarchy in classification was applied to assign patients to one of the headache groups: headache attributed to TMD, migraine, TTH, probable migraine and then probable TTH.[9] For example, if a patient scored positive on 100% of the criteria for TTH and on 75% of migraine, this patient was classified as a patient with a TTH. The concurrent (lower hierarchy) headache types were noted in the data file.

Headache pain intensity

Headache pain intensity was assessed using a numeric pain rating scale (NPRS) based on the following question: "*On a scale of 0 to 10, where 0 means no pain and 10 means the worst pain imaginable, on average, how severe is your headache?*".[27] Validity of the NPRS is considered good with a convergent validity correlated with the Visual Analog Scale, with a correlation of 0.79 to 0.95.[28]

Pain-related disability

Pain-related disability was assessed with the Graded Chronic Pain Scale (GCPS), which is a multidimensional measure that consists of eight questions about the possibility to perform normal daily tasks in the past 30 days (three questions regarding pain-intensity, one regarding the amount of days with pain, three regarding pain-related disability, and one regarding the amount of days on which a person is limited by the complaints).[29] In the current study, the three pain-related disability questions were used to assess pain-related disability, with scores that can range from 0 (no pain-related disability) to 10 (pain-related disability as bad as it could be). The outcome was the average score of the three questions. Internal consistency values of the GCPS are considered good with a Cronbach's α of 0.67 for headache and a Cronbach's α of 0.71 for painful TMD.[29]

Anxiety

The General Anxiety Disorder screener (GAD-7) is a seven-item self-report questionnaire and is used to assess anxious mood and behavior over the past 2 weeks. Anxiety is classified into four categories: no anxiety (0-4), mild anxiety (5 to 9), moderate anxiety (10 to 14),

and severe anxiety (15 to 21).[30] Psychometric values of the GAD-7 are considered good, with a convergent validity showing a correlation of 0.72 to 0.75 by correlating the GAD-7 with the Beck Anxiety Inventory and the anxiety subscale of the Symptom Checklist-90. The internal consistency of the GAD-7 is 0.92 as measured with Cronbach's α.[30]

Somatic complaints

The Patient Health Questionnaire (PHQ-15) is a 15-item self-report questionnaire and is used to assess the severity of somatic complaints. High scores on the PHQ-15 are strongly associated with functional impairment, disability, and health care use.[31] The PHQ-15 classifies somatic complaints in four categories: minimal somatization (1 to 4), low somatization (5 to 9), medium somatization (10 to 14), and high somatization (15 to 30). Internal consistency values of the PHQ-15 are considered excellent, with a Cronbach's α of 0.8.[31]

Depression

The Patient Health Questionnaire (PHQ-9) is a nine-item self-report questionnaire and is used to assess depression. Classification of depression consists of five categories: no depression (1 to 4), mild depression (5 to 9), moderate depression (10 to 14), moderately severe depression (15 to 19), and severe depression (20 to 27).[32] Psychometric values of the PHQ-9 are considered good, with a construct validity correlation of 0.33 to 0.73 by correlation the PHQ-9 to the Short Form-20 and an internal consistency of α =0.89.[32]

Optimism

The Life Orientation Test-Revised (LOT-R) is a 10-item questionnaire and is used to assess the patient's optimism in general.[33] Six of these items are to measure optimism, the other four questions are fillers and do not influence the outcome. The score ranges from 0 to 24 points. Higher scores indicate higher levels of optimism. Convergent validity using Pearson correlation of the LOT-R is -0.22 when correlated with the GAD for anxiety, and -0.31 when correlated with the PHQ-9 for depression.[34] The Cronbach's alpha coefficient of internal consistency is 0.70 for optimism.[34]

Bruxism

For measuring bruxism, the Dutch version of the Oral Behaviours Checklist (OBC) was used.[35] The OBC is a 21-item scale for quantifying the frequency of jaw-overuse behaviors, and is implemented in the DC/TMD Axis II instruments.[2] In the current study, the first four bruxism items were used to determine a bruxism score. A distinction is made between activities during sleep and activities during waking hours. Activities during sleep (two items) are scored on a five-point scale ranging from (0) 'none of the time' to (4) '4 to 7 nights a week'. Activities during waking hours (two items) are scored on a five point scale ranging from (0) 'none of the time' to (4) 'all of the time'.[35] The bruxism score used in the

current study is the average of the four bruxism items and ranges from 0 (no bruxism) to 4 (severe bruxism). Validity of the full OBC questionnaire is good with a spearman's correlation of 0.75, and test-retest reliability is excellent with an intra-class correlation coefficient (ICC) of 0.86.[35] The validity and reliability of the four-item subscale is yet to be determined.

Statistical analyses

The patients' characteristics were presented with frequencies or as mean, standard deviation (SD), and 95% confidence interval. The assumptions for linear regression models were tested as part of the regression analyses. The assumptions tested were additivity/linearity of the variables, homoscedasticity, and normally distributed errors of the standardized residuals.[36] When all assumptions were met, two regression models were built; one for the outcome measure pain intensity, and one for pain-related disability. All assumptions for linear regression were met.

Both regression models were stratified per headache type. Single linear regressions were performed to detect which psychosocial variables were associated with the outcome measures pain intensity and pain-related disability. As bruxism may have a confounding effect on the association between the outcome measures and the psychosocial variables,[6] the single regressions were corrected for the severity of bruxism. Furthermore, each single regression was also corrected for the presence of concurrent headaches. To be included in the multiple regression analyses, a significant association with the outcome measure in the corrected single linear regression model needed to be present ($p<.05$). For the multiple linear regression analyses, the step-by-step forward procedure was used, starting with the strongest variable in the model, and subsequently adding additional variables in order of their strength as based on the single regression R-Square (R^2). The R^2 was used to estimate the explained variance of the psychosocial factors on the outcome variables. For each step, improvement of the model was assessed by a significant increase in model fit.

All results were considered statistically significant at $p<.05$. Statistical analyses were performed using the IBM SPSS Statistics 26 software package (IBM Corp, Armonk, NY, USA).

Results

A total of 2,493 adult patients were screened for this study of which 323 fulfilled the inclusion criteria. Mean age of the patients was 42.9 ± 14.4 years and 61.0% was female. Myalgia was present in 283 (87.6%) of the patients, and arthralgia in 201 (62.2%) patients (see also Table 3.1). Ninety-nine patients were classified with headache attributed to TMD, of which 49 were also classified as having a migraine and 68 with a TTH. Of those not having a headache attributed to TMD, 79 patients were classified with a migraine and 145 with a TTH.

Approximately half on the TMD-pain patients with migraine (n=39) also experienced TTH, and 21 TMD-pain patients with TTH had a concurrent probable migraine.

Table 3.1: Characteristics of the study population, presented with mean and standard deviation, or with frequency by number and percentage.

	Total study population (N =323)	Migraine (N=79)	TTH (N=145)	Headache attributed to TMD (N=99)
Patient characteristics				
Gender (female); N (%)	197 (61.0)	46 (58.2)	85 (58.6)	66 (66.7)
Age in years; mean (SD)	42.9 ± 14.4	41.4 ± 13.1	43.8 ± 15.6	42.7 ± 13.7
Myalgia; N (%)	122 (37.8)	31 (39.2%)	59 (40.7%)	32 (32.3%)
Arthralgia; N (%)	40 (12.4)	8 (10.1%)	26 (17.9%)	6 (6.1%)
Combined myalgia and arthralgia); N (%)	161 (49.8)	40 (50.6%)	60 (41.4%)	61 (61.6%)
Headache pain-intensity; mean (SD)	6.2 ± 2.0	6.7 ± 1.7	5.4 ± 2.0	6.8 ± 2.0
Pain-related disability; mean (SD)	39.3 ± 30.4	40.4 ± 28.0	31.9 ± 29.4	49.2 ± 31.1
Psychosocial variables (range of instrument)				
Anxiety (0 – 21)	5.5 ± 5.1	5.9 ± 4.7	4.4 ± 4.5	7.0 ± 5.8
Somatization (1 - 30)	10.5 ± 5.0	10.9 ± 4.1	9.0 ± 4.3	12.3 ± 5.8
Depression (1 – 27)	6.9 ± 5.5	6.9 ± 5.0	6.0 ± 5.0	8.4 ± 6.3
Optimism (0 - 24)	15.6 ± 4.7	15.3 ± 4.7	15.8 ± 4.7	15.7 ± 4.8
Bruxism (0 - 4)	1.2 ± 1.0	1.2 ± 1.0	1.1 ± 0.9	1.2 ± 1.0

DC/TMD: diagnostic criteria for temporomandibular disorders; N: number of patients; SD: standard deviation; TMD: temporomandibular disorder; TTH: tension-type headache.

Headache pain intensity

For the group of TMD-pain patients with migraine, no significant associations between headache pain intensity and any of the psychosocial variables were present according to the single regression analyses. After correcting for bruxism and the presence of concurrent headache (in this case: TTH, n=39), optimism was positively associated with headache pain intensity ($R^2 = 0.143$; p=.033) No multiple regression analysis was performed.

In patients with TTH, somatic symptoms was the only significant variable associated with headache pain intensity in the single regression models (both before ($R^2 = 0.117$; p=.009) and after ($R^2 = 0.117$; p=.009) correction for bruxism and concurrent headache). No multiple regression analysis was performed.

Table 3.2: Single and multiple linear regression for headache pain intensity in TMD-pain patients with headache, stratified per headache type.

Pain intensity	Single Regression			Single regression (corrected for bruxism and concurrent headache types*)			Multiple regression (corrected for bruxism and concurrent headache types*)			
	R^2	B (95% CI)	p	R^2	B (95% CI)	p	R^2	B (95% CI)	p	Significant F change
Migraine (N=79)										
Depression	0.024	-0.054 (-0.131 - 0.024)	.107	0.136	-0.068 (-0.143-0.007)	.076	-	-	-	-
Anxiety	0.019	-0.052 (-0.136 - 0.032)	.220	0.120	-0.067 (-0.148-0.014)	.105	-	-	-	-
Somatization	0.007	0.036 (-0.059 - 0.132)	.453	0.095	0.034 (-0.062-0.129)	.481	-	-	-	-
Optimism	0.046	0.080 (-0.002 - 0.162)	.056	0.143	0.087 (0.007-0.167)	.033	-	-	-	-
Tension-Type Headache (N= 145)										
Depression	0.021	0.058 (-0.008 - 0.123)	.083	0.097	0.064 (0.000-0.128)	.051	-	-	-	-
Anxiety	0.018	0.058 (-0.012 - 0.127)	.102	0.084	0.049 (-0.022-0.120)	.176	-	-	-	-
Somatization	0.032	0.083 (0.008 - 0.157)	.031	0.117	0.099 (0.026-0.173)	.009	-	-	-	-
Optimism	0.001	-0.012 (-0.002 - 0.162)	.739	0.074	-0.019 (-0.088-0.049)	.577	-	-	-	-
Headache attributed to TMD (N=99)										
Depression	0.141	0.119 (0.058 - 0.179)	.000	0.214	0.109 (0.050-0.168)	.000	-	-	-	-
Anxiety	0.132	0.128 (0.061- 0.208)	.000	0.222	0.122 (0.059-0.185)	.000	0.222	0.122 (0.059-0.185)	.000	.000
Somatization	0.141	0.129 (0.064 - 0.194)	.000	0.213	0.117 (0.055-0.180)	.000	-	-	-	-
Optimism	0.071	-0.111 (-0.194 - -0.029)	.009	0.144	-0.089 (-0.170- -0.009)	.030	-	-	-	-

B: beta coefficient; CI: confidence interval; R2; explained variance; TMD: temporomandibular disorders; TTH: tension-type headache
*Patients may have more than one headache diagnosis. When more than one headache is present, patients were classified according to pre-defined hierarchy criteria. In this step of the analysis, the single regression outcomes are corrected for the presence of the other concurrent headaches.

Table 3.3: Single and multiple linear regression for pain-related disability in TMD-pain patients with headache, stratified per headache type.

Pain-related disability	Single Regression			Single regression (corrected for bruxism and concurrent headache types*)			Multiple regression (corrected for bruxism and concurrent headache types*)			
	R^2	B (95% CI)	p	R^2	B (95% CI)	p	R^2	B (95% CI)	p	Significant F change
Migraine (N=79)										
Depression	0.066	1.436 (0.218 - 2.653)	.021	0.103	1.367 (0.141-2.594)	.029	-	-	-	-
Anxiety	0.043	1.251 (-0.080 - 2.581)	.065	0.084	1.220 (-0.118-2.558)	.073	-	-	-	-
Somatization	0.052	1.557 (0.059 - 3.054)	.042	0.080	1.346 (-0.207-2.898)	.088	-	-	-	-
Optimism	0.001	0.212 (-1.139 - 1.563)	.756	0.046	0.279 (-1.079-1.637)	.683	-	-	-	-
Tension-Type Headache (N= 145)										
Depression	0.191	2.603 (1.723 - 3.483)	.000	0.195	2.584 (1.693-3.475)	.000	0.195	2.584 (1.693-3.475)	.000	.000
Anxiety	0.134	2.305 (1.343 - 3.266)	.000	0.126	2.258 (1.240-3.276)	.000	-	-	-	-
Somatization	0.079	1.998 (0.924 - 3.073)	.000	0.090	2.010 (0.909-3.111)	.000	-	-	-	-
Optimism	0.078	-1.757 (-2.747 - -0.768)	.001	0.079	-1.701 (-2.702- -0.699)	.001	-	-	-	-
Headache attributed to TMD (N=99)										
Depression	0.150	1.894 (0.970 - 2.818)	.000	0.160	1.962 (1.025-2.898)	.000	-	-	-	-
Anxiety	0.100	1.736 (0.672 - 2.800)	.002	0.121	1.829 (0.795-2.862)	.001	-	-	-	-
Somatization	0.148	2.103 (1.105 - 3.102)	.000	0.162	2.129 (1.119-3.139)	.000	0.162	2.129 (1.119-3.139)	.000	.000
Optimism	0.040	-1.303 (-2.602 - -0.003)	.049	0.051	-1.406 (-2.720- -0.093)	.036	-	-	-	-

B: beta coefficient; CI: confidence interval; R2; explained variance; TMD: temporomandibular disorders; TTH: tension-type headache
*Patients may have more than one headache diagnosis. When more than one headache is present, patients were classified according to pre-defined hierarchy criteria. In this step of the analysis, the single regression outcomes are corrected for the presence of the other concurrent headaches.

For patients with headache attributed to TMD, headache pain intensity was significantly associated with all psychosocial variables in the single regression models (R^2 = 0.144 – 0.222; p<.000 - .030). In the multiple regression analysis, only anxiety was retained in the regression model (R^2 = 0.222; p=.000). All outcomes are depicted in Table 3.2.

Pain-related disability

In TMD-pain patients with migraine, the variables somatization and depression were associated with pain-related disability (R^2 = 0.052 – 0.066; p<.05). After correction, only depression remained associated with pain disability (R^2 = 0.103; p=.029). Therefore, no multiple regression analysis was performed.

There was an association between pain-related disability and all psychosocial factors in TMD-pain patients with TTH in both the single regression and corrected single regression analyses (R^2 = 0.078 – 0.195; p≤.001). Depression was the strongest variable based on the multiple regression analysis (R^2 = 0.195; p=.000).

In patients with headache attributed to TMD, pain-related disability was associated with all psychosocial factors in the single regression analyses (R^2 = 0.040 – 0.150; p<.05), as well as the corrected single regression analyses (R^2 = 0.051 – 0.162; p<.05). Somatization came out as the strongest variable in the multiple regression analysis (R^2 0.162; p=.000). All outcomes are depicted in Table 3.3.

Discussion

The key findings of the current study were that in TMD-pain patients with migraine, a weak association was found between optimism and headache pain intensity, while for TMD-pain patients with TTH a (stronger) association was found between somatization and headache pain intensity. For patients with headache attributed to the TMD, all psychosocial variables showed a significant association with headache pain intensity, with anxiety presenting as the strongest variable. Optimism, depression and somatization did not further improve the explained variance of anxiety alone.

There was an association between pain-related disability and depression in TMD-pain patients with migraine. In TMD-pain patients with TTH or headache attributed to TMD, all psychosocial factors (i.e. depression, anxiety, somatization, and optimism) had a significant association with pain-related disability. Depression presented as the strongest variable in TMD-pain patients with TTH, and somatization in patients with headache attributed to TMD.

The current study was conducted at a specialized clinic for orofacial pain and dysfunction. In this clinic, all practitioners work according to the DC/TMD protocol, which enhances the reliability of the data. However, not all eligible patients could be included in the study due to missing data from their medical records. Another limitation of the current study is the use of self-administered questionnaires to gather information on many of the variables used in this study. Patients may have provided answers which they feel will help to receive the treatment they preferred. Another common disadvantage of self-reported data relates to unreliable answers due to recall bias. However, the questionnaires used to assess psychosocial factors, headache pain-intensity, and pain-related disability do have good psychometric properties.

Another strength of the current study is the multiple regression models used were built including a correction for the influence of bruxism on the studied associations. That is, because previous research has shown that bruxism is a confounding factor in the association between painful TMD and headache.[6] Moreover,, awake bruxism is associated with myofascial TMD as well as with psychosocial factors like anxiety and depression.[23,37] By correcting for bruxism, the influence of the different psychosocial factors on pain intensity and pain-related disability can be better identified.[38] Previous studies have shown various associations between painful TMD and psychosocial factors.[19,39,40] In a TMD population from an orofacial pain clinic, a positive association was found between TMD pain intensity and anxiety, somatization, and depression.[19] In the current study, similar associations as reported in the literature for TMD pain intensity were found in patients with headache attributed to TMD.

One of the findings of the current study is that higher scores on somatic complaints also predicted a higher headache pain intensity in the patient with headache attributed to TMD. Somatic complaints are multiple persistent physical complaints such as pain, fatigue or dizziness, which are all common in patients with widespread pain.[31,41,42] Widespread pain is also common in individuals with TMD, and is considered an expression of central sensitization.[43] One of the symptoms of central sensitization is hypersensitivity for pain, explaining the higher headache pain intensity scores in patients with higher levels of somatization. Furthermore, there is an association between central sensitization, pain sensitivity and depression,[44] and depression was associated with pain-related disability in all groups in the current study. Assessment of psychosocial factors like somatization and depression in the clinical setting may therefore be an important element in getting a complete image of the factors influencing the patient's pain-intensity and disability. However, as the explained variance of these factors was low, we should be aware that other factors also may have an influence on these pain outcomes. Furthermore, because psychosocial factors do have an influence on headache pain intensity and pain-related disability in TMD-pain patients with headache, this should be taken into consideration

when coming up with a treatment strategy with, for example, counselling[45] or cognitive behavioral therapy.[46]

Interestingly, where all psychosocial variables have an association with secondary headache attributed to TMD, there are fewer associations in patients with the primary headaches migraine and TTH. In TMD-pain patients with primary headaches, i.e. migraine or TTH, only optimism and somatization had an influence on the perceived pain intensity, respectively. Despite evidence stating that psychological factors can influence headache pain through central nervous system pathways,[15] this was not found in the current study in a population of TMD-pain patients with primary headache, and should therefore be studied more extensively in the future. Additionally, future research should consider prospective studies with a longitudinal design, to predict the influence of psychosocial factors on the development of pain intensity and pain-related disability in TMD-pain patients with headache.

In conclusion, pain intensity was weakly associated with optimism in TMD-pain patients with migraine, and with somatization in TMD-pain patients with TTH. In TMD-pain patients with headache attributed to TMD, all psychosocial variables were associated with headache pain intensity, with anxiety as the strongest influence. Pain-related disability was associated with depression in those with migraine or TTH, and with somatization in the patients with headache attributed to TMD.

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Conflict of interest statement
None of the authors declared a conflict of interest.

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4

Chapter 4

Is the course of headache complaints related to the course of orofacial pain and disability in patients treated for temporomandibular pain? An observational study.

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Background:
Migraine, tension-type headache (TTH) and headache attributed to temporomandibular disorders (TMD) are prevalent in patients with TMD-pain. The objective was to describe the course of headache complaints as compared to the course of TMD complaints in TMD-pain patients with headache during usual care multidisciplinary treatment for TMD.

Methods:
A 12-week longitudinal observational study following adults with TMD-pain and headache during a usual-care multidisciplinary TMD-treatment. The Graded Chronic Pain Scale was used for both TMD and headache to measure pain-related disability (primary outcome measure), pain intensity, days with pain and days experiencing disability (secondary outcome measures). Stratified for the headache type, general linear modelling for repeated measures was used to analyze changes over time in the TMD complaints and the headache complaints.

Results:
TMD-pain patients with migraine (n=22) showed significant decrease of pain-related disability for both TMD and headache complaints over time. No difference in the effect over time was found between the two complaints. Patients with TMD-pain and TTH (n=21) or headache attributed to TMD (n=17) did not improve in disability over time. For the secondary outcome measures, the results were equivocal.

Conclusion:
In TMD-pain patients with migraine, improvement in TMD-related disability was comparable to headache-related disability for TMD-pain patients with TTH or with headache attributed to TMD, no improvements in disability were found.

Practical implications:
In patients with both TMD and migraine, clinicians should consider treatment of the TMD even when the complaints of the patient focus on the usually more disabling migraine.

Introduction

One in ten adults in the general population reports the presence of pain in the temporomandibular region,[1] which could be an indication for a painful temporomandibular disorder (TMD).[2] TMDs are disorders involving the temporomandibular joint, the masticatory muscles, and associated structures.[2] Symptoms include orofacial pain, limited function of the masticatory system and joint sounds.[2] Pain in the orofacial region is the main reason patients seek care for their TMD complaints,[3] and is often accompanied by other pain complaints.[4,5] One of the most common comorbid conditions in TMD-pain patients is headache, with prevalence ranging up to 83%.[6,7] The most prevalent types of headache in TMD-pain patients are tension-type headache (TTH; 22-30%), migraine (17-55%) and headache attributed to TMD (5-19%).[6–8] Despite its high co-occurrence, there seems to be no association between the presence of TTH and TMD; i.e. the prevalence of TTH in TMD patients does not seem to exceed the prevalence of TTH in the general population.[6,9] In contrast, studies have consistently reported migraine to be more prevalent in TMD-pain patients as compared to patients with a function-related TMD, or no TMD at all.[6,7,9]

In line with the reported association between the TMD-pain and migraine, studies have shown that TMD treatment has promising outcomes on headache complaints in TMD-pain patients with concomitant migraine.[10,11] Also for headache attributed to TMD, TMD treatment is reported successful in the decrease of the headache complaints.[12] For TMD-pain patients with concomitant TTH, however, no information is available on the effect of TMD multidisciplinary treatment on the headache complaints.

To better understand the associations between different types of headache and TMD-pain, a longitudinal study following changes in severity of various types of headache in relation to changes in the TMD complaints is warranted. Therefore, the aim of this study was to describe the course of headache complaints as compared to the course of TMD complaints in TMD-pain patients with various types of headache (i.e., TTH, migraine, or headache attributed to TMD), during a 12-week usual care treatment period based on a multidisciplinary approach.

Materials and Methods

Study design, ethics and registration

A longitudinal observational study was used to monitor TMD-pain patients with headache during a 12-week treatment period in which they received usual care for their TMD complaints. This design was chosen to enhance the possibility to detect changes in their complaints and therefore to provide sufficient contrast between patients for the statistical analyses. As part of the usual care, patients received a patient-tailored treatment plan that

consisted of a combination of counseling, including pain education (in all cases), splint therapy (in case the patient reported sleep-related bruxism) and jaw exercises (in case the patient reported day-time oral behaviors, muscle tension or joint mobility problems).[13] The study was approved by the Ethical Committee of Academic Center for Dentistry Amsterdam (ACTA) [file number 2017006]. All participants signed an informed consent form before inclusion. This study has been registered in the Netherlands Trial Register (NTR6368).

Study population

Patients that sought treatment at the Orofacial Pain and Dysfunction (OPD) clinic of ACTA from October 2016 to May 2018 were invited for the study. In the OPD clinic, a multidisciplinary team collaborates in diagnosis and treatment of mostly chronic orofacial pain patients. The team consists of dentists, physical therapists, and a psychologist, all specialized in orofacial pain and dysfunction.

Patients were eligible when they had: 1) TMD-pain diagnosis; 2) headache complaints in the last year; 3) >18 years old; 4) ability to communicate in Dutch or English. Patients were excluded if: 1) no treatment was started at the OPD clinic, 2) their headache was not classified as TTH, migraine or headache attributed to TMD.

Flow of the study

Before the intake visit, patients filled out all questions from the Diagnostic Criteria for TMD (DC/TMD) axis II,[14] as well as the Headache Screening Questionnaire (HSQ).[15] At the intake visit, one of the dentists performed a standardized clinical examination, as part of the regular intake procedure, including all physical tests as described in the DC/TMD,[14] and invited the patients who fulfilled the in- and exclusion criteria to participate in the study. Included patients then received a baseline study questionnaire. The same questionnaire was sent by e-mail at four, eight and twelve weeks after the intake visit (see Figure 4.1). A reminder was sent within one week by e-mail when the patient did not fill out the questionnaire. If there was still no response, patients were contacted up to two times via telephone call. If patients did not return the baseline or the 12-week (endpoint) questionnaire, they were excluded from the analyses.

TMD-pain

Patients were diagnosed with TMD pain when they met the DC/TMD criteria for myalgia and/or arthralgia.[14] The sensitivity of the DC/TMD for TMD-pain diagnoses is 0.86, and the specificity is 0.98.[14]

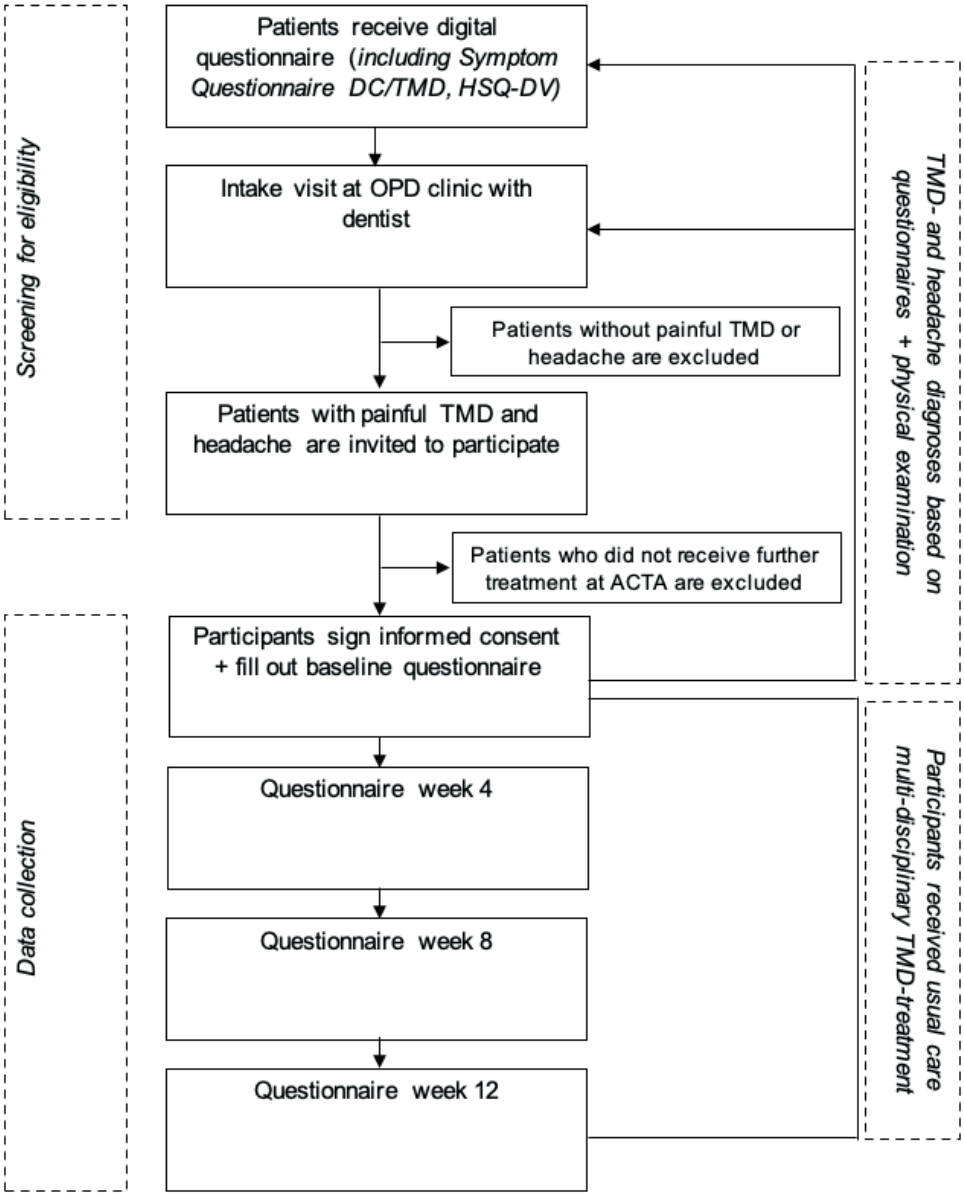

Figure 4.1: Flow of the study design, portraying each step the participants take within this study. DC/TMD: diagnostic criteria for temporomandibular disorders; HSQ-DV: headache screening questionnaire – Dutch version; ACTA: academic center for dentistry Amsterdam.

Headache

TTH and migraine were classified with the HSQ.[15] This questionnaire is based on the International Classification of Headache Disorders 3rd edition (ICHD-3) and screens for the

presence of TTH and migraine.[15,16] A patient was classified with either TTH or migraine when they obtained at least 6 (out of 8) points of that type of headache on the HSQ. The sensitivity and specificity of the HSQ are 92% and 48% respectively for TTH, and 89% and 54% for migraine.[15] In case an equal HSQ score was present for TTH and migraine (≥6 points), the patient was classified with migraine.[15,16]

Headache attributed to a TMD was established according to the DC/TMD criteria: TMD pain combined with headache complaints in the temporal region which are modified or provoked by oral function.[14,17] When patients fulfilled both the criteria of TTH or migraine and a headache attributed to TMD, the patient was classified as having a headache attributed to a TMD in accordance with the ICHD-3 criteria.[16]

Outcome measures

Patients received the Graded Chronic Pain Scale (GCPS) questionnaire,[18] which is one of the DC/TMD recommended measurement instruments to score the severity of the current pain. The GCPS is a reliable measurement instrument for patients with TMD and for patients with headache (reliability coefficients ranging from 0.67 to 1.00).[18,19] Patients were instructed to rate two sets of GCPS scores: eight questions for the TMD pain as well as for the headache complaints. The following GCPS outcome measures were extracted for both for the TMD complaints and for the headache complaints: 1) disability score (DS) – primary outcome; 2) characteristic pain intensity (CPI); 3) days with pain; and 4) days with disability.

The DS is the average score of the three disability questions (i.e. social, work and home life). The CPI score is the average score of the three questions regarding pain intensity (i.e. current, maximum, and average pain). Days with pain represents the number of days with pain experienced in the last 30 days, while days with disability represents the number of days in the last 30 days the patients perceived an impact on their life from their pain complaints.[18]

Statistical analysis

Descriptive statistics were used to characterize the study population. All the outcome measures were normally distributed and presented with means and standard deviations. The study population was stratified by type of headache: migraine, TTH or headache attributed to a TMD. For each subgroup, and for each outcome measure, a general linear modeling with repeated measures (GLM-RM) analysis was applied. This analysis shows whether 1) there are differences in the outcomes measures between the TMD complaints and the headache complaints (within-subjects effect), 2) there are changes in the complaints over time (within-subjects effect), and 3) there is evidence for a different effect in change over time between the TMD complaints and the headache complaints. When

changes over time are found, and no difference in effect over time between the TMD and headache complaints is shown, this is interpreted as 'a comparable course of TMD complaints and headache complaints over time'. Analysis of the data was performed using the *Statistical Package for the Social Sciences* (IBM SPSS) version 24.0 (SPSS Corp, Chicago, Ill, USA). In case of missing outcomes of the intermediate time points (i.e. the 4-week and the 8-week measurement), multiple imputation was applied using a linear regression model for scale variables. To account for an increased type-I error rate associated with multiple comparisons, we used Simple Interactive Statistical Analysis (http://www.quantitativeskills.com/sisa/calculations/bonfer.htm) to calculate an adjusted alpha for each headache subgroup. This adjusted Bonferroni correction is based on the mean correlation between the outcome measures, which was calculated using R statistical software. These correlations and the adjusted alphas were r=0.018 and p<0.018 for TMD-pain patients with migraine, r=0.024 and p<0.024 for patients with TTH and r=0.017 and p>0.017 for patients with headache attributed to TMD.[20]

For the DS, a clinically significant change is suggested to be 2 points.[21] A post-hoc power calculation was performed using *G*power*[22] to check if the number of patients was sufficient to show a clinically significant change based on the estimates presented in this study.

Table 4.1: Baseline demographic and diagnostic characteristics of the study population.

	Overall study population (n= 60)	Overall study population (n= 60)	TTH population (n= 21)	Headache attributed to TMD population (n= 17)
Age; mean ±sd	41.3±14.2	46.9±13.2	39.0±13.8	36.8±14.3
Gender; n (%)				
Female	50 (83.3)	20 (90.9)	15 (71.4)	15 (88.2)
Male	10 (16.7)	2 (9.1)	6 (28.6)	2 (11.8)
TMD pain subtype; n (%)				
Myalgia	37 (61.7)	13 (59.1)	13 (61.9)	11 (64.7)
Arthralgia	5 (8.3)	2 (9.1)	3 (14.3)	0 (0.0)
Combined myalgia & arthralgia	18 (30.0)	7 (31.8)	5 (23.8)	6 (35.3)
Duration of TMD pain; n (%)				
< 1 year	10 (16.7)	6 (27.3)	3 (14.3)	1 (5.9)
1 – 10 years	26 (43.3)	7 (31.8)	12 (57.1)	7 (41.2)
> 10 years	13 (21.7)	3 (13.6)	3 (14.3)	7 (41.2)
Missing	11 (18.3)	6 (27.3)	3 (14.3)	2 (11.8)

SD: standard deviation; n: number of patients; TMD: temporomandibular disorder; TTH: tension-type headache.

Results

Study population

Seventy TMD-pain patients provided informed consent for study participation, seven patients were excluded due to missing headache classification from the patient file and three were excluded because they failed to return the 12-week questionnaire. From the included 60 patients, 83.3% were female and the age ranged from 18 to 71 years. Myalgia was the most common TMD-pain subtype (61.7%), followed by a combination of myalgia and arthralgia (30.0%) and arthralgia alone (8.3%). Migraine was present in 36.5% of the sample, TTH in 35% and headache attributed to a TMD in 28.3% (Table 4.1). Based on the post-hoc power calculations with the standard deviation found in the present study (i.e. SD_{pooled}=2.6), power of 80% and $\alpha = 0.05$, the sample size needed to show a clinically significant change was 16. All headache groups consisted of more than 16 participants each.

Descriptives of the four outcome measures for TMD and headache are illustrated in Table 4.2. At baseline, the mean score for the DS was 3.4±2.9 for TMD and 4.7±2.8 for headache. At week 12, DS was 2.2±2.4 for TMD and 2.9±2.6 for headache.

Longitudinal course of TMD and migraine complaints

For the DS, the migraine complaints had overall higher scores than the TMD complaints (p=.000). There was a significant improvement over time (p=.001), and this improvement was not different for the TMD complaints as compared to the migraine complaints. CPI and days with pain also showed significant improvements over time (p<.018), which were not different for the TMD and the headache complaints. For days with disability, no changes over time were found (Table 4.2; Figures 4.2a-d).

Table 4.2: Descriptives and general linear modeling of the Graded Chronic Pain Scale on baseline, week 4, week 8 and week 12 for the complaints related to TMD-pain and to headache.

Outcome measure	Type of pain complaint	Baseline mean±sd	Week 4 mean±sd	Week 8 mean±sd	Week 12 mean±sd	Difference between complaints F (p-value)	Change over time F (p-value)	Difference between complaints over time F (p-value)
Migraine (N=22)								
Disability Score (0-10)	TMD complaints Headache complaints	2.9 ± 3.1 4.6 ± 3.0	2.9 ± 2.4 4.4 ± 2.7	2.4 ± 2.8 4.7 ± 3.4	1.0 ± 1.1 1.8 ± 2.0	17.162 (.000)	8.707 (.001)	1.928 (.159)
CPI (0-10)	TMD complaints Headache complaints	4.8 ± 2.6 5.7 ± 1.6	5.0 ± 2.6 5.7 ± 1.7	4.1 ± 2.3 4.9 ± 1.8	3.2 ± 2.0 3.8 ± 1.7	2.740 (.113)	6.229 (.004)	.578 (.637)
Days with pain (0-30)	TMD complaints Headache complaints	16.2 ± 11.1 13.3 ± 8.8	11.9 ± 8.4 9.3 ± 5.7	10.6 ± 8.1 9.6 ± 5.3	10.0 ± 9.4 5.8 ± 3.6	3.470 (.077)	4.378 (.017)	2.236 (.117)
Days with Disability (0-30)	TMD complaints Headache complaints	3.8 ± 6.0 4.6 ± 5.8	1.6 ± 2.0 3.7 ± 5.0	2.6 ± 3.6 3.5 ± 4.2	1.4 ± 2.9 1.6 ± 2.9	4.448 (.047)	1.724 (.196)	.920 (.450)
Tension-Type Headache (N=21)								
Disability Score (0-10)	TMD complaints Headache complaints	3.4 ± 2.8 4.4 ± 2.9	3.2 ± 3.0 4.1 ± 2.7	3.1 ± 2.6 3.8 ± 2.6	2.8 ± 2.8 2.9 ± 2.8	5.072 (.036)	2.111 (.135)	1.352 (.289)
CPI (0-10)	TMD complaints Headache complaints	4.8 ± 2.6 5.4 ± 2.1	5.0 ± 2.8 5.2 ± 2.1	4.5 ± 2.3 4.6 ± 2.6	4.5 ± 2.0 4.4 ± 2.4	.325 (.575)	2.533 (.089)	.634 (.603)
Days with pain (0-30)	TMD complaints Headache complaints	20.0 ± 10.4 17.9 ± 10.5	16.8 ± 11.0 18.6 ± 2.1	19.2 ± 10.2 17.4 ± 10.0	13.5 ± 10.7 11.9 ± 10.3	.248 (.624)	6.043 (.005)	2.236 (.119)
Days with Disability (0-30)	TMD complaints Headache complaints	4.0 ± 8.2 4.3 ± 8.9	3.4 ± 5.8 4.9 ± 6.8	5.9 ± 8.1 5.1 ± 6.6	2.8 ± 4.7 2.7 ± 4.7	.882 (.359)	2.758 (.072)	1.137 (.361)
Headache attributed to TMD (N=17)								
Disability Score (0-10)	TMD complaints Headache complaints	4.2 ± 2.8 5.3 ± 2.4	4.1 ± 2.9 4.7 ± 2.6	3.4 ± 2.9 4.1 ± 2.7	3.2 ± 2.3 4.2 ± 2.6	2.329 (.146)	1.659 (.221)	.274 (.843)
CPI (0-10)	TMD complaints Headache complaints	6.0 ± 2.5 6.5 ± 2.1	6.6 ± 1.5 6.2 ± 2.1	4.8 ± 2.5 5.6 ± 1.9	5.5 ± 2.2 6.2 ± 1.9	1.133 (.303)	1.975 (.164)	3.057 (.063)
Days with pain (0-30)	TMD complaints Headache complaints	21.8 ± 10.5 19.6 ± 11.6	16.1 ± 9.2 17.6 ± 10.1	16.6 ± 10.8 16.7 ± 8.9	14.1 ± 10.9 16.1 ± 10.5	.020 (.889)	3.520 (.043)	1.598 (.234)
Days with Disability (0-30)	TMD complaints Headache complaints	3.5 ± 4.5 4.4 ± 5.0	2.4 ± 2.8 4.0 ± 5.2	3.7 ± 4.9 4.5 ± 4.8	2.5 ± 5.4 4.2 ± 6.1	1.900 (.187)	.783 (.523)	.392 (.760)

TMD: temporomandibular disorder; N: number of patients; sd: standard deviation; F: F-value; CPI: characteristic pain intensity.

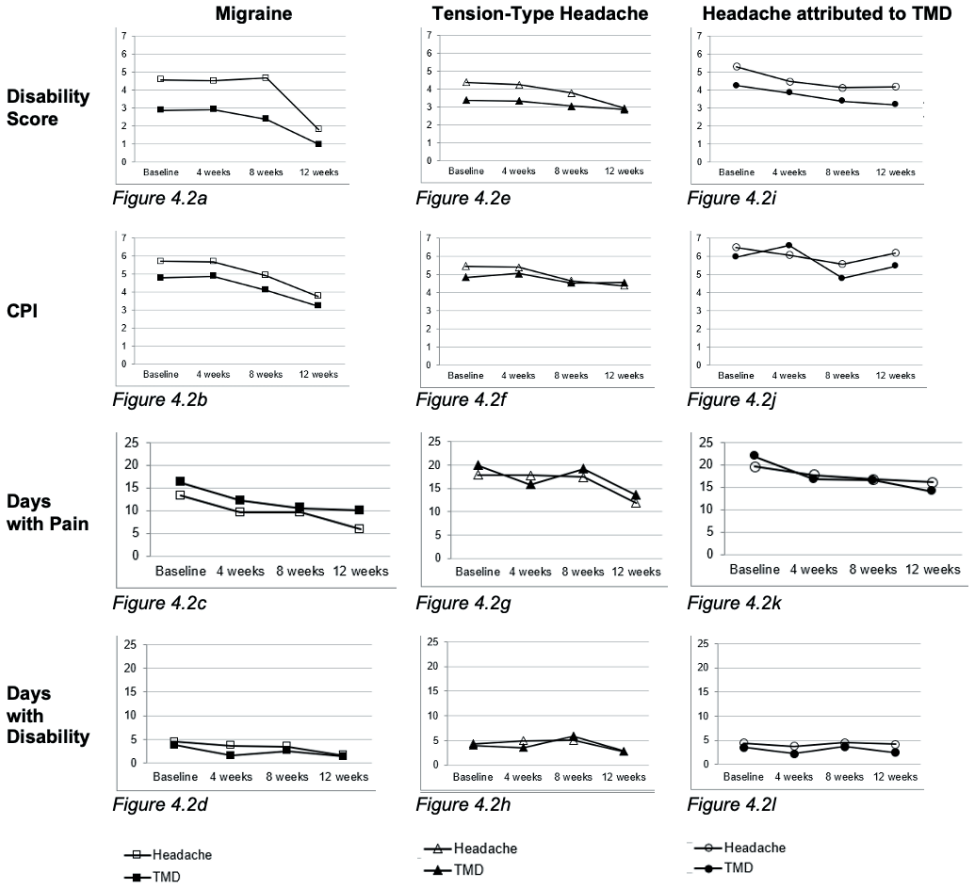

Figure 4.2: Visual representation of the outcome measures Disability Score, Characteristic Pain Intensity, Days with Pain and Days with Disability stratified per headache type. CPI: Characteristic Pain Intensity; TMD: Temporomandibular Disorder.

Longitudinal course of TMD and tension-type headache complaints

The DS was generally higher for the TTH complaints as compared to the TMD complaints, though not significant after correcting for multiple comparisons (p=.036). The DS did not change over time, and no differences between the two complaints over time were observed. Only for days with pain a significant improvement over time was found (p=.005), which was not different for the TTH complaints as compared to the TMD complaints (Table 4.2; Figures 4.2e-h).

Longitudinal course of TMD and headache attributed to TMD complaints

No difference was found in DS between the TMD complaints and the headache attributed to TMD complaints. No changes over time were found, and no differences between the TMD complaints and the headache complaints attributed to this TMD was observed.

For days with pain an improvement over time was found, though not significant after correcting for multiple comparisons (p=.043), and this change was not different for the TMD complaints and the headache complaints attributed to this TMD. For the other outcome measures no improvements over time were observed (Table 4.2; Figures 4.2i-).

Discussion

The course of TMD complaints and headache complaints is dependent on the type of headache, in a TMD patient population that was followed during usual care multidisciplinary treatment. In patients with TMD-pain and migraine, similar changes in the TMD complaints as compared to the headache complaints were observed over time. In patients with TMD-pain with TTH or headache attributed to TMD no changes over time were found, except for days with pain.

Primary outcome measure: disability score

The concomitant decrease in DS as related to TMD and to headache in patients with migraine may be attributed to the hypothesis of shared etiological factors; in case two disorders share the same etiological factors, treatment directed at these etiological factors would benefit both disorders. There is a strong association between TMD-pain and (probable) migraine,[6,7] and this association can be related to the presence of bruxism[6], indicating that bruxism may play a role in the aetiology of both disorders. One of the possible treatment options for sleep-related bruxism is splint therapy, which was not only found effective for TMD-pain, but also showed favorable effects on complaints of headache in TMD patients with migraine, in a previous study.[10] Our results add to this body of knowledge and provides additional evidence for the association between TMD and migraine.

Such associations are not found for TMD and TTH, neither in previous studies[6,9] nor in the current study. One cross-sectional study showed that there was an association between TMD and headache, specifically in patients with mild TMD-pain, but this association was no longer significant after adjusting for shared prognostic factors such as age, gender and somatization.[9] The co-occurrence between TMD-pain and TTH in some cases could be explained by shared prognostic factors, which are the underlying explanation for these comorbidities to be present at the same time.[24] Despite this overlap in shared prognostic factors, TTH and TMD-pain seem to be separate entities and should be approached as such.[24] The different effects over time between TMD-pain patients with different types of headache might indicate that different etiological processes are involved in these subtypes of patients.

Secondary outcome measures: pain intensity, days with pain and days with disability

For the secondary outcome measures used in this study, the results vary for the three subgroups. The decrease in headache pain intensity over time was comparable to the decrease in TMD-pain intensity in patients with migraine, but no decrease in pain intensity was found for TMD-pain patients with TTH or headache attributed to TMD. This corroborates the findings from the primary outcome measure in this study. In all headache groups, there was a decrease of the number of headache days as well as days with TMD-pain. According to the guidelines of the International Headache Society, 50% of reduction on the number of days with pain is considered clinically relevant in patients with migraine.[25] In the present study, the reduction in headache days reached this clinically relevant level in all three subgroups.

For the first time, the longitudinal course of TMD complaints and headache was followed in TMD-pain patients with different types of headache during a period of usual care multidisciplinary treatment. Although exploring the effects of this treatment was not the aim of this study, some interesting aspects of the treatment can be observed in our results. The treatment focused on the TMD complaints and included occlusal splints[10] and physical therapy techniques such as relaxation exercises to the jaw, myofeedback, self-massage of the masticatory muscles and advice for the management of daily parafunction. Previously, these techniques were reported to improve headache intensity and frequency.[26] Also, the treatment addressed more general aspects related to chronic pain such as pain education, focusing on the concepts of sensitization, pain modulation and self-management in pain.[27,28] Since both TMD and headaches are highly associated with psychological factors like stress and pain catastrophizing,[29–32] receiving proper pain education is important to reduce pain, disability and stress in patients with musculoskeletal pain.[33-34] This study suggests that there may be a different effect of pain education between different headache types in patients with TMD, that should be explored further.

A strength of this study is that all patients were seen in the *OPD* clinic, where standardized diagnostic procedures are implemented as part of the usual care. These procedures adhere to the full DC/TMD protocol,[14] as well as incorporate a validated instrument to screen for migraine and TTH according to the ICHD-3 criteria.[15] Often, studies regarding TMD and headaches only address self-reported headache, and not headache subtypes. Taking different subtypes into consideration increases the external validity of the results and provide relevant information on differences between TMD patients with various types of headache.

Limitations of the study

As a consequence of stratifying the analyses for the different headache types, the sample size of the subgroups (17 to 22 subjects) can be considered a limitation of the study. However, the post-hoc power calculations showed that 16 patients were sufficient to

show a clinically relevant change. Researchers have been encouraged to also present clinical relevance analysis in order to simplify the transfer of knowledge from research into practice.[35,36]

The medication use of the patients was not tracked during the study, which could have provided more information on the perception and intensity of the complaints. Furthermore, to facilitate enough change over time in this mostly chronic patient population, an observational study design was chosen in which TMD-pain patients with headache were followed during a 12-week of usual care treatment. We did not intend to study the effects of a specific TMD-treatment and therefore no control group was included. In fact, the variation within the TMD-pain groups with different types of headache allowed for the contrast needed in the regression analyses. For future studies, adding a control group which does not receive treatment, incorporate a pre-treatment period in the longitudinal design and extend the follow-up period, could make the conclusions more robust.

Practical implications

Physical therapists who frequently see patients with TMD-pain should be aware of the association between TMD-pain and different headache types. When, for example, a TMD-pain patient with migraine presents at a clinic, they should know that there is a strong association between the TMD and migraine, even during TMD-treatment. This is less so for concurrent TTH. It is therefore important that the physical therapists has a good understanding of the association between these two disorders and how thiscan be of value within the treatment process. When necessary, the physical therapist can refer the patient to a specialized dentist, neurologist, psychologist or other health professional who can support the treatment.

Conclusion

In TMD-pain patients with migraine, improvement in TMD-pain related disability was comparable to improvement in headache-related disability. For TMD-pain patients with TTH or with headache attributed to the TMD, no improvements in disability were found.

Acknowledgements

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PART II

DIAGNOSTIC PROCESS


5

Chapter 5

Development and psychometric validation of the headache screening questionnaire – Dutch Version

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Background*:*
Headache is a common disorder which may lead to substantial socio-economic loss. Treatment options include self-management strategies, medication and physiotherapy. Physiotherapists need to be able to screen for the presence of migraine and tension-type headache (TTH), so they can adjust their treatment strategies to the type of headache. A quick screening questionnaire to recognize migraine and TTH in the physiotherapy practice is needed.

Objective*:*
The aim of this study was to create a headache screening questionnaire based on the ICHD-3 beta criteria for migraine and TTH, and to establish its content and criterion validity.

Design*:*
A cross-sectional design was used during the validation phase of the study.

Methods*:*
A screening questionnaire was developed for migraine and TTH. Content validity was checked by the research group and a headache research expert. For validation of this questionnaire, patients from the headache clinic of the Canisius Wilhelmina Hospital in Nijmegen were recruited. The outcome of the questionnaire was compared to the ICHD-3 beta diagnosis of the headache specialist. For criterion validity, sensitivity, specificity, likelihood ratios, and positive- and negative predictive values were calculated.

Results*:*
A 10-item questionnaire has been developed: the Headache Screening Questionnaire. For validation of the Dutch version (HSQ-DV), 105 patients were included in the study. The sensitivity and specificity were .89 and .54 respectively for probable migraine, and for probable TTH .92 and .48 respectively.

Conclusion*:*
The HSQ-DV is a sensitive screening tool to detect patients with probable migraine and probable TTH.

Abstract

Introduction

Currently, 46% of adults worldwide are affected by headaches.[1] Of all headaches, tension-type headache (TTH) is most common (31-42%) followed by migraine (11-22%) and both have a substantial impact on quality of life.[1–4] Headaches are also important health-related drivers of economic losses [5]. The total annual cost of headache amongst adults is estimated at €173 billion in Europe.[5] Improving headache healthcare may decrease the socio-economic burden. [3–5]

Patients suffering from headache commonly use self-management strategies, including medication and physiotherapy.[6–11] A physiotherapist (PT) can contribute valuable information through clinical reasoning within their diagnostic- and therapeutic process in headache healthcare.[6,7] A PT is equipped to treat secondary headaches attributed to musculoskeletal complaints[12,13] such as cervicogenic headache,[6,14] headaches attributed to a whiplash injury,[15] and secondary headache attributed to a temporomandibular disorder (TMD).[12] Signs and symptoms that can be influenced by physiotherapy are, for example, a limited cervical range of motion in patients with cervicogenic headache[16,17] and patients with headache attributed to a whiplash injury,[18] or muscle pain in patients with a secondary headache attributed to TMD.[19]

Besides treating secondary headaches, PTs are also able to support treatment of the primary headaches migraine and TTH.[20–22] Physiotherapy focused on relaxation exercises and triggers to prevent headache episodes for migraine and TTH, is beneficial as complementary therapy.[6,12,20,23] Training motor control impairment in the deep neck flexor muscles can influence TTH,[21] while treating myofascial trigger points and relaxation therapy may influence both migraine and TTH.[21,22,24–26] The effectiveness of PT will depend on proper clinical reasoning during the physiotherapeutic diagnostic process, as not all interventions are as effective for different types of headache.[21]

Within the physiotherapeutic diagnostic process, it is important to differentiate between primary and secondary headaches. Secondary headaches attributed to musculoskeletal complaints can already properly be diagnosed by a PT using findings from the history-taking and clinical examination [14,27]. Currently, primary headaches like migraine and TTH are only recognizable during history-taking.[17] At this moment there are no clinical examination tests that can diagnose migraine or TTH. [17,27] It is therefore important that a PT should be able to recognize the symptoms of migraine and TTH while taking the history of the patient to deliver an optimal treatment appropriate for the complaints of the patient. As primary headaches are complex conditions, they need to be definitively diagnosed by a specialized neurologist. So when needed the PT can advise a patient to see a headache specialist when a suspicion of a primary headache is present.[12] To optimize history-taking by the PT a validated screening tool is needed to check for both migraine and TTH.

The International Headache Society (IHS) has created the International Classification of Headache Disorders (ICHD), a worldwide recognized standardized and validated classification system to diagnose headache disorders.[17,28,29] There are questionnaires based on the first two editions of the ICHD. The 'Lifting the Burden' campaign developed a headache questionnaire for population-based research.[30] Because of the research scope this questionnaire is not feasible as a quick screening questionnaire.[30–32] Two screening questionnaires are developed for migraine only.[33,34] To increase the effectiveness of the screening of both migraine and TTH, and to decrease administrative burden, one short questionnaire covering both headaches is favourable.

Therefore, the aim of this study is to create a headache screening questionnaire based on the ICHD-3 beta criteria for migraine and TTH, and to establish its content and criterion validity.

Methods

The six steps of measurement development of de Vet et al.[35] were used to create the headache screening questionnaire (HSQ). These six steps are: 1) definition of the construct to be measured; 2) choice of measurement method; 3) selecting items; 4) scoring issues; 5) pilot-testing; and 6) field-testing. Within this study, the first four steps are described under 'phase I: Development'. The last two steps are described under 'phase II: Validation of the HSQ-DV'.

Phase I: Development

Step 1: Definition of the construct

The researchers HAvdM, CMV, NWGN-vdS and CMS established that the constructs to be measured related to the aim of this study are the two primary headaches migraine and TTH, as described in the ICHD-3.[17]

Step 2: Choice of measurement instrument

The researchers HAvdM, CMV and CMS discussed the possibilities for measurement instruments. As migraine and TTH are disorders recognized during the history-taking of the patient, the measurement instrument had to be an addition in this process. Therefore, a questionnaire was the favourable type of measurement instrument.

Step 3: Selecting items

For the third step, HAvdM, CMV and CMS transformed the ICHD-3 criteria for migraine without aura and TTH of the domains frequency, duration, characteristics and symptoms (A to D of the ICHD-3 beta) into questions in the first draft of the Dutch Version of the Headache Screening Questionnaire (HSQ-DV; see Table 5.1). No differentiation was made

between episodic and chronic migraine, nor between infrequent, frequent, and chronic TTH. The last domain "headache is not better accounted for by another ICHD-3 diagnosis" was left out; this domain is not relevant for this screening instrument.

Thereafter, the HSQ-DV was translated into the English version (HSQ-EV) by an independent researcher (JT). JT is a native English speaker and fluent in Dutch. Simultaneously, the original ICHD-3 beta criteria were translated into layman English by another independent researcher and native English speaker (DT). JT and DT were both blinded for all other HSQ development steps.

The layman English ICHD-3 beta criteria were compared to the HSQ-EV and differences were discussed (HAvdM, CMV and CMS), resulting in adjustments in phrasing and word-use of the HSQ-EV. This HSQ-EV was back-translated into Dutch (HAvdM), which resulted in adjustments of the HSQ-DV.

Step 4: Scoring issues
For part A to D of the ICHD-3 beta criteria, 2 points can be scored (Table 1). Question 1 is related to the domain "frequency" for TTH, corresponding with part A from the ICHD-3 criteria. For migraine, question 2 corresponds with part A (Table 1). Parts B-D are translated into the same questions for both migraine and TTH, but different answers correspond with each headache.

The HSQ provides 2 final scores: 0-8 points for migraine and 0-8 points for TTH (Figures 5.1 and 5.2). In case all ICHD-3 beta criteria are met for migraine and/or TTH, a person receives the maximum score of 8 points for migraine and/ or TTH. As people may have concurrent migraine and TTH [36], it is possible for patients to receive 8 points for each headache. When at least 6 points are appointed, migraine or TTH is considered 'probably present'; hereafter named 'probable' migraine or 'probable' TTH.

Table 5.1: ICHD-3 beta criteria for migraine and Tension-Type Headache and the corresponding question numbers of the Headache Screening Questionnaire (HSQ).

Migraine		Tension-Type Headache	
ICHD-3 beta criteria	**Corresponding question number HSQ**	**ICHD-3 beta criteria**	**Corresponding question number HSQ**
A. At least five attacks fulfilling criteria B-D	2	A. At least 10 episodes of headache occurring on 1-14 days per month on average for >3 months (≥12 and <180 days per year) and fulfilling criteria B-D	1 (3)
B. Headache attacks lasting 4-72 hr (untreated or unsuccessfully treated)	4	B. Lasting from 30 min to 7 days	4
C. Headache has at least two of the following four characteristics:		C. At least two of the following four characteristics:	
1. unilateral location	6	1. bilateral location	6
2. pulsating quality	5	2. pressing or tightening (non-pulsating) quality	5
3. moderate or severe pain intensity	7	3. mild or moderate intensity	7
4. aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)	8, 9	4. not aggravated by routine physical activity such as walking or climbing stairs	8
D. During headache at least one of the following:		D. Both of the following:	
1. nausea and/or vomiting	10	1. no nausea or vomiting	10
2. photophobia and phonophobia	10	2. no more than one of photophobia or phonophobia	10

HSQ-DV: Headache Screening Questionnaire Dutch Version.

Phase II: Validation of the HSQ-DV

Step 5: Pilot testing

Within this study, the HSQ-DV was presented to three bachelor students physiotherapy and eight master students orofacial physiotherapy. They tested the HSQ-DV on written case reports and each other. Their feedback regarding the scoring system was used to finalize the HSQ-DV before field-testing with patients and resulted in the development of the algorithms.

Steps 6: Field testing

A cross-sectional study was conducted at the Canisius-Wilhelmina Hospital (CWZ) headache clinic of Nijmegen. Applying convenience sampling, patients entering the clinic in the period between December, 2013 and August, 2015 were asked to participate in this study. To be included, patients had to: 1) be at least 18 years of age; 2) visit the neurologist for an intake; and 3) be able to understand and read Dutch. No exclusion criteria were applied. A medical ethical waiver was obtained from the medical ethics committee at the

Radboud university medical center of Nijmegen [file number 2013/453]. Written informed consent for participation in the study was obtained from all patients. Gender, age and headache pain intensity based on the numeric pain rating scale (NPRS) [37] were obtained from all patients.

Patients received the HSQ-DV before their visit to the neurologist, which then was collected by a nurse at the clinic. The neurologist took the patient's medical history, performed complementary clinical tests when needed for a diagnosis and wrote the ICHD-3 beta diagnosis on a separate form. This separate form was also collected by this nurse who also appointed participant numbers to anonymize the forms. The HSQ-DV and neurologist's diagnosis were anonymously collected for analysis by HAvdM.

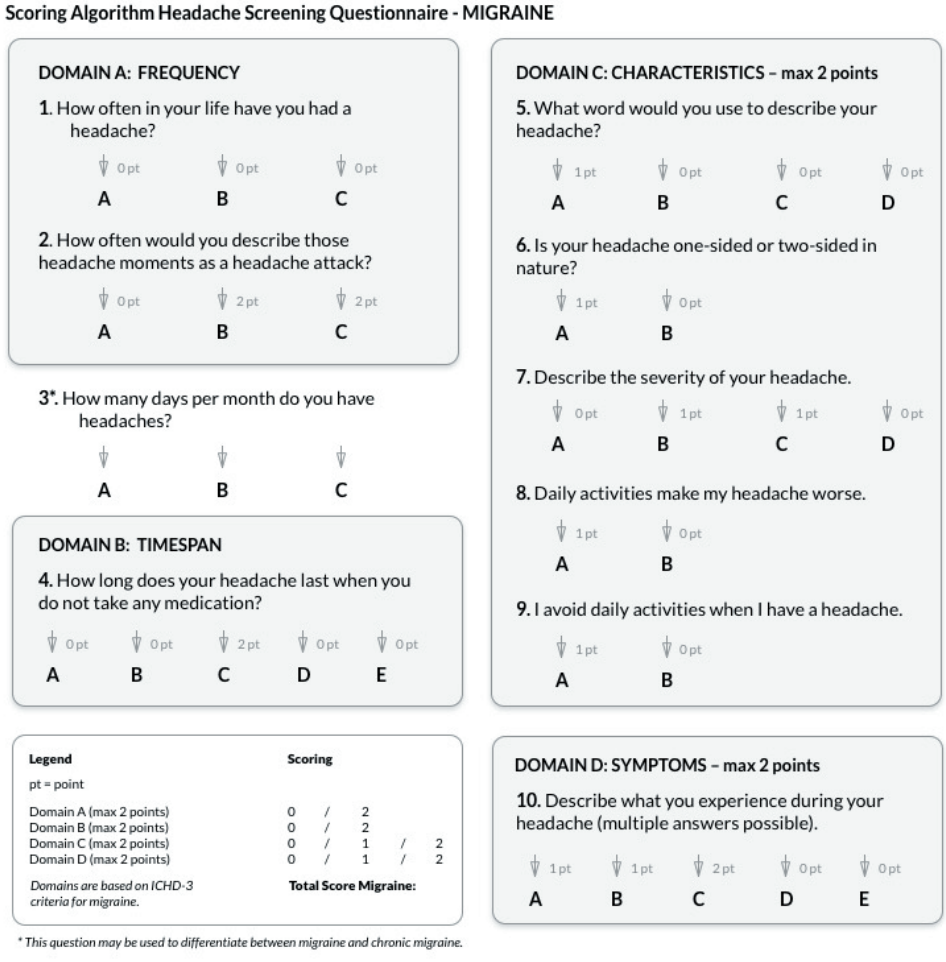

Figure 5.1: Scoring algorithm for migraine on the Headache Screening Questionnaire.

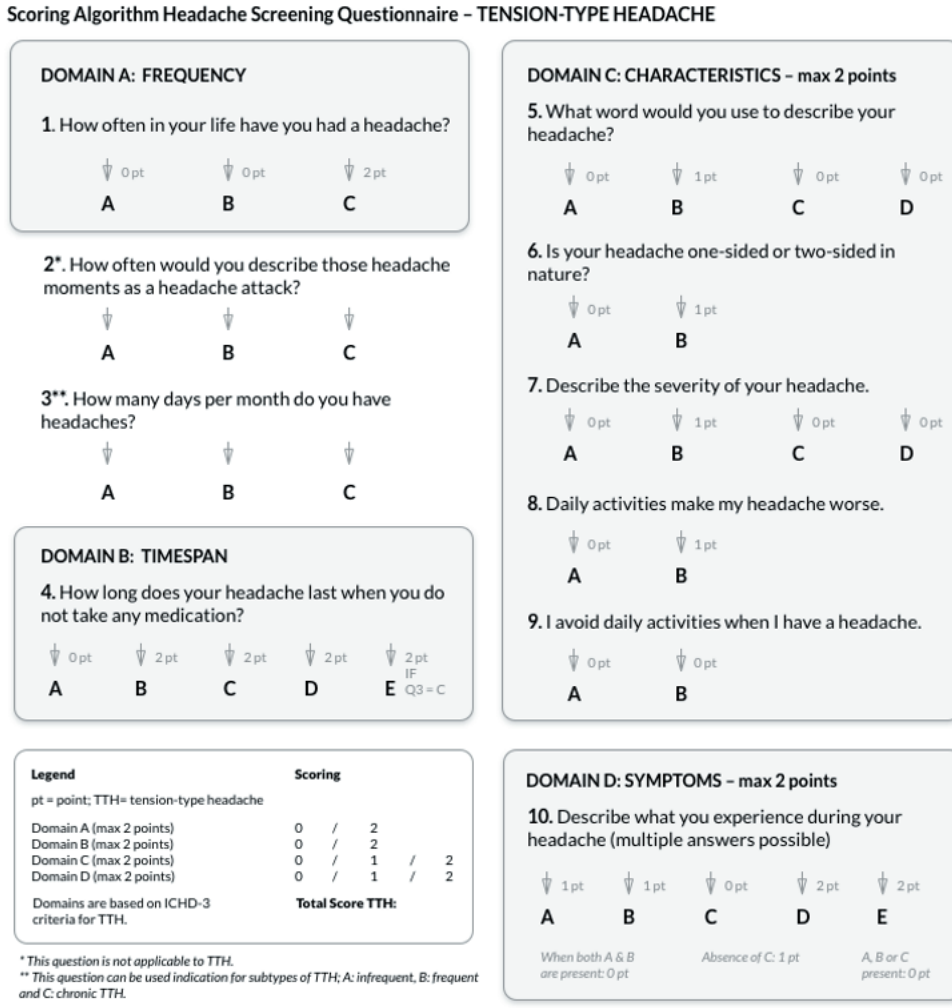

Figure 5.2: Scoring algorithm for Tension Type Headache on the Headache Screening Questionnaire

Data analysis

Face validity, as a sub form of content validity, was checked by examining the degree to which the content of the HSQ was an adequate reflection of the construct to be measured.[38] To establish this, the HSQ-DV and HSQ-EV were compared to the ICHD-3 beta criteria by an expert in headache research (DG). Adjustments were made to both the HSQ-DV and HSQ-EV. To establish clinical utility the HSQ-DV was shown to a group of 10 PTs for their feedback regarding the clinical utility on face value.

Criterion validity is the degree to which the scores of an instrument are consistent with hypotheses based on the assumption that the instrument validly measures the construct to be measured.[38] The ICHD-3 beta diagnosis of the neurologist was used as gold standard. This diagnosis was compared with the outcome of the HSQ-DV (migraine yes/no and TTH yes/no). Agreement (percentage [%] and kappa [K]) between the neurologist and HSQ-DV were calculated. Kappa values below .20 were considered slight agreement, between .21 - .40 fair, between .41 - .60 moderate, 0.61-0.80 as substantial and between .81 - 1 almost perfect agreement.[39]

Related to criterion validity, sensitivity and specificity were calculated for migraine, probable migraine, TTH and probable TTH. Furthermore the positive likelihood ration (LR+), the negative likelihood ratio (LR-), and the positive predictive value (PPV) and negative predictive value (NPV) were calculated.[40] The PPV and NPV were calculated using the prevalence numbers from the validation study, but also applied to the general population. For migraine, the prevalence range of 11-22% is used.[1,3] When considering probable migraine, it is estimated that the prevalence numbers double so the range 22-44% was used. For TTH, the prevalence range of 31-42% was used.[1,3] There were no estimates available for probable TTH. Likelihood ratios can range from 0 to infinity, where the value 1 lacks diagnostic value, values greater than 1 increase the probability of disease (LR+) and values below 1 decrease the probability of disease (LR-).[41]

Analysis of the data was performed using the *Statistical Package for the Social Sciences* (IBM SPSS) version 22.0 (SPSS Corp, Chicago, Ill, USA).

Table 5.2: Basic demographics.

Gender	
Male; *n*(%)	23 (21.9)
Female; *n*(%)	82 (78.1)
Age; mean (*SD*)	40.3 (14.5)
Marital status	
Single; *n*(%)	27 (25.7)
Married; *n*(%)	46 (43.8)
Living together; *n*(%)	22 (21.0)
Divorced; *n*(%)	6 (5.7)
Widow(er) ; *n*(%)	2 (1.9)
Missing; *n*(%)	2 (1.9)
Education	
Primary school; *n*(%)	2 (1.9)
High school; *n*(%)	38 (36.2)
Community college; *n*(%)	32 (30.5)
University applied sciences; *n*(%)	20 (19.0)
University; *n*(%)	10 (9.5)
Missing; *n*(%)	3 (2.9)
Medication usage	
None; *n*(%)	21 (20.0)
Light painkillers <15 days p/m; *n*(%)	17 (16.2)
Light painkillers ≥15 days p/m; *n*(%)	19 (18.1)
Heavy painkillers <10 days p/m; *n*(%)	15 (14.3)
Heavy painkillers ≥10 days p/m; *n*(%)	17 (16.2)
Light and heavy painkillers; *n*(%)	10 (9.5)
Missing	6 (5.7)
Body Mass Index; mean (*SD*)	24.9 (4.6)
Headache NPRS; mean (*SD*)	7.7 (1.3)
Headache Diagnoses [ICHD-3 beta code]*	
Migraine [1]; *n*(%)	55 (52.4)
Tension-Type Headache [2]; *n*(%)	36 (34.3)
Cluster Headache [3.1]; *n*(%)	5 (4.8)
Hemicrania continua [3.4]; *n*(%)	1 (1.0)
Hypnic Headache [4.9]; *n*(%)	2 (1.9)
New Daily Persistent Headache [4.10]; *n*(%)	1 (1.0)
Post-traumatic Headache [5.1]; *n*(%)	1 (1.0)
Headache attributed to whiplash [5.3]; *n*(%)	1 (1.0)
Headache attributed to giant cell arteritis [6.4.1]; *n*(%)	2 (1.9)
Headache attributed to spontaneous intracranial hypotension [7.2.3]; *n*(%)	1 (1.0)
Medication-overuse Headache; *n*(%)	9 (8.6)
Headaches attributed to disorder of the neck [11.2]; *n*(%)	2 (1.9)
Headaches attributed to temporomandibular disorder [11.7]; *n*(%)	3 (2.9)
Occipital neuralgia [13.4]; *n*(%)	1 (1.0)

SD: standard deviation; NPRS: numeric pain rating scale.* patients may have been diagnosed with multiple headache types.

Results

Study population

In total, 125 patients participated in this study, of whom 20 were excluded based on missing data. Of the included 105 patients, 82 were female (Table 5.2). The mean headache pain intensity was 7.7 (±1.3). The neurologist diagnosed 55 migraines, 36 TTHs and 29 other headaches (Table 5.2). Five patients with the diagnosis medication-overuse headache were also diagnosed with migraine. Three other patients with medication-overuse headache were also diagnosed with TTH.

Content validity

The questionnaire consisted of 10 items corresponding to the ICHD-3 beta A, B, C, and D criteria for migraine and TTH. To optimize face validity, the feedback from the headache expert (DG) resulted in adjusting question 3 to improve the accuracy of headache frequency by changing how many 'times' to how many 'days' they have experienced a headache. The content validity was established, as all the questions from the HSQ-DV and HSQ-EV are a direct derivative off the ICHD-3 beta criteria. The ICHD-3 beta criteria and the corresponding question numbers of the HSQ-DV are shown in Table 5.1. The final 10-item version of the HSQ-EV can be found in Appendix 5.1.

Table 5.3: Sensitivity, specificity, positive and negative likelihood ratios of questionnaire diagnostic performance of the HSQ-DV for migraine and probable migraine compared to the diagnosis of the neurologist.

		HSQ-DV			Sens (95%CI)	Spec (95%CI)	LR+	LR-
		Migraine	**No Migraine**	***Total***				
Neurologist	Migraine	38	17	55	.69 (.55 - .80)	.90 (.77 - .96)	6.91	.34
	No Migraine	5	45	50				
	Total	43	62	105				

		'Probable' HSQ-DV			Sens (95%CI)	Spec (95%CI)	LR+	LR-
		Migraine	**No Migraine**	***Total***				
Neurologist	Migraine	49	6	55	.89 (.77 - .95)	.54 (.39 - .68)	1.94	.20
	No Migraine	23	27	50				
	Total	72	33	105				

HSQ-DV score = 8 points; "probable" HSQ-DV score ≥ 6 points; Sens: sensitivity; Spec: specificity; CI: Confidence Interval; LR+: positive likelihood ratio; LR-: negative likelihood ratio.

Criterion validity

For migraine, there was a moderate overall agreement between the ICHD-3 beta diagnoses and the HSQ-DV of 79.0% (K=.585; p=.000).[39] The concomitant sensitivity is .69 and the specificity is .90. For a diagnosis of probable migraine (≥6 points), the overall agreement dropped to 72.4% (moderate kappa value; K=.438; p=.000) [39] with a sensitivity of .89 and specificity of .54 (Table 5.3).

For TTH, the overall agreement between the diagnosis of the neurologist based on the ICHD-3 beta criteria and the HSQ-DV was 68.6%. The kappa value between the two diagnoses was fair (K=.237; p=.011).[39] The sensitivity was .36, and the specificity was .86. For the recognition of a probable TTH (≥6 points), the overall agreement was 62.9% with a fair kappa value (K=.324; p=.000).[39] The sensitivity was .92, and the specificity was .48 (Table 5.4).

The PPV and NPV for both the study population in the headache clinic and the general population are depicted in Table 5.5.

Table 5.4: Sensitivity, specificity, positive and negative likelihood ratios of questionnaire diagnostic performance for TTH and probable TTH compared to the diagnosis of the neurologist.

		HSQ-DV			Sens (95%CI)	Spec (95%CI)	LR+	LR-
Neurologist		**TTH**	**No TTH**	***Total***				
	TTH	38	17	55	.36 (.21 - .54)	.86 (.74 - .92)	2.49	.75
	No TTH	5	45	50				
	Total	43	62	105				

		'Probable' HSQ-DV			Sens (95%CI)	Spec (95%CI)	LR+	LR-
Neurologist		**TTH**	**No TTH**	***Total***				
	TTH	49	6	55	.92 (.76 - .98)	.48 (.36 - .60)	1.76	.17
	No TTH	23	27	50				
	Total	72	33	105				

HSQ-DV score = 8 points; "probable" HSQ-DV score ≥ 6 points; TTH: tension-type headache; Sens: sensitivity; Spec: specificity; CI: Confidence Interval; LR+: positive likelihood ratio; LR-: negative likelihood ratio.

Table 5.5: Sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) for combinations of HSQ-DV outcomes in relation to headache diagnosis made by neurologist.

	Sensitivity	Specificity	General Population [a]		Headache Clinic [b]	
			PPV	**NPV**	**PPV**	**NPV**
Migraine	0.69	0.90	0.46 - 0.66	0.96 – 0.91	0.88	0.73
Probable Migraine [c]	0.89	0.54	0.35 – 0.60	0.95 – 0.86	0.68	0.82
TTH	0.36	0.86	0.53 – 0.65	0.75 – 0.65	0.57	0.72
Probable TTH [d]	0.92	0.48	n/a	n/a	0.48	0.92

[a] With prevalence range for general practice 11%-22% for migraine and 31%-42% for TTH.
[b] With a prevalence for migraine of 52.4% and a prevalence for TTH of 34.3%.
[c] With an estimation of double the prevalence of strict migraine: 22%-44% for general practice.
[d] Prevalence is unknown for general practice.
n/a: not applicable.

Clinical utility

A group of 10 PTs received the HSQ-DV to establish the face value clinical utility. The length of the questionnaire and algorithms were seen as positive attributes, provided that the questionnaire is available.

Discussion

In this study the 10-item Headache Screening Questionnaire for migraine and TTH was constructed in both English (HSQ-EV) and Dutch (HSQ-DV) based on the ICHD-3 beta criteria. As the HSQ-DV was in part a literal translation of the ICHD-3 beta criteria, the questions reflect the construct that was measured (migraine and TTH) well for content validity. The criterion validity was established for two cut-off points per headache: ≥6 points (probable migraine or probable TTH) or 8 points (migraine or TTH). The criterion validity was moderate for probable migraine and migraine, and fair for probable TTH and TTH.

The sensitivity to recognize migraine with the HSQ-DV using a full score of 8 points was .69 and the specificity was .90. When applying a cut-off point of ≥6 points, the sensitivity increased to .89 and the specificity decreased to .54. Since a screening tool primarily aims to recognize the patients with the disorder of interest, a high sensitivity is preferred over high specificity.[42] Therefore, the cut-off point of ≥6 is recommended to use when screening for migraine in the clinical practice. With this cut-off point, the HSQ-DV performed well in excluding people who do not have migraine because the NPV of the HSQ for migraine is .82, and the LR- is .20. With a cut off value of ≥6 point on the HSQ-DV, most people with migraine were accurately detected, even though the lower PPV (.68) indicates that also quite some patients with headache are incorrectly suspected of having migraine.

To recognize TTH with the HSQ-DV, the sensitivity using a full score of 8 points was .36 and the specificity was .86. When applying a cut-off point of ≥6 points, the sensitivity increased to 0.92 and the specificity decreased to .48. The use of ≥6 points is favourable when screening for TTH in the clinical practice, as the sensitivity is higher than for the full 8 points.[42] The HSQ-DV also performed well in excluding people who do not have TTH, because the NPV is .92 and the LR- is .17. All of these findings indicate that most people with TTH were accurately detected with a cut off value of ≥6 point on the HSQ-DV. However, there may also have been some patients with headache who were incorrectly suspected of having a TTH, indicated by a low PPV (.48).

This study was performed in a headache clinic in the Netherlands, where the female gender was predominant, and the mean age was 40.3 years. These findings are similar to other studies.[43] In this study, 64.8% was married or living with their partner, compared to 69.0% in the general Dutch population.[3] Within this study, 59.0% went through higher education and 38.1% did not meet this educational level. However, most studies report

the opposite.[44] It is important to note that the prevalence of a specific headache in the headache clinic is different from the prevalence of a specific headache in the general population or PT practice. In a higher prevalence population, a test is more likely to be positive and is therefore not always a good representation of the general population. In this study, we compared the headache clinic with the general population to show the change in PPV/NPV when the prevalence changes. When we extrapolated our findings to the general population for the PPV and NPV (Table 5.5), the PPV for migraine decreased. In this study, 52.4% was diagnosed with a migraine by the neurologist, whereas the prevalence of migraine in the general population is between 11-22%.[1,3] For TTH, the findings in the headache clinic (34.3%) are comparable to the general population (31-42%).[1,3] However, within the PT practice, the HSQ-DV will only be used in patients with headaches and it is reasonable to assume that the prevalence of migraine and TTH will be higher in the PT practice than in the general population. We therefore recommend considering the population in which the HSQ-DV is used, before interpreting the results.

Due to the absence of specific and distinguishing features, TTH is a difficult headache to diagnose and often diagnosed by exclusion.[45,46] Within this study, similar to validating headache questionnaire studies,[34,47] the headache specialist's diagnosis was seen as the gold standard. This can be debated for two reasons: 1. the wide clinical spectrum of TTH (i.e. diversity of symptoms, frequency and intensity) frequently challenges the physician's diagnostic judgement[46,48] and 2. the ICHD-3 beta system provides the gold standard based on both empirical evidence and clinical experience.[49] A patient might have TTH according to the HSQ-DV, based on the ICHD-3 beta criteria, but clinically shows different features to which the headache specialist diagnoses another headache, applying criterion D from the ICHD-3 beta, which states 'that the headache may not be better accounted for by another ICHD-3 diagnosis'. The HSQ-DV, however, did not use this criterion in order to include more headaches. Therefore, it is important for PTs to use the outcome of the HSQ-DV as an indication for the presence of migraine or TTH, and continue their diagnostic process to confirm or reject their differential diagnoses. This is especially important for TTH, as the HSQ-DV shows a high number of false positives. The results from a recently published Delphi round show the recommended physical examination tests for different types of headache within the PT practice.[27] The outcome of the HSQ-DV combined with these tests, can result in patient specific treatment plans.

Within this study no discrimination was made between episodic and chronic migraine, nor between infrequent, frequent or chronic TTH. If a healthcare provider is interested in the specific subtype of migraine or TTH with regard to its frequency, question 3 ('how many days per month do you have a headache') can be used. Based on the HSQ and physical examination outcomes, a PT can discuss with the patient, by shared decision making [50], if the headache diagnosis of a headache specialist is needed.

For migraine the findings of this study are similar to other screening questionnaires.[33,51,52] An English 3-item screening questionnaire showed a sensitivity of 81% and a specificity of 75%.[33] This screening questionnaire only included disability, nausea and sensitivity to light items from the ICHD-II criteria. A Spanish 5-item screening questionnaire for migraine showed a sensitivity of 93% and a specificity of 81% when 4 of the 5 items were positive.[52] This questionnaire, however, did not completely use items from the ICHD-II criteria, but more general questions such as: "Do you have frequent or intense headaches?". Deviating from the exact ICHD-II wording negatively impacted on the content validity of this questionnaire in our opinion.

After the development of the HSQ, a German 22-item questionnaire was discovered, which is very similar to the HSQ-DV. The German questionnaire consists of 7 items for migraine, 7 items for TTH and 6 items for trigeminal autonomic cephalgias. The migraine component showed a sensitivity of 73% and a specificity of 96%. The TTH part showed a sensitivity of 85.0% and a specificity of 98.2%.[51] Even though the German questionnaire shows better overall validity, it was created for research purposes and may therefore not be applicable in the clinical setting, whereas the HSQ-DV was developed for clinical use and the clinical utility tested on face value. For use in clinical practice, a high sensitivity is preferred[42] and the HSQ-DV has a higher sensitivity when using cut-off point of ≥6 points than the German questionnaire.

The HSQ-DV is a short 10-item screening tool that can be used by PTs, but also by other health care providers. A study performed in 15 countries looked into the overlap between the diagnosis 'migraine' given by a family practitioner (FP) and given by an expert panel based on the ICHD-II criteria.[53] This study showed that of the patients diagnosed with migraine by the FP, 97% fulfilled the criteria according to the ICHD-II. However, of the patients diagnosed with a non-migraine primary headache by the FP, 48% fulfilled the criteria for migraine. This shows that screening by a FP may lead to an underestimation of migraine.[53] Using the validated HSQ-DV may increase the number of accurately recognized migraineurs, as the HSQ-DV only missed 10.9% of the migraineurs, when applying the ≥6 points cut-off, compared to the 48% the FP missed.

Limitations and strengths of this study

A limitation of this study is that the HSQ-DV was validated in a headache clinic where no PT was present, whereas the intention of the HSQ-DV is to be used in a clinical setting such as a PT practice. However, the clinical utility and usability in a patient population has been established through field-testing, which created the opportunity to compare the results of the HSQ-DV with the diagnosis of the neurologist. The usability of the HSQ-DV as a screening tool in the PT practice, however, still needs to be established in future research.

Another limitation of the study is the use of convenience sampling, which may have led to selection bias of the participants.

One of the strengths of this study is the use of the six steps of development of a measurement instrument to create the HSQ-DV.[35] Another strength is that the questionnaire is based on the validated criteria for migraine and TTH as described in the ICHD-3.[17]

Implications for future research

Future research is needed to test the clinical utility of the HSQ-DV in the PT practice. For this we propose a mixed-methods study including a decision model for comparing three strategies (a test-and-treat strategy, a treat-all strategy, and a wait-in-all strategy) and the experiences of the PT using the HSQ-DV.[54] Therefore, we will perform further research to validate the HSQ-DV and HSQ-EV in PT practice.

Implications for practice

We expect that with the HSQ-DV or HSQ-EV and associated algorithm, PTs are facilitated to screen for the presence of migraine and/or TTH and adjust their clinical examination and treatment plan to the findings.

In conclusion, the HSQ-DV can be used as a screening tool for the recognition of probable migraine (sensitivity .89) and probable TTH (sensitivity .92) by PTs and other health care providers. Physical examination tests for migraine, TTH or other musculoskeletal headaches need to be performed to optimize a personal treatment plan.

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Appendix 5.1. Headache Screening Questionnaire – English Version

1 How often in your life have you had a headache?
- o 1 – 4 times
- o 5 – 9 times
- o ≥ 10 times

2 Looking back at the last question, how often would you describe those headache moments as a headache-attack?
- o 0 – 4 times
- o 5 – 9 times
- o ≥ 10 times

3 How many days per month do you have headaches?
- o < 1 per month
- o ≥1 - <15 per month
- o ≥15 per month

4 How long does your headache last when you do not take any medication?
- o 0 - 30 minutes
- o 30 minutes - 4 hours
- o 4 hours – 3 days
- o 3 – 7 days
- o >7 days

5 What word would you use to describe your headache?
- o Pulsating feeling
- o Tight or pressing feeling
- o Burning or stabbing feeling
- o Other, such as…….

6 Is your headache one-sided or two-sided in nature?
- o One-sided
- o Two-sided

7 Describe the severity of your headache
- o Mild
- o Moderate
- o Severe
- o Very severe

Indicate by the following statements if these are applicable to you when you have a headache.

8 Daily activities (such as climbing stairs or walking) make my headache worse.
- ○ Yes
- ○ No

9 I avoid daily activities when I have a headache.
- ○ Yes
- ○ No

10 Describe what you experience during your headache (multiple answers possible).
- ○ Sensitivity to light
- ○ Sensitivity to sound
- ○ Nausea and/or vomiting
- ○ None of the above
- ○ Other, such as ……..


6

Chapter 6

The diagnostic accuracy of headache measurement instruments: A systematic review and meta-analysis focusing on headaches associated with musculoskeletal symptoms

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Aim:
To systematically review the available literature on the diagnostic accuracy of questionnaires and measurement instruments for headaches associated with musculoskeletal symptoms.

Design:
Articles were eligible for inclusion when the diagnostic accuracy (sensitivity / specificity) was established for measurement instruments for headaches associated with musculoskeletal symptoms in an adult population. The databases searched were PubMed [1966-2018], Cochrane [1898-2018] and Cinahl [1988-2018]. Methodological quality was assessed with the QUADAS-2 and COSMIN checklist for criterion validity. When possible, a meta-analysis was performed. The GRADE recommendations were applied to establish the level of evidence per measurement instrument.

Results:
From 3450 articles identified, 31 articles were included in this review. Eleven measurement instruments for migraine were identified, of which the ID-Migraine is recommended with a moderate level of evidence and a pooled sensitivity of 0.87 (95%CI: 0.85-0.89) and specificity of 0.75 (95%CI: 0.72-0.78). Six measurement instruments examined both migraine and tension-type headache and only the Headache Screening Questionnaire – Dutch version has a moderate level of evidence with a sensitivity of 0.69 (95%CI 0.55-0.80) and specificity of 0.90 (95%CI 0.77-0.96) for migraine, and a sensitivity of 0.36 (95%CI 0.21-0.54) and specificity of 0.86 (95%CI 0.74-0.92) for tension-type headache. For cervicogenic headache, only the cervical flexion rotation test was identified and had a very low level of evidence with a pooled sensitivity of 0.83 (95%CI 0.72-0.94) and specificity of 0.82 (95%CI 0.73-0.91).

Discussion:
The current review is the first to establish an overview of the diagnostic accuracy of measurement instruments for headaches associated with musculoskeletal factors. However, as most measurement instruments were validated in one study, pooling was not always possible. Risk of bias was a serious problem for most studies, decreasing the level of evidence. More research is needed to enhance the level of evidence for existing measurement instruments for multiple headaches.

Abstract

Introduction

Primary headaches like tension-type headache (TTH) and migraine are associated with various musculoskeletal factors. TTH is, for example, associated with pericranial tenderness, myofascial trigger points and lower muscle coordination of the upper neck flexors.[1–4] Furthermore, migraine may be triggered by myofascial trigger points or bruxism.[1,5–7] These primary headaches are not caused by musculoskeletal disfunction, but are associated with different musculoskeletal symptoms.[8] There are several secondary headaches that are actually caused by musculoskeletal problems, such as cervicogenic headache (CGH), headache after whiplash trauma and secondary headache attributed to temporomandibular dysfunction (TMD).[8] The physiotherapist (PT) is a specialist in the musculoskeletal field, and often treats patients with headaches associated with musculoskeletal symptoms . The type of headache must be diagnosed within the physiotherapeutic diagnostic process to choose the proper treatment options and collaborate with medical specialists when needed.[9]

The International Headache Society (IHS) published the International Classification of Headache Disorders – 3rd edition (ICHD-3) which contains clear diagnostic criteria for all types of headache.[8] Several headache measurement instruments are developed for PTs and other health care professionals to classify different headache types.[10–14] The ability of a test to discriminate between the target condition and health or not having the target condition, is called the diagnostic accuracy of the test.[15] The diagnostic accuracy is often quantified through measures of sensitivity and specificity.[15] Insight in the diagnostic accuracy, of these instruments for headaches associated with musculoskeletal symptoms is needed to determine the type of headache. Currently there is, to our knowledge, no overview of diagnostic accuracy of the different headache measurement instruments related to the level of evidence. Therefore, the aim of this study was to systematically review the available literature on the diagnostic accuracy of questionnaires and measurement instruments for headaches associated with musculoskeletal symptoms.

Methods

Protocol and registration

This review has been performed according to the PRISMA statement[17] and registered in PROSPERO (registration number: CRD42017062472). Due to the magnitude of articles found within the original search strategy, there were two review questions created. The focus of the current review is the diagnostic accuracy of measurement instruments for headaches associated with musculoskeletal symptoms. A second review (*in preparation*) will focus on the clinimetric properties of the instruments that measure other outcomes, based on the International Classification of Functioning, Disability and Health.[16] For

example, measurement instruments for pain, range of motion, limitations in activity and quality of life.

Eligibility criteria

Only full text original articles were included concerning the diagnostic accuracy, expressed in sensitivity and specificity, of diagnostic headache tests usable for PTs. Further inclusion criteria were: 1) adult patients (≥18 years) and 2) patients experienced headaches associated with musculoskeletal symptoms. These include migraine, TTH, CGH, headache after whiplash and headache attributed to TMD.[8,19,20] There was no minimum sample size for inclusion. No restrictions were put on the year of publication. Intervention studies, prediction models and measurement instruments not useable for PTs (e.g. imaging, nerve blocks)[21] were excluded. Only English articles were included.

Information sources

The electronic databases PubMed [1966 – 2018], Cochrane [1898 – 2018] and Cinahl [1988 – 2018] were searched for literature. The last search was performed on October 25th of 2018. If full texts could not be obtained, the corresponding author was contacted through email to request full text.

Search

The search strategies included search terms for the construct (e.g. pain, diagnosis), the target population (e.g. migraine, TTH), the instrument (e.g. questionnaire, test) and the methodological PubMed search filter for measurement instruments.[21] The search filters for the Cochrane and Cinahl databases were derivatives from the PubMed search filter. The full search strategies for each database can be found in Appendix 6.1. References of retrieved articles were screened for additional relevant studies.

Study selection

Two reviewers (HvdM, CMV) independently assessed titles, abstracts and reference lists of the studies, using the online program Covidence.[22] In case of disagreement between the two reviewers, a third reviewer (CMS) made the decision regarding inclusion of the article. After initial screening of the titles and abstracts, HvdM and CMV read the full texts of included articles and screened these for eligibility. All reviewers are orofacial physiotherapists and researchers in this field.

Data collection process

Two reviewers (HvdM, CMS) independently extracted data from the included articles and registered this in a pre-made, empty Table 1 format. The data extracted were: first author, year of publication, target population, information about the index test (aim, language and name), reference test, study population, diagnostic accuracy (sensitivity / specificity).

Risk of bias in individual studies

The methodological quality of the included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies tool (QUADAS-2).[23,24] This tool assesses the risk of bias within four domains: patient selection, index test, reference standard, and flow and timing.[24] Concerns regarding applicability were also determined for the first three domains.[24] Methodological quality of studies regarding the criterion validity was assessed using the COSMIN checklist.[25] Criterion validity is defined as the degree to which the scores of an instrument are an adequate reflection of a gold standard.[26] Within diagnostic accuracy, criterion validity is an essential measurement property. For criterion validity, box H of the COSMIN was used.[25]

Data extraction and assessment of methodological quality were performed by two reviewers independently (HvdM, CMS). HvdM was trained to use the QUADAS-2 tool and CMS was trained by the COSMIN team on quality appraisal and data extraction. The protocol for methodological assessment using the QUADAS-2 tool for this review was made available for the review authors (Appendix 6.2). The protocol for the COSMIN checklist is published elsewhere.[25]

Summary measures

Sensitivity and specificity were used as measures of diagnostic accuracy.

Synthesis of results

A best evidence synthesis was performed using the GRADE recommendations for diagnostic accuracy studies with the GRADE pro online software.[27] These recommendations provide a step-by-step assessment to determine the certainty of evidence of a diagnostic test, which results in a comprehensive and transparent approach for developing the recommendations for these tests. To determine the impact of the test, both sensitivity and specificity of the test must be known as well as the prevalence of the target condition.[27] Based on the prevalence of the target population, the pre-test probability of the presence of the headache was determined for a population of 1.000 people.[27] The test sensitivity and specificity was used to determine how many people would be accurately diagnosed (true positive) or excluded from having the headache (true negative).

A pooled sensitivity and specificity were used for each measurement instrument when there were multiple studies for one measurement tool. The pooled measurements were calculated using the 'rmeta' package for the R statistical software.[28] A bivariate model resulting in a summary estimate for sensitivity and specificity together was used, as recommended by the Cochrane Collaboration.[29,30] This model takes potential threshold effects and the correlation between sensitivity and specificity into account.[29,30] The pooled sensitivity and specificity were used for the GRADE recommendations. When there was

only one study for a measurement instrument, the published sensitivity and specificity of that measurement instrument were used. Finally, a summary receiver operating characteristics (S-ROC) curve was created using the 'mada' package for the R statistical software.[29,31,32]

Factors determining the quality of evidence according to the GRADE approach are: 1) limitations in study design or execution (risk of bias); 2) inconsistency of results; 3) indirectness of evidence; 4) imprecision; and 5) publication bias.[27] For limitations, the risk of bias assessment from the QUADAS-2 was used to determine if downgrading of the evidence was needed. When ≥50% of the assessed domains scored a 'high' or 'unclear' risk of bias, this was considered 'serious' and the level of evidence was downgraded by one. When ≥75% of the assessed domains scored a 'high' or 'unclear' risk of bias, this was considered 'very serious' and the level of evidence was downgraded by two. Inconsistency refers to unexplained heterogeneity of the results between multiple studies, after which the level of evidence may be downgraded. The indirectness of evidence was determined by the applicability assessment of the QUADAS-2 tool with the same rules as the risk of bias assessment. In case of only one article studying a measurement tool, the evidence was downgraded for imprecision. All steps of the synthesis of results are depicted in Figure 6.1.

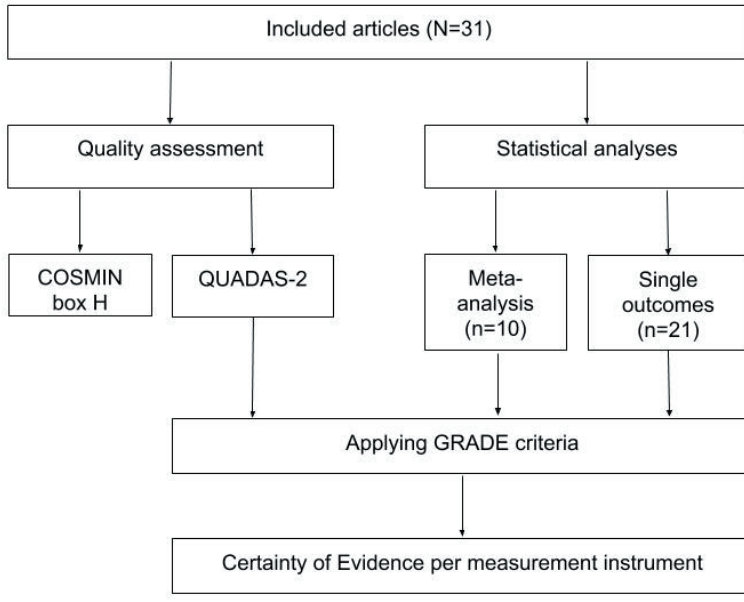

Figure 6.1: Flowchart of the steps taken in this review after inclusion.

Risk of bias across studies

Methods to detect publication bias are not very reliable in diagnostic accuracy studies.[30] As diagnostic accuracy studies have sensitivity and specificity values as outcome measures rather than a stated null hypothesis with a p-value, it is unlikely for publication bias to be associated with statistical nonsignificance.[33] Therefore, no publication bias assessment was applied in this review.

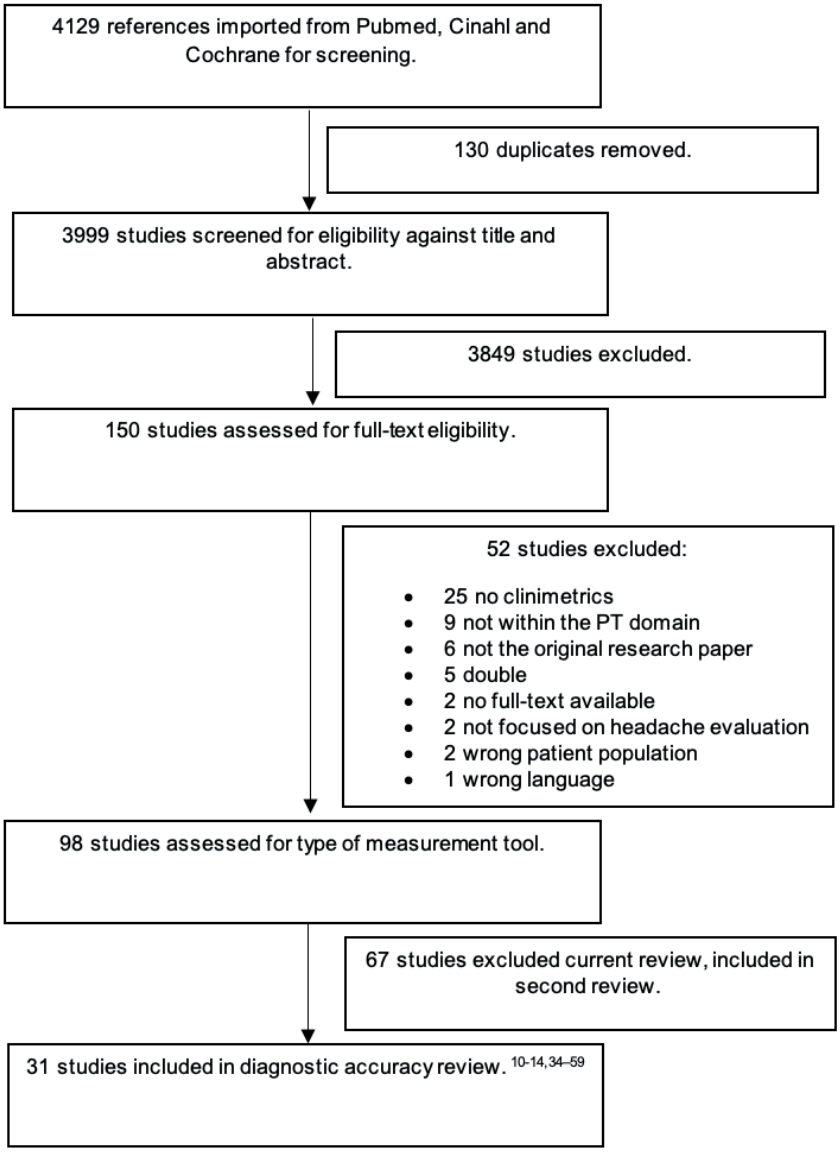

Figure 6.2: Flowchart of the study.

Results

Study selection

The search in all three databases resulted in 4129 articles which were imported in Covidence.[22] After removing duplicates and assessment of eligibility on title/abstract, 150 articles remained to be assessed full text. Of these, 52 articles were excluded based on the in- and exclusion criteria (Appendix 6.3) and 67 articles assessed other clinimetric outcome measures than diagnostic accuracy. These 67 articles will be included in the second review regarding clinimetric outcome measures based on the ICF. This resulted in 31 articles to be included in the current review. The complete flowchart of the study selection can be found in Figure 6.2. No authors were contacted to obtain the full-texts of any study.

Study characteristics

The included headaches associated with musculoskeletal symptoms in this review are migraine, TTH and CGH. No measurement instruments were found that studied the diagnostic accuracy for instruments related to secondary headache attributed to TMD or headache attributed to whiplash injury. Table 6.1 shows the study characteristics of the 31 included studies, stratified by target population of the measurement instrument. From the 31 studies, 22 articles had migraine as the target population.[10-12,34–51] Seven articles had both migraine and TTH as target population,[13,14,52–56] and two articles examined patients with CGH.[57,58] A total of 28,246 people were included in the 31 studies. Of the included population, 64% was female, though three articles did not describe the gender distribution.[38,54,55] Mean age varied from 19[42] to 52 years.[53]

For migraine, 11 different measurement instruments were studied.[10-12,34–37,40–43,44–51,59] ID-Migraine was the most studied measurement instrument with nine studies in five languages.[12,34,40,44–47,49,50] Eight of these instruments were screening instruments, one was a replacement test for the diagnostic process and for two instruments the aim of the test was unclear. Out of the seven studies for both migraine and TTH, only two articles looked at the same questionnaire.[13,56] From the seven instruments, one was a screening test, three were replacement tests and of two the aim was unclear. Both studies on CGH researched the cervical flexion-rotation test (CFRT).[57,58] The aim of the CFRT compared to the ICHD-3 criteria for cervicogenic headache is unclear.

Table 6.1: Study characteristics of included articles stratified for the target populations of patients with Migraine, Migraine & Tension-Type Headache and Cervicogenic Headache.

Measurement instrument	Author, year	Index Test		Reference Test	Population		Diagnostic accuracy	
		Language of index test	Aim of index test		N (%F)	Age; mean±SD	Sensitivity	Specificity
Target population: Migraine								
3 Question Screen	† Cady, 2004[10]	English	Triage	ICHD[2]	3014 (85.2)	40.0± -	0.78*	0.27*
	Pryse-Phillips, 2002[59]	English	Triage	Neurologist	476 (81.9)	40.4± -	0.86	0.73
	† Wahab, 2016[41]	English	Triage	ICHD-3[15]	1513 (50.1)	23.3±2.5	0.66	0.98
Diagnostic screen	Michel, 1993 (II)[37]	English	Triage	Neurologist	160 (83.3)	39.9±0.7	0.44	0.93
ID- Migraine	Brighina, 2006[44]	Italian	Triage	ICHD-II[4]	222 (73.4)	37.8±11.0	0.95	0.72
	de Mattos, 2017[45]	Portuguese	Triage	ICHD-II[4]	232 (82.0)	48.9±11.2	0.92	0.60
	Ertas, 2008[46]	Turkish	Triage	ICHD-II[4]	2625 (58.5)	43.3-47.3 ±16-18	0.80 – 0.88	0.74 – 0.76
	† Gil-Gouveia, 2009[47]	Portuguese	Triage	ICHD-II[4]	142 (82.8)	39.2±13.9	0.94	0.60
	† Karli, 2007[49]	Turkish	Triage	ICHD-II[4]	3682 (62.9)	45.2±17.0	0.92	0.63
	Kim, 2006[50]	Korean	Triage	ICHD-II[4]	176 (81.2)	30.7±9.3	0.58	0.98
	Lipton, 2003[12]	English	Triage	ICHD[2]	451 (75.6)	39.3±10.1	0.81	0.75
	† Lipton, 2016[34]	English	Triage	ICHD-3[15]	111 (82.9)	46.2±13.4	0.81	0.89
	† Siva, 2008[40]	Turkish	Triage	ICHD-II[4]	227 (65.6)	31.9±5.9	0.71	0.79
MSMDQ	Rueda-Sanchez, 2004[38]	Spanish	Unclear	Neurologist	170 ()	-	0.38	0.99
Migraine Assessment Tool	Marcus, 200435	English	Triage	Neurologist	80 (88.8)	33.7±9.9	0.89	0.79
Migraine Screen Questionnaire	Láinez, 2005[11]	English	Triage	ICHD[2]	140 (73.0)	39.2±13.0	0.93	0.81
	Láinez, 2010[51]	English	Triage	ICHD-II[4]	9670 (61.9)	48.9±17.2	0.82	0.97
Migraine-specific questionnaire	Kallela, 2001[48]	Finnish	Triage	ICHD[2]	94 (71.3)	44.6±18.0	0.99	0.96
Migraine-4	Walters, 2015[42]	English	Triage	ICHD-3[15]	1829 (71.5)	19.1±2.1	0.94	0.92
Modified Algorithm for IHS Migraine	Michel, 1993 (I)[36]	English	Replacement	Neurologist	267 (70.3)	-	0.95 – 0.98	0.53 – 0.78
Screening items	Wang, 2008[43]	-	Triage	ICHD-II[4]	755 (71.0)	37±15	0.89*	0.67*
Structured Migraine Interview Questionnaire	Shaik, 2015[39]	Malay	Unclear	ICHD-II[4]	157 (100)	26.8±8.3	0.97	0.63

Table 6.1: Continued.

Measurement instrument	Author, year	Index Test		Reference Test	Population		Diagnostic accuracy	
		Language of index test	Aim of index test		N (%F)	Age; mean±SD	Sensitivity	Specificity
Target population: MMigraine and tension-type headache								
Computerized Headache Assessment Test	Maizels, 2007[54]	English	Replacement	Headache nurse	117 (-)	-	M: 0.83-1.00 TTH: 1.00	- -
German language questionnaire	† Fritsche, 2007[13]	German	Replacement	ICHD-II[4]	278 (51.1)	43.9± -	M: 0.73 TTH: 0.85	M: 0.96 TTH: 0.98
	† Yoon, 2008[56]	German	Replacement	ICHD-II[4]	193 (68.4)	45.4±12.4	M: 0.85 T: 0.60	M: 0.85 T: 0.88
Headache Screening Questionnaire – Dutch version	van der Meer, 2017[14]	Dutch	Triage	ICHD-3[15]	105 (78.1)	40.3±14.5	M: 0.69 PM: 0.89 TTH: 0.36 PTTH: 0.92	M: 0.90 PM: 0.54 TTH: 0.86 PTTH: 0.48
Headache questions	Hagen, 2010[53]	Norwegian	Unclear	ICHD-II[4]	297 (49.0)	52.3± -	M:0.49-0.67 TTH: 0.96 CT: 0.64	M: 0.91-0.95 TTH: 0.69 CTTH: 1.00
Self-administered headache questionnaire	Rasmussen, 1991[55]	Danish	Replacement	Neurologist	713 (-)	-	M: 0.51 TTH: 0.43	M: 0.92 TTH: 0.96
Structured Headache Questionnaire	el-Sherbiny, 2017[52]	Arabic	Unclear	ICHD-3[15]	232 (72.8)	41.2±10.9	M: 0.86 CM: 0.71 TTH: 0.93 CTTH: 0.70	M: 0.94 CM: 0.98 TTH: 0.93 CTTH: 0.96
Target population: MMigraine and tension-type headache								
Cervical Flexion-Rotation Test (CFRT)	† Hall, 2010[57]	n/a	Unclear	Sjaastad criteria[32]	60 (63.3)	30-35 ± 6.5-10.9	0.70	0.70
	† Ogince, 2007[58]	n/a	Unclear	Sjaastad criteria[32]	58 (65.5)	37-46 ± -	0.91	0.91

* Not given in article therefore calculated based on the published 2x2 table. † Articles included in meta-analysis as shown as in Table 6.3.
MSMDQ: Michel's Standardized Migraine Diagnosis Questionnaire; - missing data; F: female; SD: standard deviation; M: migraine; CM: chronic migraine; PM: probable migraine; TTH: tension-type headache; CTTH: chronic tension-type headache; PTTH: probable tension-type headache; n/a: not applicable.

Risk of bias within studies

The risk of bias was assessed for patient selection, index test, reference standard and flow and timing. The summarized assessment of the QUADAS-2 can be found in Table 6.2. The complete assessment including reasons for the given scores can be found in Appendix 6.4. Only one study received a low risk of bias on all domains.[43] Twenty-two articles received a 'high' risk of bias on ≥1 domain.[10-14,35,37,39–41,43,45–50,55–59] The remaining articles received an 'unclear' risk of bias on ≥1 domain. [12,35,37,41,50–53] Risk of bias for the index test and the reference standard was generally scored unclear, because there was uncertainty if the index test was conducted and interpreted without knowledge of the results of the reference standard.

The clinimetric evaluation of the criterion validity was established with the COSMIN Box H. One study scored excellent[14], one good[35], 21 fair[11,12,34,36–48,50–53,57] and the remaining eight scored poor[10,13,50,55–57,59]. Of the studies scoring poor, all but two[54,55] also scored a high risk of bias on ≥2 domains.[10,12,13,50,55,57,59]

Migraine Measurement Instruments

Results of individual studies

The sensitivity of the measurement instruments for migraine ranged from 0.38[38] to 0.99[48] (see Table 6.1). Only three studies had a sensitivity below 0.70[38,41,50] and eight studies found a sensitivity of 0.90 or higher.[11,39,42,44,45,47–49] Half of these studies with a high sensitivity were researching the ID-Migraine.[44,45,47,49] Specificity ranged from 0.27[10] to 0.99[37]. Six studies found a specificity of 0.70 or lower,[10,39,43,45,47,49] and a specificity above 0.90 was found in six other studies.[38,41,42,48,50,51] Eleven studies had both sensitivity and specificity above 0.70,[11,12,34,35,40,42,44,46,48,51,59] of which two studies had both above 0.90.[42,48]

Table 6.2: Methodological Quality Assessment with QUADAS-2 and Clinimetric Evaluation of the Criterion Validity with the COSMIN checklist Box H.

Measurement instrument	Study	Risk of Bias				Applicability concerns			COSMIN Box H
		1a. Patient selection	2a. Index test	3a. Reference standard	4. Flow and timing	1b. Patient selection	2b. Index test	3b. Reference standard	
Target population: Migraine									
3 Question screen	Cady, 2004	High	Unclear	Unclear	High	Low	Low	Low	Poor
	Pryse-Phillips, 2002	High	Unclear	High	High	Low	Low	Low	Poor
	Wahab, 2016	Unclear	Unclear	Unclear	Low	Low	Low	Low	Fair
Diagnostic Screen	Michel, 1993 II	Unclear	Unclear	Unclear	High	Low	Low	Low	Fair
ID-Migraine	Brighina, 2006	Low	Low	Low	Low	Low	Low	Low	Fair
	de Mattos, 2017	High	Low	Low	Unclear	Low	Low	Low	Fair
	Ertas, 2008	High	Low	Unclear	Low	Low	Low	Low	Fair
	Gil-Gouveia, 2009	High	Low	Low	Low	Low	Low	Low	Fair
	Karli, 2007	High	Unclear	Unclear	High	Low	Low	Low	Poor
	Kim, 2006	Unclear	Low	Unclear	Low	Low	Low	Low	Fair
	Lipton, 2003	Unclear	Unclear	Low	Unclear	Low	Low	Low	Fair
	Lipton, 2016	High	Unclear	Unclear	Unclear	Low	Low	Low	Fair
	Siva, 2008	High	Low	Low	Unclear	Low	Low	Low	Fair
MSMDQ	Rueda-Sánchez, 2004	Low	Unclear	Unclear	High	Low	Low	Low	Fair
MAT	Marcus, 2004	Low	Low	Unclear	Low	Low	Low	Low	Good
Migraine Screen Questionnaire	Lainez, 2010	Low	Low	Unclear	Low	Low	Low	Low	Fair
	Lainez, 2005	High	High	Low	Unclear	Low	Low	Low	Fair
MSQ	Kallela, 2001	Low	Low	Unclear	High	Low	Low	Low	Fair
Migraine-4	Walters, 2015	Low	Unclear	Unclear	High	Low	Low	Low	Fair
MA-HIS-M	Michel, 1993 I	Unclear	Low	Low	Unclear	Low	Low	Low	Fair
Screening items	Wang, 2008	Unclear	Unclear	Unclear	High	Low	Low	Low	Fair
SMIQ	Shaik, 2015	High	Unclear	Unclear	Low	Low	Low	Low	Fair

Table 6.2: Continued.

Measurement instrument	Study	Risk of Bias				Applicability concerns			COSMIN Box H
		1a. Patient selection	2a. Index test	3a. Reference standard	4. Flow and timing	1b. Patient selection	2b. Index test	3b. Reference standard	
Target population: Migraine and tension-type headache									
CHAT	Maizels, 2007	High	Low	Unclear	Unclear	Low	Low	Low	Poor
German Language Questionnaire	Fritsche, 2007	High	Low	Low	High	Low	Low	Low	Poor
	Yoon, 2008	High	Low	Unclear	High	Low	Low	Low	Poor
HSQ-DV	van der Meer, 2017	Low	Low	Low	High	Low	Low	Low	Excellent
Headache questions	Hagen, 2010	Low	Unclear	Unclear	Unclear	Low	Low	Low	Fair
SAHQ	Rasmussen, 1991	Low	Low	High	Unclear	Low	Low	Low	Poor
SHQ	El-Sherbiny, 2017	Unclear	Low	Unclear	Unclear	Low	Low	Low	Fair
Target population: Cervicogenic headache									
Cervical Flexion-Rotation Test	Hall, 2010	High	Low	Unclear	Unclear	Low	Low	Low	Fair
	Ogince, 2005	High	Unclear	Unclear	High	Low	Low	Low	Poor

MSMDQ: Michel's Standardized Migraine Diagnosis Questionnaire; MAT: Migraine Assessment Questionnaire; MSQ: Migraine-specific questionnaire; MA-IHS-M; Modified Algorithm for IHS Migraine; SMIQ: Structured Migraine Interview Questionnaire; CHAT: Computerized Headache Assessment Test; HSQ-DV: Headache Screening Questionnaire – Dutch Version; SAHQ: Self-Administered Headache Questionnaire; Structured Headache Questionnaire. An extended version of this table including explanation of judgement can be found in Appendix 4.

Table 6.3: Pooled sensitivity and specificity of the 3-Question screen, ID-Migraine, German language questionnaire and Cervical Flexion-Rotation Test.

Measurement instrument	Target population	N of studies; author, year	Pooled sensitivity (95% CI)	Pooled specificity (95% CI)
3-Question screen	Migraine	2; Cady, 2004[10] Wahab, 2016[41]	0.73 (0.71 – 0.75)	0.93 (0.92 – 0.94)
ID-Migraine	Migraine	4; Lipton, 2016[34] Siva, 2008[40] Gil-Gouveia, 2009[47] Karli, 2007[49]	0.87 (0.85 – 0.89)	0.75 (0.72 – 0.78)
German language questionnaire	Migraine TTH	2;Fritsche, 2007[13] Yoon, 2008[56]	0.69 (0.63 – 0.75) 0.81 (0.75 – 0.87)	0.90 (0.86 – 0.94) 0.96 (0.94 – 0.98)
Cervical Flexion-Rotation Test	Cervicogenic Headache	2; Hall, 2010[57] Ogince, 2007[58]	0.83 (0.72 – 0.94)	0.82 (0.73 – 0.91)

N: number; CI: confidence interval; TTH: tension-type headache.

Synthesis of results

For two measurement instruments the sensitivity and specificity could be pooled. For the 3-question Screen the pooled sensitivity was 0.73 and specificity was 0.93 (Table 6.3) based on two[10,41] out of three studies, due to missing data in one article[59]. The pooled sensitivity for the ID-Migraine was 0.87 and specificity was 0.75 (Table 3, Figures 6.3a and 6.3b). The results were based on four studies,[34,40,47,49] as the other five studies[12,44–46,50] did not have sufficient data available to perform the analyses.

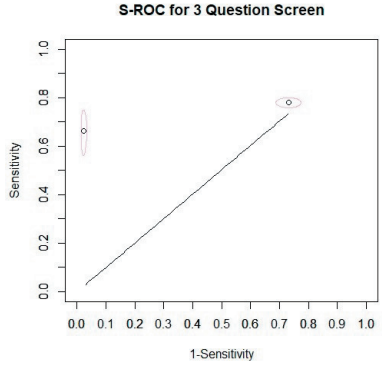

Figure 6.3a: S-ROC curve for 3 Question screen.

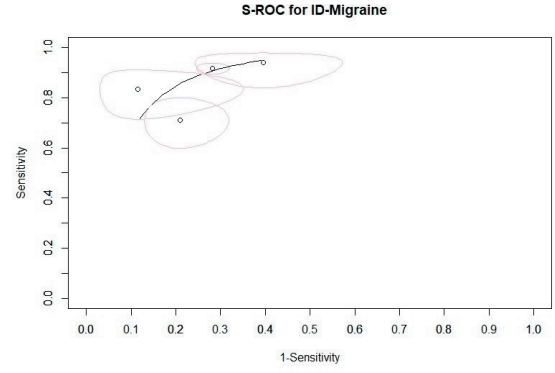

Figure 6.3b: S-ROC curve for the ID-migraine.

There was a very low level of evidence for six measurement instruments for migraine related to the GRADE recommendations: Diagnostic Screen,[37] Michel's Standardized Migraine Diagnosis Questionnaire,[38] Migraine Specific Questionnaire,[48] Migraine-4,[42] Modified Algorithm for IHS Migraine,[36] Screening Items,[43] and the Structured Migraine Interview Questionnaire (see Table 6.4).[39] For two measurement instruments, there was a low level of evidence: the 3-question Screen[10,41] and the Migraine Screen Questionnaire.[11,51] There

was a moderate level of evidence for the ID-Migraine[34,40,47,49] and also for the Migraine Assessment Tool.[35]

Combined migraine and TTH measurement instruments

Results of individual studies

The aim of the index tests differed between the included seven articles, where four 'replacement' tests,[13,54–56] one 'triage' test[14] and two aims were unclear.[52,53] Three articles established the diagnostic accuracy for several migraine and TTH ICHD diagnoses aside from the 'standard' diagnoses, including chronic migraine, chronic TTH, probable migraine, and probable TTH.[14,52,53] For migraine the sensitivity ranged from 0.49[53] to 1.00[54] and the specificity ranged from 0.85[56] to 0.96.[13] For chronic migraine the sensitivity and specificity were 0.71 and 0.98 respectively.[52] Probable migraine had a sensitivity of 0.89 and a specificity of 0.54.[14] The sensitivity for TTH ranged from 0.36[14] to 1.00[54] and the specificity range was 0.69[53] to 0.98.[13] One study did not establish the specificity results from their test.[54] Chronic TTH was tested in two studies, for which the sensitivity was 0.64[53] to 0.70[52] and the specificity 0.96[52] to 1.00.[53] The test for probable TTH had a sensitivity of 0.92 and a specificity of 0.48.[14]

For migraine, chronic migraine, and probable migraine[13,14,52,54,56] five studies had a sensitivity above 0.70, which was also found for TTH, chronic TTH, and probable TTH in five studies (see Table 6.1).[13,14,52–54] All six studies that reported specificity, had a specificity of 0.70 or higher for migraine, chronic migraine, and probable migraine and for TTH chronic TTH, and probable TTH.[13,14,52,53,55,56]

Table 6.4: GRADE recommendations for measurement instruments for target population Migraine, stratified per measurement instrument.

Measurement Instrument	Sensitivity (95% CI) / Specificity (95% CI)	Outcome	Nº of studies (Nº of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested*	Test accuracy CoE
					Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 14.7%*	
3-question screen[10,41,59]	**0.73 (0.71-0.75)‡**	**TP**	2 studies 2539 patients	cross-sectional (cohort type accuracy study)	serious±	not serious	serious	not serious	none	107 (104 to 110)	⊕⊕◯◯ LOW
		FN								40 (37 to 43)	
	0.93 (0.92-0.94)‡	**TN**	2 studies 1988 patients		serious±	not serious	serious	not serious	none	793 (785 to 802)	⊕⊕◯◯ LOW
		FP								60 (51 to 68)	
Diagnostic Screen[37]	**0.44 (0.35 – 0.53)**	**TP**	1 study 125 patients	cross-sectional (cohort type accuracy study)	very serious¥	not serious	not serious	serious×	none	65 (51 to 78)	⊕◯◯◯ VERY LOW
		FN								82 (69 to 96)	
	0.93 (0.85 – 1.00)	**TN**	1 study 41 patients		very serious¥	not serious	not serious	serious×	none	793 (725 to 530)	⊕◯◯◯ VERY LOW
		FP								60 (0 to 128)	
ID-Migraine [34,40,47,49]	**0.87 (0.85-0.89)‡**	**TP**	4 studies 1257 patients	cross-sectional (cohort type accuracy study)	serious±	not serious	serious	not serious	none	128 (125 to 131)	⊕⊕⊕◯ MODERATE
		FN								19 (16 to 22)	
	0.75 (0.72-0.78)‡	**TN**	4 studies 1109 patients		serious±	not serious	serious	not serious	none	640 (614 to 665)	⊕⊕⊕◯ MODERATE
		FP								213 (188 to 239)	
Michel's Standardized Migraine Diagnosis Questionnaire [38]	**0.38 (0.26-0.52)**	**TP**	1 study ? patients	cross-sectional (cohort type accuracy study)	very serious¥	serious	not serious	serious×	none	56 (38 to 76)	⊕◯◯◯ VERY LOW
		FN								91 (71 to 109)	
	0.99 (0.95-1.00)	**TN**	1 study ? patients		very serious¥	serious	not serious	serious×	none	844 (810 to 853)	⊕◯◯◯ VERY LOW
		FP								9 (0 to 43)	
Migraine Assessment Tool[35]	**0.89 (0.80-0.98)‡**	**TP**	1 study 46 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious×	none	131 (118 to 144)	⊕⊕⊕◯ MODERATE
		FN								16 (3 to 29)	
	0.79 (0.65-0.93)‡	**TN**	1 study 34 patients		not serious	not serious	not serious	serious×	none	674 (554 to 793)	⊕⊕⊕◯ MODERATE
		FP								179 (60 to 299)	
Migraine Screen Questionnaire [11,51]	**0.82 – 0.93**	**TP**	2 studies ? patients	cross-sectional (cohort type accuracy study)	serious±	serious [b]	not serious	not serious	none	121 to 137	⊕⊕◯◯ LOW
		FN								10 to 26	
	0.81 – 0.97	**TN**	2 studies ? patients		serious±	serious [b]	not serious	not serious	none	691 to 827	⊕⊕◯◯ LOW
		FP								26 to 162	

Table 6.4: Contineud.

Measurement Instrument	Sensitivity (95% CI) / Specificity (95% CI)	Outcome	Nº of studies (Nº of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested*	Test accuracy CoE
					Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 14.7%*	
Migraine Specific Questionnaire[48]	**0.99 (0.97-1.00)‡**	**TP**	1 study	cross-sectional (cohort type accuracy study)	serious±	serious	not serious	serious×	none	146 (143 to 147)	⊕○○○
		FN	69 patients							1 (0 to 4)	VERY LOW
	0.96 (0.88-1.00)‡	**TN**	1 study		serious±	serious	not serious	serious×	none	819 (751 to 853)	⊕○○○
		FP	25 patients							34 (0 to 102)	VERY LOW
Migraine-4[42]	**0.94 (0.87 – 0.98)**	**TP**	1 study	cross-sectional (cohort type accuracy study)	very serious¥	not serious	not serious	serious×	none	138 (128 to 144)	⊕○○○
		FN	? patients							9 (3 to 19)	VERY LOW
	0.92 (0.90 – 0.94)	**TN**	1 study		very serious¥	not serious	not serious	serious×	none	785 (768 to 802)	⊕○○○
		FP	? patients							68 (51 to 85)	VERY LOW
Modified Algorithm for IHS Migraine[36]	**0.95 – 0.98**	**TP**	1 study	cross-sectional (cohort type accuracy study)	serious±	serious	serious	serious×	none	144 to 144	⊕○○○
		FN	126 patients							3 to 7	VERY LOW
	0.53 – 0.78	**TN**	1 study		serious±	serious	serious	serious×	none	452 to 665	⊕○○○
		FP	141 patients							188 to 401	VERY LOW
Screening Items[43]	**0.89 (0.86-0.92)‡**	**TP**	1 study	cross-sectional (cohort type accuracy study)	very serious¥	not serious	not serious	serious×	none	131 (126 to 135)	⊕○○○
		FN	363 patients							16 (12 to 21)	VERY LOW
	0.67 (0.63-0.72)‡	**TN**	1 study		very serious¥	not serious	not serious	serious×	none	572 (537 to 614)	⊕○○○
		FP	392 patients							281 (239 to 316)	VERY LOW
Structured Migraine Interview Questionnaire[39]	**0.97 (0.94-1.00)‡**	**TP**	1 study	cross-sectional (cohort type accuracy study)	very serious¥	not serious	not serious	serious×	none	143 (138 to 147)	⊕○○○
		FN	100 patients							4 (0 to 9)	VERY LOW
	0.63 (0.50-0.76)‡	**TN**	1 study		very serious¥	not serious	not serious	serious×	none	542 (427 to 648)	⊕○○○
		FP	57 patients							316 (205 to 426)	VERY LOW

* Prevalence in the general population of 14.7% is used.65 CoE: certainty of evidence.
± 'Unclear' or 'high' risk of bias on ≥50<75% of the domains on QUADAS-2; ¥ 'Unclear' or 'high' risk of bias on ≥75% of the domains on QUADAS-2.
× Results based on the outcome of one single study. ‡95% confidence interval (CI) calculated by reviewers

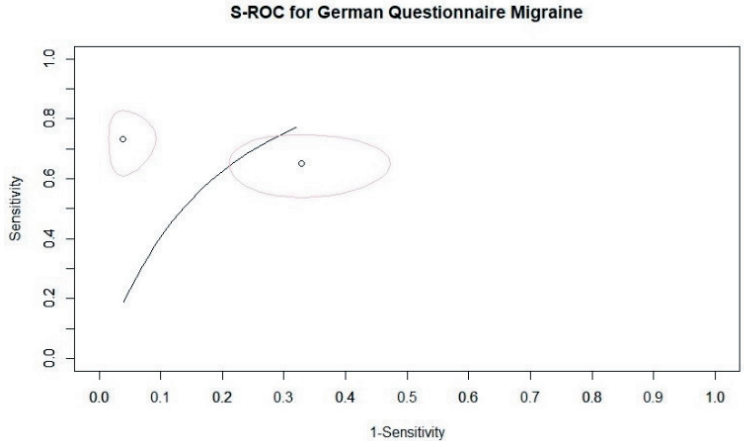

Figure 6.3c: S-ROC curve for the German Questionnaire for migraine.

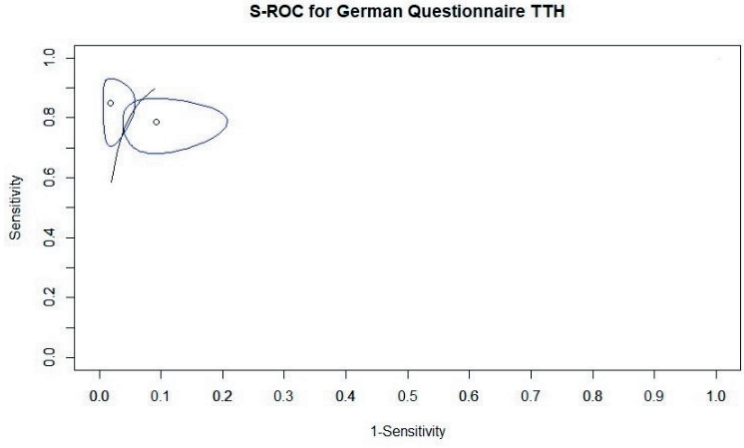

Figure 6.3d: S-ROC curve for the German Questionnaire for tension-type headache.

Synthesis of results

One instrument, the German Language Questionnaire, was supported by two studies.[13,56] The pooled sensitivity and specificity for migraine were 0.69 and 0.90 respectively (Table 6.3, Figure 6.3c). For TTH the pooled sensitivity and specificity were 0.81 and 0.96 respectively (Table 6.3, Figure 6.3d). The five other measurement instruments[14,52–55] were supported by one study and therefore downgraded for imprecision (see also Table 6.5).

There was a very low level of evidence for the Computerized Headache Assessment Test (CHAT),[54] the use of Headache Questions[53] and the Structured Headache Questionnaire.[52] The German Language Questionnaire[13,54] and the Self-Administered Headache Questionnaire[55] both are supported with a low level of evidence. Only the Headache Screening Questionnaire (HSQ)– Dutch Version was found to have a moderate level of evidence.[14]

Cervicogenic headache measurement instruments

Results of individual studies

The two included studies for CGH established the diagnostic accuracy of the Cervical Flexion-Rotation Test (CFRT).[57,58] Both sensitivity and specificity ranged from 0.70[57] to 0.91.[58]

Synthesis of results

The pooled sensitivity was 0.83 and the pooled specificity was 0.82 (Table 6.3, Figure 6.3e). Based on the GRADE recommendations (Table 6.6) there is a low level of evidence for the use of the CFRT for patients with cervicogenic headache.[57,58]

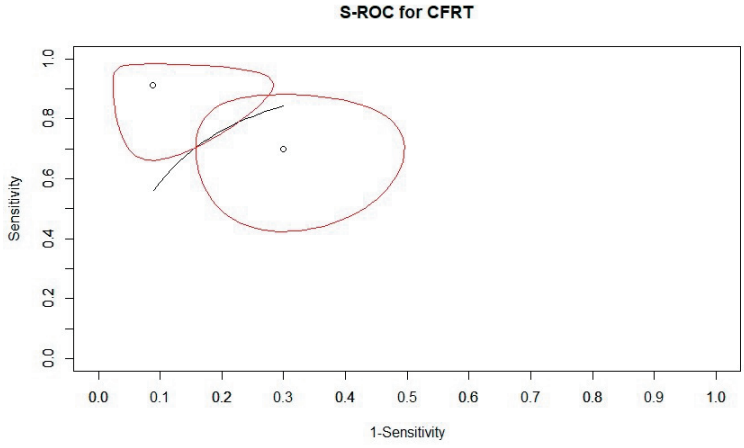

Figure 6.3e: S-ROC curve for the Cervical Flexion Rotation Test.

Table 6.5: GRADE recommendations for measurement instruments for target populations Migraine and Tension-Type Headache, stratified per measurement instrument.

Measurement Instrument	Target population	Sensitivity (95% CI) / Specificity (95% CI)	Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested*	Test accuracy CoE
						Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 14.7%* / 62.6%**	
Computerized Headache Assessment Test (CHAT)[54]	Migraine	**0.98**‡ **(0.93-1.00)**	**TP** **FN**	1 study 41 patients	cross-sectional (cohort type accuracy study)	very serious¥	serious	not serious	serious×	none	144 (137 to 147) 3 (0 to 10)	⊕◯◯◯ LOW
		1.00‡ **(1.00-1.00)**	**TN** **FP**	1 study 76 patients		very serious¥	very serious	not serious	serious×	none	853 (853 to 853) 0 (0 to 0)	⊕◯◯◯ LOW
	TTH	**1.00**‡ **(1.00-1.00)**	**TP** **FN**	1 study 14 patients		very serious¥	serious	not serious	serious×	none	626 (626 to 626) 0 (0 to 0)	⊕◯◯◯ VERY LOW
		1.00‡ **(1.00-1.00)**	**TN** **FP**	1 study 14 patients		very serious¥	very serious	not serious	serious×	none	374 (374 to 374) 0 (0 to 0)	⊕◯◯◯ VERY LOW
German Language Questionnaire[13,56]	Migraine	**0.69**‡ **(0.63-0.75)**	**TP** **FN**	2 studies 217 patients	cross-sectional (cohort type accuracy study)	serious±	serious	not serious	not serious	none	101 (81 to 118) 46 (29 to 66)	⊕⊕◯◯ LOW
		0.90‡ **(0.86-0.94)**	**TN** **FP**	2 studies 254 patients		serious±	serious	not serious	not serious	none	768 (657 to 819) 85 (34 to 196)	⊕⊕◯◯ LOW
	TTH	**0.81**‡ **(0.75-0.87)**	**TP** **FN**	2 studies 177 patients		serious±	serious	not serious	not serious	none	507 (470 to 545) 119 (81 to 156)	⊕⊕◯◯ LOW
		0.96‡ **(0.94-0.98)**	**TN** **FP**	2 studies 294 patients		serious±	serious	not serious	not serious	none	359 (352 to 367) 15 (7 to 22)	⊕⊕◯◯ LOW
Headache Screening Questionnaire – Dutch Version[14]	Migraine	**0.69** **(0.55-0.80)**	**TP** **FN**	1 study 55 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious×	none	101 (81 to 118) 46 (29 to 66)	⊕⊕⊕◯ MODERATE
		0.90 **(0.77-0.96)**	**TN** **FP**	1 study 50 patients		not serious	not serious	not serious	serious×	none	768 (657 to 819) 85 (34 to 196)	⊕⊕⊕◯ MODERATE
	TTH	**0.36** **(0.21-0.54)**	**TP** **FN**	1 study 36 patients		not serious	not serious	not serious	serious×	none	225 (131 to 338) 401 (288 to 495)	⊕⊕⊕◯ MODERATE
		0.86 **(0.74-0.92)**	**TN** **FP**	1 study 69 patients		not serious	not serious	not serious	serious×	none	322 (277 to 344) 52 (30 to 97)	⊕⊕⊕◯ MODERATE

Table 6.5: Continued.

Measurement Instrument	Target population	Sensitivity (95% CI) / Specificity (95% CI)	Outcome	Nº of studies (Nº of patients)	Study design	Factors that may decrease certainty of evidence: Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Effect per 1.000 patients tested* pre-test probability of 14.7%* / 62.6%**	Test accuracy CoE
Headache Questions[53]	Migraine	**0.49** (-)†	**TP** **FN**	1 study ? patients	cross-sectional (cohort type accuracy study)	very serious¥	not serious	serious	serious×	none	72 (- to -) 75 (- to -)	⊕◯◯◯ VERY LOW
		0.91 (-)†	**TN** **FP**	1 study ? patients		very serious¥	not serious	serious	serious×	none	776 (- to -) 77 (- to -)	⊕◯◯◯ VERY LOW
	TTH	**0.96 (0.94-0.98)**	**TP** **FN**	1 study ? patients		very serious¥	not serious	not serious	serious×	none	601 (588 to 613) 25 (13 to 38)	⊕◯◯◯ VERY LOW
		0.69 (0.63-0.75)	**TN** **FP**	1 study ? patients		very serious¥	not serious	not serious	serious×	none	258 (236 to 281) 116 (93 to 138)	⊕◯◯◯ VERY LOW
Self-administered Headache Questionnaire[55]	Migraine	**0.51‡ (0.41-0.61)**	**TP** **FN**	1 study 93 patients	cross-sectional (cohort type accuracy study)	serious±	not serious	not serious	serious×	none	75 (60 to 90) 72 (57 to 87)	⊕⊕◯◯ LOW
		0.92‡ (0.90-0.94)	**TN** **FP**	1 study 619 patients		serious±	not serious	not serious	serious×	none	785 (768 to 802) 68 (51 to 85)	⊕⊕◯◯ LOW
	TTH	**0.43‡ (0.39-0.47)**	**TP** **FN**	1 study 468 patients		serious±	not serious	not serious	serious×	none	269 (244 to 294) 357 (332 to 382)	⊕⊕◯◯ LOW
		0.96‡ (0.94-0.98)	**TN** **FP**	1 study 244 patients		serious±	not serious	not serious	serious×	none	359 (352 to 367) 15 (7 to 22)	⊕⊕◯◯ LOW
Structured Headache Questionnaire[52]	Migraine	**0.86 (0.78-0.97)**	**TP** **FN**	1 study ? patients	cross-sectional (cohort type accuracy study)	very serious¥	not serious	not serious	serious×	none	126 (115 to 143) 21 (4 to 32)	⊕◯◯◯ VERY LOW
		0.94 (0.86-0.98)	**TN** **FP**	1 study ? patients		very serious¥	not serious	not serious	serious×	none	802 (734 to 836) 51 (17 to 119)	⊕◯◯◯ VERY LOW
	TTH	**0.93 (0.79-0.98)**	**TP** **FN**	1 study ? patients		very serious¥	not serious	not serious	serious×	none	582 (495 to 613) 44 (13 to 131)	⊕◯◯◯ VERY LOW
		0.93 (0.86-1.00)	**TN** **FP**	1 study ? patients		very serious¥	not serious	not serious	serious×	none	348 (322 to 374) 26 (0 to 52)	⊕◯◯◯ VERY LOW

* Prevalence in the general population of 14.7% is used for migraine.** Prevalence in the general population of 62.6% is used for TTH[65] CoE: certainty of evidence.± 'Unclear' or 'high' risk of bias on ≥50<75% of the domains on QUADAS-2. ¥ 'Unclear' or 'high' risk of bias on ≥75% of the domains on QUADAS-2.
× Results based on the outcome of one single study. ‡95% confidence interval (CI) calculated by reviewers. †Not possible to calculate 95%CI.

Table 6.6: GRADE recommendations for measurement instruments for target population Cervicogenic Headache.

Measurement Instrument	Sensitivity (95% CI) / Specificity (95% CI)	Outcome	Nº of studies (Nº of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested*	Test accuracy CoE
					Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 4.1%*	
Cervical Flexion Rotation Test[57,58]	**0.83‡ (0.72-0.94)**	**TP**	2 studies	cross-sectional (cohort type accuracy study)	very serious¥	not serious	serious	not serious	none	34 (30 to 39)	⊕◯◯◯
		FN	43 patients							7 (2 to 11)	VERY LOW
	0.82‡ (0.73-0.91)	**TN**	2 studies		very serious¥	not serious	serious	not serious	none	786 (700 to 873)	⊕◯◯◯
		FP	74 patients							173 (86 to 259)	VERY LOW

* Prevalence in the general population of 4.1% is used.[76] CoE: certainty of evidence.
¥ 'Unclear' or 'high' risk of bias on ≥75% of the domains on QUADAS-2. ‡95% confidence interval (CI) calculated by reviewers.

Discussion

Within this review, for migraine alone eleven tools were identified, [10-12, 34–37,40–51,59] for the combination of migraine and TTH six, [13,14,52–56] and for CGH one tool.[57,58] The sensitivity and specificity of the measurement instruments for migraine ranged from 0.38[38] to 0.99[48] and 0.27[10] to 0.99[37] respectively. The sensitivity and specificity for migraine based on the combined measurement instruments ranged from 0.49[53] to 1.00[54] and 0.85[56] to 0.96[13] respectively. For TTH the sensitivity and specificity ranged from 0.36[14] to 1.00[54] and 0.59[53] to 0.98[13] respectively. For the CFRT, the only measurement instrument for cervicogenic headache, both the sensitivity and specificity ranged from 0.70[57] to 0.91[58]. All measurement tools for migraine and TTH were questionnaires. The measurement tool for CGH was a physical examination test. Migraine and TTH are solely based on information from the history of the patient,[15] allowing the diagnosis to be derived from a questionnaire. However, the choice of gold standard within headache research is inconsistent. Some studies used the International Classification of Headache Disorders (ICHD) first, second or third edition,[15,60,61] others used the diagnosis of a neurologist or a headache nurse and for CGH the Sjaastad criteria were used.[62] As the ICHD is based on the most recent scientific findings and clinical expertise from experts worldwide, the newest version of de ICHD is recommended as the gold standard.[15,63]

The aim of each measurement instrument was described in Table 6.1. This was unclear for five measurement instruments. Nine measurement instruments are meant to be used as a screening tool in a broader population before seeing a medical specialist for a definitive diagnosis. These screening instruments are recommended for health care providers like PTs, as they are not trained for medical diagnoses but do see these patients often and can refer them to the medical specialist.[64] Three measurement instruments studied were meant as a replacement test for the gold standard. This may be efficient for research purposes, as this allows the researchers to diagnose the patients without an extensive visit to a specialist. However, no conclusion was drawn from the included articles if the measurement instruments were better than the gold standard (the medical specialist), therefore the presence of a medical specialist is still recommended in clinical practice.

For each measurement tool, the cut-off criteria to recognize headache should be described to allow for comparison of outcomes between studies. In reality, cut-off criteria differed between studies, which resulted in highly variable sensitivity and specificity. The lack of established cut-off points was taken into account within the 'Index Test' domain when assessing both methodological qualities and risk of bias.

Migraine Measurement Instruments

From the 11 measurement instruments found for migraine, only three were supported by evidence of two or more articles: the 3-question screen,[10,41,59] the ID-migraine[12,34,40,44–47,49,50] and the Migraine Screen Questionnaire.[11,51] Several studies introduced serious patient selection bias by only recruiting patients with the headache they were interested in studying.[10] By doing so, there were no false positives or true negatives present, which resulted in more favourable diagnostic accuracy outcome measures. Other studies excluded participants who had a secondary headache,[45] or who did not screen positive for a preliminary screening for migraine.[45,46,49] One study selected their participants so 50% had a confirmed migraine diagnosis prior to the index test and 50% did not have migraine.[11] This also introduced selection bias in favour of the outcomes, as the prevalence of the studied disorder (50% in tested group versus 14.7% in general population) determines the pre-test probability and thus the chance of correct diagnosis.[65,66]

Furthermore, serious bias was introduced in the 'flow and timing' section of the articles as some articles did not properly describe the order of receiving the index test and the reference standard diagnosis. Other studies did not include all participants in the analysis.[11,12,34,37,38,40,42,43,48,49,59] The introduced biases on both domains resulted in a downgrade of the certainty of evidence on all measurement instruments, except for the Migraine Assessment Tool.[35] However, as this tool is only studied in one article, the level of evidence was also downgraded for imprecision. Therefore, there are no measurement instruments for migraine with a high level of evidence.

Combined migraine and TTH measurement instruments

Out of the six measurement instruments that looked at both migraine and TTH, only the German language questionnaire is supported by two articles.[13,57] However, due to a serious risk of bias and indirectness, there is only a low level of evidence for this questionnaire. In both studies, only patients with headaches that were also studied in the questionnaire were included, which introduced a serious selection bias.[13,57] Similarly, the Computerized Headache Assessment Tool (CHAT) presented a sensitivity of 1.00 for both migraine and TTH, but no true negatives or false positives were available, and no specificity was presented.[54] In this study, the gold standard was the diagnosis established by a headache nurse.[54] As stated before, this is an unreliable gold standard for a headache diagnosis.[63]

The seven articles differed in population. Some study samples were retrieved from the general population,[53,55,56] others from urgent care or family practice[54] and others from a headache clinic.[13,14] In one study the sample origin was unclear.[52] The prevalence used in the GRADE recommendations was for the general population, but in health care settings the prevalence is higher. This increases the pre-test probability of a positive headache

diagnosis. This must be taken into consideration when interpreting the results of those studies.[14,54,56]

In regards to the flow and timing of these studies, not all participants received both the index test and reference standard.[52–54,56] Other studies did not include all participants in the final analyses.[13,14,53,55] By excluding participants in these ways, the generalization of results is compromised. All these components resulted in very low to moderate level of evidence for the six combined migraine and TTH measurement instruments.

Cervicogenic headache measurement instruments

Both articles studying the diagnostic accuracy of the cervical flexion rotation test (CFRT) for CGH showed selection bias, as participants were selected based on headache type.[57,58] In one study the sensitivity and specificity were both 0.70,[57] whereas in the other study the sensitivity was 0.91 and the specificity 0.90.[58] In the study with lower diagnostic accuracy, the control group consisted of other headache forms (migraine or multiple headache forms).[57] This makes differentiating between headache types more difficult as other headaches are related to neck problems.[5,67,68] The study with higher diagnostic accuracy compared patients with CGH with asymptomatic participants and several patients with migraine,[58] which made it easier to recognize the CGH. When this test is applied in the clinic, patients will have a headache complaint and will not be asymptomatic, so the sensitivity and specificity of 0.70 will likely be more accurate.

Just as in the current review, another recent systematic review describing physical examination tests for screening and diagnosis of CGH, the CFRT was determined to be the most useful test with the highest reliability and strongest diagnostic accuracy.[69] There is, however, a debate in the literature on the reliability of manual ROM tests of the spine.[70] Inter-examiner reliability for the cervical spine passive ROM ranged from poor to substantial. The manual tests of the upper cervical spine (C1/2, C2/3) have a fair to substantial level of reliability.[70]The reliability of the CFRT has been established to be good to excellent.[71] However, CFRT reliability was established by comparing a manual diagnosis of C1/2 dysfunction with the outcome of the CFRT.[71] If the reliability of the manual diagnosis of dysfunction is only fair, then the reliability of the CFRT is questionable. However, in another study where the cervical ROM was measured with a device (CROM), a significant difference was found between the ROM in patients with CGH compared to patients with migraine and healthy subjects, which confirms the findings of the included papers of this review.[57,58,72] In conclusion, the CFRT is a valid and reliable measure to recognize CGH, though the reliability is higher when using a CROM device rather than assessing the ROM manually.

Strengths and limitations of the study

The current review is, to the authors' knowledge, the first review establishing an overview of the diagnostic accuracy of measurement instruments for headaches associated with musculoskeletal symptoms. By using the QUADAS-2 and COSMIN tool, the methodological quality was assessed in a well-known and internationally accepted manner.[24,25] By using the GRADE recommendations, the findings of this review are transparent and easy to translate to the clinical practice.[27]

There are, however, also a few limitations of this study. Comparison between index and reference test was not easy, as the validation of the index test was performed in a different population compared to the population in which the reference standard was developed. Itis important to keep in mind that the diagnostic accuracy is dependent on the prevalence of the target condition in the population, the study sample needs to be taken into consideration when interpreting the results. The prevalence of the target condition is the pre-test probability of a person having that condition, and a good measurement instrument will increase the chance of recognizing the target condition correctly. However, if the study sample is biased by having a very high prevalence in the target condition, whereas the measurement instrument would normally be used in a setting with a low prevalence of the target condition, the diagnostic accuracy is not valid for that specific population. Validation studies of measurement instruments should therefore always test the measurement instrument in the population and setting for which it is being validated.

Also, some measurement tools were used in different languages and cultures, which must also be considered when interpreting these results. In this review great variability was found between the different studies, as illustrated in the S-ROC curves in figures 3a and 3c. These S-ROC curves show the uncertainty of the findings compared to reality, so the pooled data should be used with caution. The clear gap between the diagnostic accuracy of some measurement instruments between studies showed the necessity of conformation by multiple studies within the same population and against the same reference standard.

Implications for practice

The findings of the current review support the use of the ID-Migraine questionnaire to diagnose migraine with a moderate level of certainty (Table 6.4). However, patients with headaches often experience multiple headache forms.[7,13,74] This warrants a measurement instrument that can diagnose more than one headache. From the questionnaires that looked at both migraine and TTH, the HSQ has the highest level of evidence within this review (Table 6.5). To establish if there is a migraine and/ or a TTH is present, this questionnaire is therefore recommended. As CGH need to be confirmed by physical examination,[15] the CFRT is recommended (Table 6.6). No other measurement instruments for secondary headache related to musculoskeletal complaints were found. Therefore, for

these headache types, such as secondary headache attributed to temporomandibular disorders or headache attributed to whiplash injury, no recommendations can be made.

Implications for future research

Currently, for migraine and TTH there are many of questionnaires, most of them validated by one study. Future research should use the recommended measurement instruments and validate them in different samples of the same population to increase the level of certainty that the diagnostic accuracy is realistic. The QUADAS-2 and COSMIN tools should be used when designing their studies to enhance their methodological quality.

Furthermore, additional clinimetric properties of measurement instruments for headache should be examined. Clinimetric properties such as reliability and responsiveness are important to enhance the care of headache complaints and monitor the course of these complaints. For that reason, the authors are conducting a complementary review to establish the clinimetric properties of measurement instruments for these symptoms and factors (Figure 6.2).

In conclusion, only a few measurement instruments reached a moderate level of evidence for the diagnostic accuracy. For migraine, the ID-Migraine is recommended. For migraine and TTH, the HSQ is recommended, and the CFRT is advised to be used for CGH. However, more studies are needed to validate these instruments further to enhance the level of evidence.

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Appendix 6.1. Search strategies

Performed October 25th, 2018.

Suggested by Terwee et al:	Search Strategy Pubmed:	Number of articles
#1: construct	((((((((((pain measurement[MeSH Terms]) OR pain[Title/Abstract]) OR mouth opening[Title/Abstract]) OR range of motion[MeSH Terms]) OR range of motion[Title/Abstract]) OR quality of life[MeSH Terms]) OR quality of life[Title/Abstract]) OR stability[Title/Abstract]) OR coordination[Title/Abstract]) OR muscle performance[Title/Abstract]) OR function impairment[Title/Abstract]) OR diagnosis[Title/Abstract]	2603868
#2: population	(((((((primary headache disorder[MeSH Terms]) OR secondary headache disorder[MeSH Terms]) OR cervicogenic headache[MeSH Terms]) OR disorder, migraine[MeSH Terms]) OR tension type headache[MeSH Terms]) OR headache[Title/Abstract]) OR migraine[Title/Abstract]	87490
#3: instrument	(((((questionnaire[MeSH Terms]) OR questionnaire[Title/Abstract]) OR physical examination[MeSH Terms]) OR physical examination[Title/Abstract]) OR performance based[Title/Abstract]) OR physical test[Title/Abstract]	2305843
#4: filter	(((instrumentation[sh] OR methods[sh] OR Validation Studies[pt] OR Comparative Study[pt] OR "psychometrics"[MeSH] OR psychometr*[tiab] OR clinimetr*[tw] OR clinometr*[tw] OR "outcome assessment (health care)"[MeSH] OR outcome assessment[tiab] OR outcome measure*[tw] OR "observer variation"[MeSH] OR observer variation[tiab] OR "Health Status Indicators"[Mesh] OR "reproducibility of results"[MeSH] OR reproducib*[tiab] OR "discriminant analysis"[MeSH] OR reliab*[tiab] OR unreliab*[tiab] OR valid*[tiab] OR coefficient[tiab] OR homogeneity[tiab] OR homogeneous[tiab] OR "internal consistency"[tiab] OR (cronbach*[tiab] AND (alpha[tiab] OR alphas[tiab])) OR (item[tiab] AND (correlation*[tiab] OR selection*[tiab] OR reduction*[tiab])) OR agreement[tiab] OR precision[tiab] OR imprecision[tiab] OR "precise values"[tiab] OR test-retest[tiab] OR (test[tiab] AND retest[tiab]) OR (reliab*[tiab] AND (test[tiab] OR retest[tiab])) OR stability[tiab] OR interrater[tiab] OR inter-rater[tiab] OR intrarater[tiab] OR intra-rater[tiab] OR intertester[tiab] OR inter-tester[tiab] OR intratester[tiab] OR intra-tester[tiab] OR interobserver[tiab] OR inter-observer[tiab] OR intraobserver[tiab] OR intra-observer[tiab] OR intertechnician[tiab] OR inter-technician[tiab] OR intratechnician[tiab] OR intra-technician[tiab] OR interexaminer[tiab] OR inter-examiner[tiab] OR intraexaminer[tiab] OR intra-examiner[tiab] OR interassay[tiab] OR inter-assay[tiab] OR intraassay[tiab] OR intra-assay[tiab] OR interindividual[tiab] OR inter-individual[tiab] OR intraindividual[tiab] OR intra-individual[tiab] OR interparticipant[tiab] OR inter-participant[tiab] OR intraparticipant[tiab] OR intra-participant[tiab] OR kappa[tiab] OR kappa's[tiab] OR kappas[tiab] OR repeatab*[tiab] OR ((replicab*[tiab] OR repeated[tiab]) AND (measure[tiab] OR measures[tiab] OR findings[tiab] OR result[tiab] OR results[tiab] OR test[tiab] OR tests[tiab])) OR generaliza*[tiab] OR generalisa*[tiab] OR concordance[tiab] OR (intraclass[tiab] AND correlation*[tiab]) OR discriminative[tiab] OR "known group"[tiab] OR factor analysis[tiab] OR factor analyses[tiab] OR dimension*[tiab] OR subscale*[tiab] OR (multitrait[tiab] AND scaling[tiab] AND (analysis[tiab] OR analyses[tiab])) OR item discriminant[tiab] OR interscale correlation*[tiab] OR error[tiab] OR errors[tiab] OR "individual variability"[tiab] OR (variability[tiab] AND (analysis[tiab] OR values[tiab])) OR (uncertainty[tiab] AND (measurement[tiab] OR measuring[tiab])) OR "standard error of measurement"[tiab] OR sensitiv*[tiab] OR responsive*[tiab] OR ((minimal[tiab] OR minimally[tiab] OR clinical[tiab] OR clinically[tiab]) AND (important[tiab] OR significant[tiab] OR detectable[tiab])) AND (change[tiab] OR difference[tiab])) OR (small*[tiab] AND (real[tiab] OR detectable[tiab]) AND (change[tiab] OR difference[tiab])) OR meaningful change[tiab] OR "ceiling effect"[tiab] OR "floor effect"[tiab] OR "Item response model"[tiab] OR IRT[tiab] OR Rasch[tiab] OR "Differential item functioning"[tiab] OR DIF[tiab] OR "computer adaptive testing"[tiab] OR "item bank"[tiab] OR "cross-cultural equivalence"[tiab]))))	8757688
#5:	#1 AND #2 AND #3 AND #4	4652
#6: NOT filter	((("addresses"[Publication Type] OR "biography"[Publication Type] OR "case reports"[Publication Type] OR "comment"[Publication Type] OR "directory"[Publication Type] OR "editorial"[Publication Type] OR "festschrift"[Publication Type] OR "interview"[Publication Type] OR "lectures"[Publication Type] OR "legal cases"[Publication Type] OR "legislation"[Publication Type] OR "letter"[Publication Type] OR "news"[Publication Type] OR "newspaper article"[Publication Type] OR "patient education handout"[Publication Type] OR "popular works"[Publication Type] OR "congresses"[Publication Type] OR "consensus development conference"[Publication Type] OR "consensus development conference, nih"[Publication Type] OR "practice guideline"[Publication Type]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) OR (cancer[sb] OR veterinary[sb] OR aids[sb] OR bioethics[sb] OR jsubsetd OR jsubsets OR jsubsete OR jsubsetq OR jsubsetqis)))	12975051

#7	#5 NOT #6	3631

Suggested by Terwee et al:	**Search Strategy Cinahl:**	**Number of articles**
S1	MM pain OR AB pain OR AB mouth opening OR MM range of motion OR AB range of motion OR MM quality of life OR AB quality of life OR AB stability OR AB coordination OR AB muscle performance OR AB function impairment OR AB diagnosis	488267
S2	MJ headache OR TI headache OR AB headache OR TI migraine OR AB migraine	27971
S3	MH questionnaire OR AB questionnaire OR MH physical examination OR AB physical examination OR AB performance based test OR AB physical test	193293
S4	(MH "Psychometrics") or (TI psychometr* or AB psychometr*) or (TI clinimetr* or AB clinimetr*) or (TI clinometr* OR AB clinometr*) or (MH "Outcome Assessment") or (TI outcome assessment or AB outcome assessment) or (TI outcome measure* or AB outcome measure*) or (MH "Health Status Indicators") or (MH "Reproducibility of Results") or (MH "Discriminant Analysis") or ((TI reproducib* or AB reproducib*) or (TI reliab* or AB reliab*) or (TI unreliab* or AB unreliab*)) or ((TI valid* or AB valid*) or (TI coefficient or AB coefficient) or (TI homogeneity or AB homogeneity)) or (TI homogeneous or AB homogeneous) or (TI "coefficient of variation" or AB "coefficient of variation") or (TI "internal consistency" or AB "internal consistency") or (MH "Internal Consistency+") or (MH "Reliability+") or (MH "Measurement Error+") or (MH "Content Validity+") or "hypothesis testing" or "structural validity" or "cross-cultural validity" or (MH "Criterion-Related Validity+") or "responsiveness" or "interpretability" or (TI reliab* or AB reliab*) and ((TI test or AB test) OR (TI retest or AB retest)) or (TI stability or AB stability) or (TI interrater or AB interrater) or (TI inter-rater or AB inter-rater) or (TI intrarater or AB intrarater) or (TI intra-rater or AB intrarater) or (TI intertester or AB intertester) or (TI inter-tester or AB inter-tester) or (TI intratester or AB intratester) or (TI intra-tester or AB intra-tester) or (TI interobserver or AB interobserver) or (TI inter-observer or AB inter-observer) or (TI intraobserver or AB intraobserver) or (TI intra-observer or AB intra-observer) or (TI intertechnician or AB intertechnician) or (TI inter-technician or AB inter-technician) or (TI intratechnician or AB intratechnician) or (TI intra-technician or AB intra-technician) or (TI interexaminer or AB interexaminer) or (TI inter-examiner or AB inter-examiner) or (TI intraexaminer or AB intraexaminer) OR (TI intra-examiner or AB intra-examiner) or (TI intra-examiner or AB intraexaminer) or (TI interassay or AB interassay) or (TI inter-assay or AB inter-assay) or (TI intraassay or AB intraassay) or (TI intra-assay or AB intra-assay) or (TI interindividual or AB interindividual) or (TI inter-individual or AB inter-individual) OR (TI intraindividual or AB intraindividual) or (TI intra-individual or AB intra-individual) or (TI interparticipant or AB interparticipant) or (TI inter-participant or AB inter-participant) or (TI intraparticipant or AB intraparticipant) or (TI intra-participant or AB intra-participant) or (TI kappa or AB kappa) or (TI kappa's or AB kappa's) or (TI kappas or AB kappas) or (TI repeatab* or AB repeatab*) or (TI responsive* or AB responsive*) or (TI interpretab* or AB interpretab*)	496904
S5	S1 AND S2 AND S3 AND S4	388

Suggested by Terwee et al:	**Search Strategy Cochrane:**	**Number of articles**
#1	"pain":ti,ab,kw or "mouth opening" or "range of motion":ti,ab,kw or "quality of life":ti,ab,kw or "stability" or "coordination":ti,ab,kw or "muscle performance" or "function impairment":ti,ab,kw (Word variations have been searched)	191444
#2	"headache":ti,ab,kw or "migraine":ti,ab,kw (Word variations have been searched)	25131
#3	"questionnaire":ti,ab,kw or "test":ti,ab,kw or "performance test":ti,ab,kw or "physical examination":ti,ab,kw (Word variations have been searched)	215482
#4	"validation studies" or "validation study":ti,ab,kw or "psychometrics":ti,ab,kw or "clinimetrics":ti,ab,kw or "Outcome and Assessment Information Set":ti,ab,kw or "outcome measure":ti,ab,kw (Word variations have been searched) or observer variation:ti,ab,kw or "reproducability":ti,ab,kw or "reliability":ti,ab,kw or standard error of measurement:ti,ab,kw (Word variations have been searched)	33005
#5	#1 AND #2 AND #3 AND #4	110

Appendix 6.2 – Indicators for the assessment of quality using the QUADAS-2.

Domain	Signaling questions and indicators
Patient selection	*Was the spectrum of patients representative of the patients who will receive the test in practice?* Patients with an unclassified headache will receive the tests in practice, therefore this should be the sample used in the studies. • **Classify as 'yes'** if (1) patient enrollment was consecutive or random, (2) a case-control design was avoided and (3) inappropriate exclusions were avoided. Information should be given about clinical setting, recruitment of patients and the in- and exclusion criteria. o When all three items are classified as yes, there was considered to be a **low risk of bias**. • **Classify as 'no'** if (1) patient enrollment was not consecutive or random, or (2) a case-control design was applied or (3) inappropriate exclusions were present. Examples of inappropriate exclusions are: (1) excluding secondary headaches when the test was aimed at diagnosing primary headaches or (2) excluding patients with multiple headache types (*patients in practice may have a second(ary) headache, the test should be able to discriminate between the headaches properly to be used in practice*) o When one or more items were classified as no, there was considered to be a **high risk of bias**. • **Classify as 'unclear'** if the information stated above was not available or unclear from the article. o When one or more items were classified as unclear and no items were classified as no, the **risk of bias** was considered to be **unclear**.
Index test	*Is the index test likely to classify the target condition correctly? Could the conduct or interpretation of the index test have introduced bias?* Blinding of the results of other tests or specific patient population will decrease the risk of bias. Using pre-specified thresholds when applicable will also decrease the chance that bias is introduced after the index test is applied. As different index tests were included, no definition can be given for the index test. • **Classify as 'yes'** if (1) the index tests results were interpreted without knowledge of the results of the reference standard and (2) if the threshold used was pre-specified (when applicable). The index test should be clearly described as well as how the diagnosis was determined (cut-off points, thresholds or criteria). o When both items are classified as yes, there was considered to be a **low risk of bias**. • **Classify as 'no'** if (1) the index tests results were interpreted with knowledge of the results of the reference standard or (2) if the threshold used was determined after the test was applied (when applicable). o When one or more items were classified as no, there was considered to be a **high risk of bias**. • **Classify as 'unclear'** if the information stated above was not available or unclear from the article. o When one or more items were classified as unclear and no items were classified as no, the **risk of bias** was considered to be **unclear**.
Reference standard	*Is the reference standard likely to classify the target condition correctly? Could the conduct or interpretation of the reference standard have introduced bias?* Blinding of the results of other tests or specific patient population will decrease the risk of bias. The reference test should be the gold standard: ICHD, ICHD-II or ICHD-3 or a headache specialist trained in using these criteria. • **Classify as 'yes'** if (1) the reference standard is the gold standard (ICHD, ICHD-II or ICHD-3) or otherwise likely to correctly classify the target condition and (2) the reference standard results were interpreted without knowledge of the results of the index test. o When both items are classified as yes, there was considered to be a **low risk of bias**. • **Classify as 'no'** if (1) the reference standard is not the gold standard and not likely to correctly classify the target condition (e.g. interview with someone other than a trained headache specialist) and (2) the reference standard results were interpreted with knowledge of the results of the index test. o When one or more items were classified as no, there was considered to be a **high risk of bias**. • **Classify as 'unclear'** if the information stated above was not available or unclear from the article. For example: when the diagnosis from a neurologist was the reference standard, without explicitly stating the neurologist is trained in, or used the ICHD criteria. o When one or more items were classified as unclear and no items were classified as no, the **risk of bias** was considered to be **unclear**.
Flow and timing	*Was the application of the index test and reference standard adequate in terms of interval between the two tests and inclusion of all participants?* Ideally the index test and reference standard should be carried out on the same day. However, it is unlikely that headache complaints will change within 0 – 4 weeks, so this time interval was determined to be adequate. By including all participants in the analyses, the results will be most accurate and true to reality. • **Classify as 'yes'** if (1) an appropriate time interval between the index test and reference standard was present, (2) all patients received (the same) reference standard and (3) all patients were included in the analysis. o When all three items are classified as yes, there was considered to be a **low risk of bias**. • **Classify as 'no'** if (1) there was not an appropriate interval between the index test and reference standard, or (2) not all patients received (the same) reference standard or (3) not all patients were included in the analysis. o When one or more items were classified as no, there was considered to be a **high risk of bias**. • **Classify as 'unclear'** if the information stated above was not available or unclear from the article. o When one or more items were classified as unclear and no items were classified as no, the **risk of bias** was considered to be **unclear**.

Appendix 6.3. List of studies excluded during the full-text screening process of the current review and reasons for exclusion.

Nr. of studies	Reason of exclusion	References
25	No measurement instrument with clinimetric outcome measures (following diagnostic accuracy or the ICF model)	1–25
9	Not within the domain of a physical therapist	26–34
6	Not the original research paper	35–40
5	Duplicate	41–45
2	No full-text available	46,47
2	Not focused on headache evaluation	48,49
2	Wrong patient population	50,51
1	Wrong language	52

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Appendix 6.4: Clarification of Methodological Quality Assessment with QUADAS-2 and Clinimetric Evaluation of the Criterion Validity with the COSMIN checklist Box H per study (extended version Table 6.2).

Measurement instrument	Study	Risk of Bias				Applicability concerns			COSMIN Box H
		1a. Patient selection	2a. Index test	3a. Reference standard	4. Flow and timing	1b. Patient selection	2b. Index test	3b. Reference standard	
Target population: Migraine									
3 Question screen	**Cady, 2004**	**High:** method of selection unclear. Inappropriate exclusions were not avoided.	**Unclear:** index test was after reference / inclusion; unclear if results were known.	**Unclear:** reference test before index test and different criteria were used.	**High:** reference before index; time interval unknown.	**Low**	**Low**	**Low**	**Poor:** important flaws in the design / methods of the study.
	Pryse-Phillips, 2002	**High:** method of selection unclear. Enrolment was not random or consecutive.	**Unclear:** moment of interpretation unclear. Use of threshold unclear.	**High:** gold standard was not used.	**High:** not all participants were included in analysis. Time interval unknown.	**Low**	**Low**	**Low**	**Poor:** gold standard was not used.
	Wahab, 2016	**Unclear:** method and design of selection unclear.	**Unclear:** moment of interpretation unclear.	**Unclear:** moment of interpretation unclear. Unclear how diagnosis was actually made.	**Low**	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete.
Diagnostic Screen	**Michel, 1993 II**	**Unclear:** method and design of selection unclear.	**Unclear:** use of threshold unclear.	**Unclear:** index test before reference test, moment of interpretation unclear.	**High:** not all participants were included in analysis. Time interval unknown.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete.
ID-Migraine	**Brighina, 2006**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete.

Measurement instrument	Study	Risk of Bias				Applicability concerns			COSMIN Box H
		1a. Patient selection	2a. Index test	3a. Reference standard	4. Flow and timing	1b. Patient selection	2b. Index test	3b. Reference standard	
ID-Migraine (Continued)	**de Mattos, 2017**	**High:** inappropriate exclusions were not avoided.	**Low**	**Low**	**Unclear:** time interval unknown.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete. Some flaws in the design / methods of the study.
	Ertas, 2008	**High:** inappropriate exclusions were not avoided.	**Low**	**Unclear:** moment of interpretation unclear.	**Low**	**Low**	**Low**	**Low**	**Fair:** some flaws in the design / methods of the study.
	Gil-Gouveia, 2009	**High:** inappropriate exclusions were not avoided.	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete. Some flaws in the design / methods of the study.
	Karli, 2007	**High:** inappropriate exclusions were not avoided.	**Unclear:** moment of interpretation unclear.	**Unclear:** moment of interpretation unclear.	**High:** not all participants received reference test or were included in the analysis.	**Low**	**Low**	**Low**	**Poor:** important flaws in the design / methods of the study.
	Kim, 2006	**Unclear:** method and design of selection unclear.	**Low**	**Unclear:** moment of interpretation unclear.	**Low**	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete.
	Lipton, 2003	**Unclear:** method and design of selection unclear.	**Unclear:** use of threshold unclear.	**Low**	**Unclear:** time interval unclear. Inclusion for analysis unclear.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete.

Measurement instrument	Study	Risk of Bias				Applicability concerns			COSMIN Box H
		1a. Patient selection	2a. Index test	3a. Reference standard	4. Flow and timing	1b. Patient selection	2b. Index test	3b. Reference standard	
ID-Migraine (Continued)	**Lipton, 2016**	**High:** patient sampling was not random nor consecutive.	**Unclear:** moment of interpretation unclear.	**Unclear:** moment of interpretation unclear.	**Unclear:** time interval unclear. Inclusion for analysis unclear.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete. Some flaws in the design / methods of the study.
	Siva, 2008	**High:** patient sampling was not random nor consecutive.	**Low**	**Low**	**Unclear:** unclear who received the tests and was included in analysis from the complete sample.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete.
MSMDQ	**Rueda-Sánchez, 2004**	**Low**	**Unclear:** use of threshold unclear.	**Unclear:** moment of interpretation unclear. Unclear how diagnosis was actually made.	**High:** not all participants received reference test or were included in the analysis.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete. Some flaws in the design / methods of the study.
MAT	**Marcus, 2004**	**Low**	**Low**	**Unclear:** moment of interpretation unclear.	**Low**	**Low**	**Low**	**Low**	**Good**
Migraine Screen Questionnaire	**Lainez, 2010**	**Low**	**Low**	**Unclear:** moment of interpretation unclear.	**Low**	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete.
	Lainez, 2005	**High:** patient sampling was not random nor consecutive.	**High:** threshold not pre-specified. Moment of interpretation unclear.	**Low**	**Unclear:** time interval unclear.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete.

Measurement instrument	Study	Risk of Bias				Applicability concerns			COSMIN Box H
		1a. Patient selection	2a. Index test	3a. Reference standard	4. Flow and timing	1b. Patient selection	2b. Index test	3b. Reference standard	
MSQ	**Kallela, 2001**	**Low**	**Low**	**Unclear:** moment of interpretation unclear. Unclear how diagnosis was actually made.	**High:** not all participants received reference test or were included in the analysis. Time interval unclear.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete. Some flaws in the design / methods of the study.
Migraine-4	**Walters, 2015**	**Low**	**Unclear:** use of threshold unclear.	**Unclear:** moment of interpretation unclear. Unclear how diagnosis was actually made.	**High:** not all participants were included in the analysis.	**Low**	**Low**	**Low**	**Fair:** some flaws in the design / methods of the study.
MA-HIS-M	**Michel, 1993 I**	**Unclear:** method and design of selection unclear.	**Low**	**Low**	**Unclear:** time interval unclear.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete.
Screening items	**Wang, 2008**	**Unclear:** method and design of selection unclear.	**Unclear:** use of threshold and moment of interpretation unclear.	**Unclear:** moment of interpretation unclear. Unclear how diagnosis was actually made.	**High:** not all participants were included in the analysis. Time interval unclear.	**Low**	**Low**	**Low**	**Fair:** some flaws in the design / methods of the study.
SMIQ	**Shaik, 2015**	**High:** inappropriate exclusions were not avoided.	**Unclear:** use of threshold unclear.	**Unclear:** moment of interpretation unclear. Unclear how diagnosis was actually made.	**Low**	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete. Some flaws in the design / methods of the study.

Measurement instrument	Study	Risk of Bias				Applicability concerns			COSMIN Box H
		1a. Patient selection	2a. Index test	3a. Reference standard	4. Flow and timing	1b. Patient selection	2b. Index test	3b. Reference standard	
Target population: Migraine and tension-type headache									
CHAT	**Maizels, 2007**	**High:** inappropriate exclusions were not avoided.	**Low**	**Unclear:** moment of interpretation unclear. Unclear how diagnosis was actually made.	**Unclear:** time interval unclear.	**Low**	**Low**	**Low**	**Poor:** sensitivity and specificity not properly described. Unclear if reference test can be used as golden standard.
German Language Questionnaire	**Fritsche, 2007**	**High:** inappropriate exclusions were not avoided.	**Low**	**Low**	**High:** not all participants were included in the analysis.	**Low**	**Low**	**Low**	**Poor:** important flaws in the design / methods of the study.
	Yoon, 2008	**High:** inappropriate exclusions were not avoided.	**Low**	**Unclear:** moment of interpretation unclear.	**High:** not all participants received reference test or were included in the analysis. Time interval unclear.	**Low**	**Low**	**Low**	**Poor:** important flaws in the design / methods of the study.
HSQ-DV	**van der Meer, 2017**	**Low**	**Low**	**Low**	**High:** not all participants were included in the analysis.	**Low**	**Low**	**Low**	**Excellent**
Headache questions	**Hagen, 2010**	**Low**	**Unclear:** use of threshold unclear.	**Unclear:** moment of interpretation unclear.	**Unclear:** time interval unclear.	**Low**	**Low**	**Low**	**Fair:** description of how missing items were handled not complete. Some flaws in the design / methods of the study.
SAHQ	**Rasmussen, 1991**	**Low**	**Low**	**High:** gold standard was not used. Moment of interpretation unclear.	**Unclear:** time interval unclear.	**Low**	**Low**	**Low**	**Poor:** gold standard was not used.

Measurement instrument	Study	Risk of Bias				Applicability concerns			COSMIN Box H
		1a. Patient selection	2a. Index test	3a. Reference standard	4. Flow and timing	1b. Patient selection	2b. Index test	3b. Reference standard	
SHQ	**El-Sherbiny, 2017**	**Unclear:** method and design of selection unclear.	**Low**	**Unclear:** moment of interpretation unclear.	**Unclear:** time interval unclear. Unclear if all participants received reference test.	**Low**	**Low**	**Low**	**Fair:** some flaws in the design / methods of the study.
Target population: Cervicogenic headache									
Cervical Flexion-Rotation Test	**Hall, 2010**	**High:** patient sampling was not random nor consecutive.	**Low**	**Unclear:** moment of interpretation unclear. Unclear if criteria used can be considered gold standard.	**Unclear:** time interval unclear.	**Low**	**Low**	**Low**	**Fair:** some flaws in the design / methods of the study.
	Ogince, 2005	**High:** patient sampling was not random nor consecutive. Inappropriate exclusions were not avoided.	**Unclear:** moment of interpretation unclear.	**Unclear:** unclear if criteria used can be considered gold standard.	**High:** not all participants received reference test or were included in the analysis. Time interval unclear.	**Low**	**Low**	**Low**	**Poor:** important flaws in the design / methods of the study.

MSMDQ: Michel's Standardized Migraine Diagnosis Questionnaire; MAT: Migraine Assessment Questionnaire; MSQ: Migraine-specific questionnaire; MA-IHS-M; Modified Algorithm for IHS Migraine; SMIQ: Structured Migraine Interview Questionnaire; CHAT: Computerized Headache Assessment Test; HSQ-DV: Headache Screening Questionnaire – Dutch Version; SAHQ: Self-Administered Headache Questionnaire; Structured Headache Questionnaire. Reasons for QUADAS-2 domains were given when studies scored high risk of bias or unclear risk of bias. Reasons for COSMIN was given when studies scored poor or fair methodological quality.

PART III

THERAPEUTIC PROCESS


7

Chapter 7

Effects of physical therapy for temporomandibular disorders on headache pain intensity: A systematic review

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Effects of physical therapy for temporomandibular disorders on headache pain intensity: A systematic review

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and

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Background:
Physical therapy is regarded an effective treatment for temporomandibular disorders (TMD). Patients with TMD often report concomitant headache. There is, however, no overview of the effect of physical therapy for TMD on concomitant headache complaints.

Objectives:
The aim of this study is to systematically evaluate the literature on the effectiveness of physical therapy on concomitant headache pain intensity in patients with TMD.

Data sources:
PubMed, Cochrane and PEDro were searched.

Study eligibility criteria: Randomized or controlled clinical trials studying physical therapy interventions were included.

Participants:
Patients with TMD and headache.

Appraisal:
The Cochrane risk of bias tool was used to assess risk of bias.

Synthesis methods:
Individual and pooled between-group effect sizes were calculated according to the standardized mean difference (SMD) and the quality of the evidence was rated using the GRADE approach.

Results:
Five studies were selected and analyzed by two reviewers. All articles had a high risk of bias on the RoB assessment**.** The pooled data analysis showed small, but not significant, overall effect in favor of TMD-focused physical therapy compared to control interventions. A subgroup analysis considering the different modalities showed promising results for static stretching and manual therapy on both orofacial region and cervical spine**.** There is a very low level of certainty that TMD-treatment is effective on headache pain intensity, downgraded by high risk of bias, inconsistency, and imprecision**.**

Limitations:
The methodological quality of most included articles was poor, and the interventions included were very different.

Conclusions:
Physical therapy interventions presented small, but not significant, effect on reducing headache pain intensity on subjects with TMD, with low level of certainty. More studies of higher methodological quality are needed so better conclusions could be taken.

Abstract

Introduction

One in five adults in Europe are estimated to have a perceived dysfunction of their masticatory system, which is related to temporomandibular disorders (TMD).[1,2] TMDs are defined according to the Diagnostic Criteria for TMD (DC/TMD) as complaints involving the masticatory system and can be stratified into myalgia (pain in the masticatory muscles), arthralgia (pain in the temporomandibular joint), or functional complaints of the joint, like clicking or locking.[3] Up to 85% of patients with TMD complain about myalgia.[4] Physical therapists are equipped to treat patients with these musculoskeletal complaints. In the last five years, six reviews, discuss the effectiveness of several physical therapy modalities on TMD complaints.[5–10] The most recent review and meta-analysis concluded that exercise therapy is effective in reducing TMD-pain. Even though headache is a common symptom in TMD,[11] headache pain intensity was not taken into consideration in these reviews.

Patients with TMD report headache more frequently (68 – 85%) than the general population (50%).[12–16] Most common headaches in patients with TMD are Tension-Type Headache (TTH), migraine and headache attributed to TMD.[13,14] These headaches are classified by the International Classification for Headache Disorders 3rd edition (ICHD-3).[17] In contrast to the primary headaches TTH and migraine, headache attributed to TMD has a known cause for the headache complaints which is the TMD. This underlying TMD condition needs to be treated in order to decrease the headache complaints attributed to TMD. Another secondary headache that may be frequent in patients with TMD is a cervicogenic headache, as patients with TMD often report cervical dysfunction and patients with cervicogenic headache frequently report signs of a TMD.[18–20]

The high co-morbidity between TMD and cervical impairments,[19] as well as the neuroanatomical relationship between these two areas,[21–23] may explain why physical therapy can have an effect on headache through treatment of the temporomandibular system.[20,24–26] Besides manual physical therapy and exercise therapy, some of the common approaches for treating TMD or headache are focusing on more general aspects of pain, like pain education and counselling. This has also been found effective for patients with migraine,[27] TTH[28] and TMD.[29] As these physical therapy modalities may be an effective treatment for both TMD and headaches, it may be interesting to see how headache pain intensity responds to TMD-treatment. There is currently, however, no overview of the effect of physical therapy interventions for TMD on concomitant headache pain intensity. We hypothesized that TMD-treatment would have a positive effect on headache pain intensity, but that this may differ between different headaches types. Therefore, the aim of this study is to systematically evaluate the literature on the effectiveness of physical therapy interventions on concomitant headache pain intensity in patients with TMD.

Methods

Protocol and registration

This review has been reported in accordance with PRISMA recommendations[30] and is registered on PROSPERO (registration number CRD42017062487).

Eligibility criteria

Studies had to meet the following inclusion criteria to be eligible: 1) adult participants with TMD based on the diagnostic criteria for TMD (DC/TMD)[3,31]; 2) headache pain intensity as outcome measure; 3) randomized controlled trial (RCT) or controlled clinical trial (CCT); 4) TMD-treatment within the physical therapy domain[32]; and 5) article is published in English or Dutch. Articles were excluded when an occlusal device (e.g. a stabilization splint) was the only intervention. There were no restrictions on publication dates, or on age and gender of the participants. All headache types were included in the review.

Information sources

Literature searches to identify studies were performed in the electronic databases PubMed [1966 – 2020], Cochrane [1993 – 2020] and Physiotherapy Evidence Database (PEDro) [1999 – 2020]. The electronic search was supplemented by snowballing of full articles retrieved. The search was conducted on August 3, 2020.

Search

Key words used in the search strategy were, amongst others: "physical therapy", "physiotherapy", "temporomandibular disorder" and "headache". In PubMed, we used a combination of MeSH Terms and title/abstract searches and different physical therapy modalities were described. The search strategy for PEDro and Cochrane required adaptation from the PubMed search strategy. The complete search strategies can be found in Appendix 7.1. There was no hand search. Grey literature was not included.

Study selection

Duplicates were removed and title/abstracts of all retrieved records were screened for eligibility by two researchers blinded to each other's results (HvdM, CMS). The full texts of the remaining articles were obtained and the full texts were assessed to see if the studies met the inclusion criteria for this review. In case of disagreement between the two reviewers, a third reviewer (RE) made the decision regarding inclusion of the article.

Data collection process, data items and summary measures

Data extraction was performed by one reviewer (HvdM). A second reviewer (LBC) checked the extracted data for accuracy. The following key data were extracted: 1) study characteristics: first author, year of publication, type of study, sample size; 2) participant

characteristics: age, gender, and TMD diagnosis[3]; 3) intervention characteristics: type of intervention(s)[32], frequency, and follow-up; and 4) outcome measures: intensity of headache[17] according to Visual Analog Scale (VAS) or similar tools and the statistical significance for both within-group and between-group analyses when available. The mean and standard deviations were extracted from the included studies for further statistical analysis.

Risk of bias in individual studies

Quality assessment of the studies was performed using the Cochrane 'risk of bias (RoB)' tool, in contrast with what was registered in PROSPERO, because the Cochrane RoB tool is recommended over the use of the PEDro score.[33] The Cochrane RoB tool assesses five domains regarding bias: selection bias, performance bias, detection bias, attrition bias and reporting bias. The tool focuses on the internal validity and does not lead to a quality score.[34] This tool shows if there is a high, low, or unclear risk of bias within the study which may influence the internal validity of the study.[34] Two independent reviewers performed the quality assessment blinded to each other's results (HvdM, LBC). Any discrepancies were discussed and, when needed, a third reviewer (CMS) made the decision regarding the final quality score of the article. A risk of bias graph and risk of bias summary were extracted from the program Review Manager 5.3.[35]

Synthesis of results and additional analyses

For each study, between-group effect sizes were calculated according to the standardized mean difference (SMD),[36] using the follow-up data. When means and standard deviations were unavailable, the first author was contacted for the details. All contacted authors provided information needed. In case only one article studied an intervention, the between-group SMD was considered. When multiple studies were available, the outcomes were pooled using Review Manager 5.3 and forest plots were provided.[35] Effect sizes were classified as small (<0.20), moderate (≥0.20 and ≤0.80) or large (>0.80), according to Cohen's criteria.[37]

To assess the certainty of the findings, the GRADE recommendations were followed considering the following domains: trial design limitations (using the RoB tool), inconsistency of results, indirectness, imprecision of results and publication bias.[38–40] The certainty was classified as one of the four levels: high, moderate, low, or very low. The details of this method have been reported previously.[10,41,42]

Table 7.1: Characteristics of included studies considering study design, subjects, interventions and outcome.

Author, year	Complaints	Intervention group			Control group			Therapist	Follow-up	Headache VAS outcomes				
		Population	Intervention		Population	Control intervention				Intervention group		Control group		Between group p-value
		N(%F) Age±SD	Type	Freq.	N(%F) Age±SD	Type	Freq.			B m(SD)	FU m(SD)	B m(SD)	FU m(SD)	
Costa, 2015(36)	Myofascial TMD and headache	30(90) 36±6.7	Counseling, relaxation exercises, stretching and auto-massage jaw muscles	3-5x / week 30min for 5mo.	30(90) 27.5±6.7	Counseling and occlusal appliance	1x	Therapist (undefined)	5 months	7.6 (2.2)	4.4 (2.5)	6.5 (1.6)	3.4 (2.2)	NS
Maluf, 2010(37)	TMD-pain	12 (100) 30.1±7.1	Static stretching of cervical spine, upper limbs, and mandibular muscles	1x / week 40min for 2mo.	12 (100) 30.0±4.3	Global posture reeducation	1x / week 40min for 2mo.	Therapist (undefined)	8 weeks	65.7 (21.7)	16.4 (16.6)	73.5 (26.2)	39.2 (29.8)	?
Michelotti, 2004(38)	TMD-pain	26(86.1) 28.2±8.8	Education + home exercises	7x / week ? min for 3mo.	23 (91.2) 31.8±13.0	Education	1x	Dentist	3 months	26.1 (29.7)	11.2 (17.4)	13.3 (19.7)	12.1 (17.0)	NS
Michelotti, 2012(39)	Myogenous TMD-pain	23 (82.6) 30.2±13.0	Education + home exercises	7x / week ? min for 3mo.	21 (71.4) 30.3±11.4	Splint	1x	Mandibular surgeon	3 months	33.3 (19.6)	33.7 (19.2)	33.9 (21.1)	33.7 (19.2)	NS
Von Piekartz, 2013(40)	CGH and TMD symptoms	22 (63.6) 34.7±7.1	Jaw muscle and -joint exercises combined with cervical manual therapy	1-2x / week 30min for 3-6 weeks	21 (66.7) 36.1±6.5	Cervical manual therapy	1-2x / week 30min for 3-6 weeks	Physical therapist	6 months	7.4* (1.1)	3.5* (2.0)	7.1* (1.1)	6.7* (1.2)	<.001

All included studies are Randomized Controlled Trials; TMD: temporomandibular disorder; CGH: cervicogenic headache; N: number of study participants; F: female; VAS: visual analog scale; m: mean; SD: standard deviation; N/A: not applicable; (?): missing; B: baseline; FU: follow-up; p: p-value; NS: not significant; mo.: months. * Measured with CAS: colored analog scale.

Results

Study selection

The search strategy revealed 87 initial articles from PubMed, 52 from Pedro and 6 from Cochrane (see Figure 7.1). After applying inclusion and exclusion criteria, five articles were included.[43–47] The list of excluded studies can be found in Appendix 7.2.

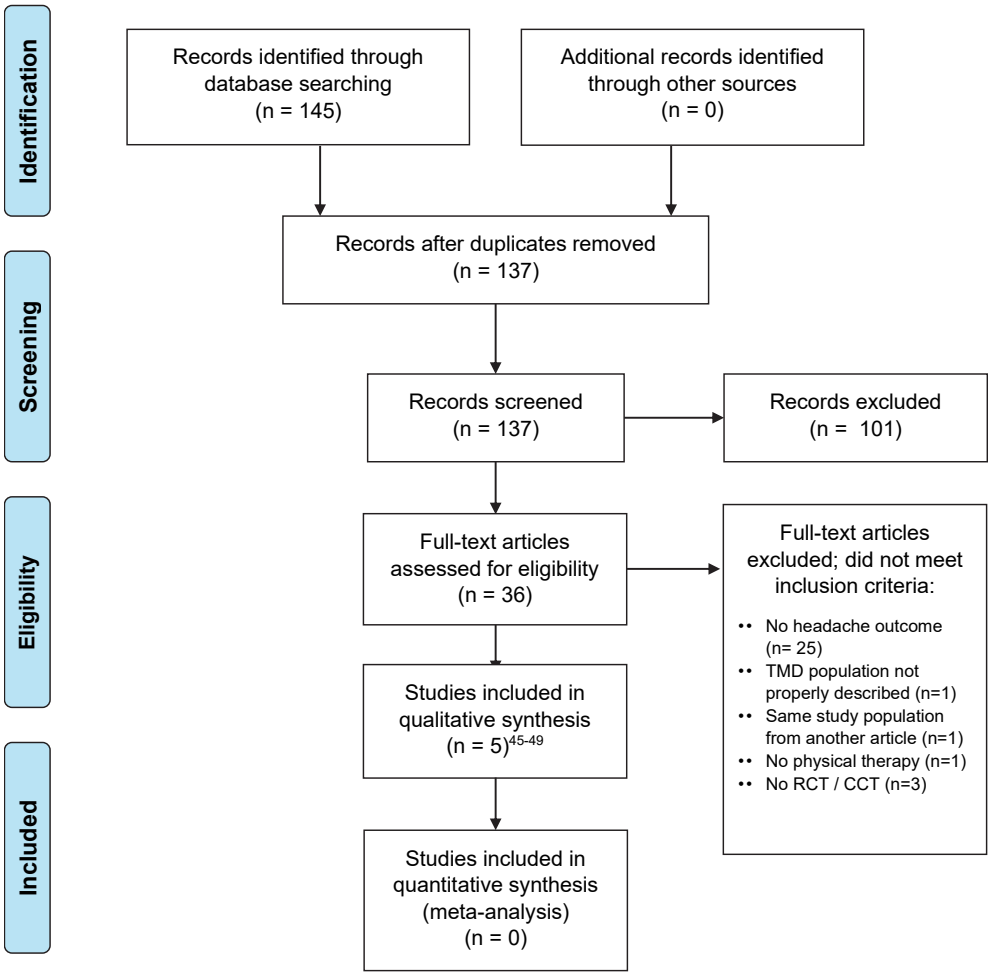

Figure 7.1: PRISMA Flow Diagram.

Risk of bias within studies

All articles received were classified as a high risk of bias on blinding of participants and personnel, and unclear risk on selective reporting (Figures 7.2 and 7.3).

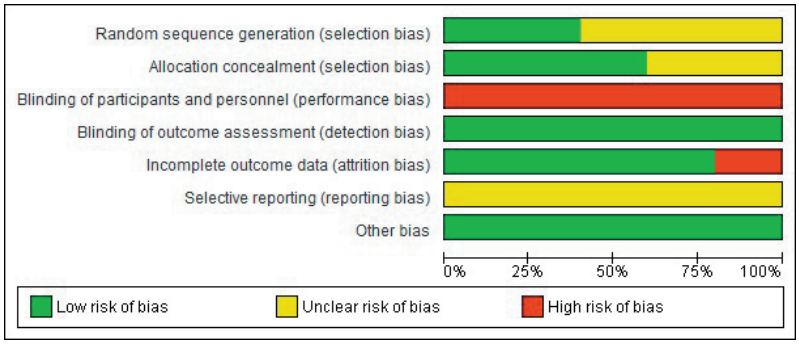

Figure 7.2: Risk of bias graph.

Characteristics and results of individual studies

In the five included RCTs[43–47] the study population ranged from 28 to 54 persons (see Table 7.1). The follow-up period ranged from two weeks to six months. Four articles used the VAS for headache intensity as an outcome measure.[43–46] One article used a colored analog scale (CAS) to rate headache pain intensity.[47] The frequency of the interventions ranged from daily for three months[45,46] to weekly for eight weeks.[44] The session time ranged from several minutes for home therapy[45,46] to full 30 to 40 minute sessions with a therapist.[43,44,47]

Although all included studies were RCTs, there was variation in the applied protocols regarding the therapy modality and the type of control intervention.

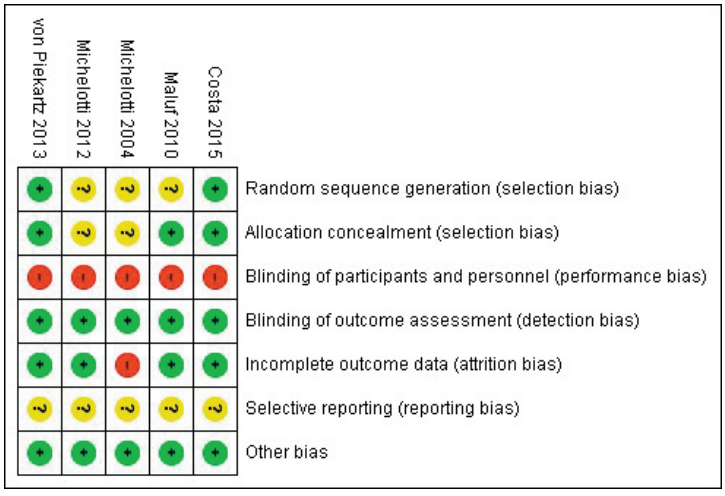

Figure 7.3: Risk of bias summary.

Table 7.2: Between-group and within-group effect sizes for individual studies stratified for different types of physical therapy compared to control interventions.

Overall PT for TMD *versus* control interventions						
Outcome	**Trial**	**Overall PT**		**Comparison**		**Beween-group ES**
		n	**Within-group ES**	**n**	**Within-group ES**	
Headache pain - VAS	Costa(36)	30	1.34	30	1.59	0.05
	Maluf(37)	12	2.46	12	1.18	0.60
	Michelotti(38)	26	0.60	23	0.06	0.62
	Michelotti(39)	23	-0.02	21	0.01	-0.03
	Von Piekartz(40)	19	2.37	17	0.34	-2.42
Counseling and exercise *versus* counseling and / or splint therapy						
Outcome	**Trial**	**Counseling + exercise**		**Comparison**		**Beween-group ES**
		n	**Within-group ES**	**n**	**Within-group ES**	
Headache pain - VAS	Costa(36)	30	1.34	30	1.59	0.05
	Michelotti(38)	26	0.60	23	0.06	0.62
	Michelotti(39)	23	-0.02	21	0.01	-0.03
Static stretching *versus* global stretching						
Outcome	**Trial**	**Static stretching**		**Comparison**		**Beween-group ES**
		n	**Within-group ES**	**n**	**Within-group ES**	
Headache pain - VAS	Maluf(37)	12	2.46	12	1.18	0.60
Orofacial and cervical manual therapy *versus* cervical manual therapy						
Outcome	**Trial**	**Static stretching**		**Comparison**		**Beween-group ES**
		n	**Within-group ES**	**n**	**Within-group ES**	
Headache pain - CAS	Von Piekartz(40)	19	2.37	17	0.34	-2.42

PT: physical therapy; TMD: temporomandibular disorder; n: number of participants; ES: effect size; VAS: visual analog scale; CAS: colored analog scale; N/A: not applicable.

Effect of the interventions and level of evidence

The GRADE criteria were applied for all therapy modalities. The studies were split in 3 subgroups, according to the intervention type and also analyzed together (Table 7.2). For two studies[43,47], additional data were collected from the authors to calculate the effect sizes.

Counseling and exercise versus counseling and/or splint

Three articles studied the effect of a multimodal intervention of counseling and exercises.[43,45,46] The control interventions were splint therapy (i.e. a removable artificial occlusal surface placed on the upper or lower dental arch)[48], counseling, or a combination of both counseling and splint therapy.

On the individual analysis, there was a small between-group effect size for Costa et al (2015) (SMD: 0.42; 95%CI: -0.09, 0.51), showing no clinically relevant difference between the multimodal therapy or combined counselling and splint therapy. The two other articles studied counseling and home exercises for three months.[45,46] One study[46] compared education to splint therapy and showed small between-group effect size (SMD: 0.00; 95%CI: -0.59, 0.59). The other study[45] compared education and education combined with physical therapy for TMD. The physical therapy regimen contained self-relaxation exercises, self-massage of the masticatory muscles, application of moist heat pads on the painful muscles, stretching, and coordination exercises. There was a moderate between-group effect size (SMD: -0.05; 95%CI: -0.61, 0.51)

Figure 7.4 shows the pooled mean difference, which is 0.15 (95%CI: -0.17, 0.46), indicating there is no difference in effect for counseling and exercises compared to counseling and/or splint therapy. Based on the GRADE recommendations (Table 3), we see that there is a low certainty of the found effects, downgraded by risk of bias and imprecision.

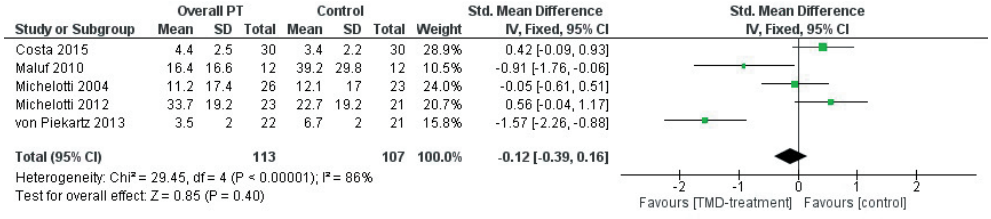

Figure 7.4: Forest plot of comparison overall physical therapy versus control interventions.

Table 7.3: Summary of findings table according to the GRADE recommendations for studies comparing different types of PT for TMD applied to patients with TMD and headache.

Overall PT for TMD *versus* control interventions			
Outcome	**N patients (studies)**	**Standardized Mean Difference (95%CI)**	**Certainty of the evidence (GRADE quality)**
Headache pain - VAS	220 (5 RCTs)[45-49]	-0.12 (-0.39, 0.16)	⊕◯◯◯ VERY LOW Due to risk of bias, inconsistency and imprecision.
Counseling and exercise *versus* counseling and / or splint therapy			
Outcome	**N patients (studies)**	**Standardized Mean Difference (95%CI)**	**Certainty of the evidence (GRADE quality)**
Headache pain - VAS	153 (3 RCTs)[45,47,48]	0.15 (-0.17, 0.46)	⊕⊕◯◯ LOW Due to risk of bias and imprecision.
Static stretching *versus* global stretching			
Outcome	**N patients (studies)**	**Standardized Mean Difference (95%CI)**	**Certainty of the evidence (GRADE quality)**
Headache pain - VAS	24 (1 RCT)[46]	-0.91 (-1.76, -0.06)	⊕⊕◯◯ LOW Due to risk of bias and imprecision.
Orofacial and cervical manual therapy *versus* cervical manual therapy			
Outcome	**N patients (studies)**	**Standardized Mean Difference (95%CI)**	**Certainty of the evidence (GRADE quality)**
Headache pain - VAS	43 (1 RCT)[49]	-1.57 (-2.26, -0.88)	⊕⊕◯◯ LOW Due to risk of bias and imprecision.

GRADE: Grades of Recommendation, Assessment, Development, and Evaluation; PT: physical therapy; TMD: temporomandibular disorder; n: number of participants; VAS: visual analog scale; CAS: colored analog scale.
* Methodological quality limitations based on the Cochrane Risk of Bias tool (high risk: serious -1 or very serious -2; unclear risk; not serious or serious -1).
GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Static stretching versus global stretching

One study[44] compared static stretching techniques for the cervical spine, upper limbs and mandibular muscles with postural re-education. This study showed a large between-group effect size in favor of static stretching (SMD: -0.91; 95%CI: -1.76, -0.06) on reducing headache pain intensity. There is a low certainty of evidence, downgraded by risk of bias and inconsistency, that static stretching of the cervical spine, upper limbs and mandibular muscles is more effective than global postural re-education for headache pain intensity.

Orofacial and cervical manual therapy versus cervical manual therapy

One study[47] applied orofacial therapy (i.e. jaw muscle and -joint exercises) combined with cervical manual therapy and compared this to cervical manual therapy alone. The between-group effect size was large (SMD: -1.57; 95%CI: -2.26, -0.89) showing that the intervention was superior to control intervention on reducing headache pain intensity. The level of certainty regarding the evidence was moderate, downgraded by inconsistency.

Overall effect on headache by physical therapy focused on TMD

When taking all included studies together as TMD physical therapy, this review shows that there is a very low level of certainty for TMD-treatment on reducing headache pain intensity, downgraded by high risk of bias, inconsistency and imprecision.[41] The pooled data analysis showed small overall effect (SMD: -0.12; 95%CI: -0.39, 0.16), in favor of TMD-focused physical therapy compared to control interventions (see also Figure 7.5).

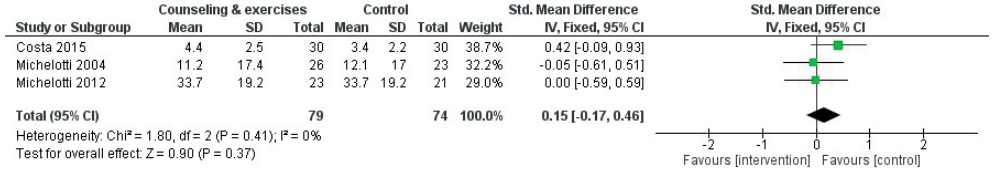

Figure 7.5: Forest plot of comparison counselling and exercise versus counselling and/or splint therapy.

Discussion

The aim of this study was to systematically evaluate the literature on the effectiveness of physical therapy for TMD on concomitant headache pain intensity. The therapy modalities varied across the five included articles. The certainty of the findings was very low for the effectiveness of physical therapy for TMD on headache intensity.

The influence of headache types in TMD-treatment

Two studies described a specific headache diagnosis based on the ICHD-II, which were headache related to masticatory myofascial pain and cervicogenic headache.[43,47,49] The other three studies did not describe the headache types,[44–46] but they may have been at least a part of patients with primary headache as these are very prevalent (10 to 63%) in patients with TMD.[11,14,50,51] The presence of a primary headache may have negatively interfered with the efficacy of the different musculoskeletal TMD treatments on TMD complaints.[52] This is possibly due to peripheral or central mechanisms. For instance, one theory states that the increase in pain transmission from peripheral tissues, such as the masticatory system, to the trigeminal system negatively interferes with the efficacy of the treatment.[52] Central sensitization (CS) can also play a role in the efficacy of treatment, as patients with multiple complaints such as chronic TTH, migraine and TMD tend to

show more signs of CS.[23,53–55] Patients with signs of CS manifest pain hypersensitivity and hyperalgesia, for whom certain therapies may increase the pain rather than decrease it.[54,56] A combination of peripheral and central mechanisms can also contribute to the etiology and interference with therapy: input from the periphery (i.e. masticatory system) may turn to painful output due to CS.[54,55] However, combining a TMD treatment with specific medication for migraine is found to be more effective as compared to a single treatment for either TMD or migraine.[57] Thus, it is important to know which type of headache is the concomitant headache with the TMD complaints.

The role of the muscles and the cervical spine

In this review, two studied interventions (stretching and orofacial therapy) focused on myogenous problems rather than arthrogenous.[44,47] Headache is more prevalent in patients with muscle-related TMD than in patients with joint-related TMD,[13,51,58] and some headaches, for example TTH, are similar to certain muscular referred pain patterns.[59,60] This may explain the effectiveness of the muscle-oriented physical therapy for TMD on headache intensity. Both stretching and orofacial therapy aim at relaxing the muscles and by that decreasing the TMD-pain and headache pain intensity.[44,47] Additionally, both studies showed that combining treatment regarding the temporomandibular area (jaw, masseter muscle, temporal muscle) and cervical area (spine and muscles) are effective for headache intensity.[44,47]

Other studies have also shown that exercises for the cervical spine can decrease both TMD complaints as well as headache complaints.[10,61–63] Three studies included applied home exercises as part of the physical therapy for TMD.[43,45,46] However, it is unclear which specific home exercises were applied and if they were only addressed to the jaw or also the cervical spine. Furthermore, there is debate about the effectiveness of home exercises compared to supervised exercises. For other disorders such as knee osteoarthritis, chronic neck pain and shoulder impingement, both types of exercise were effective, but when at least one supervised training was done the effect increased and lasted longer.[64–66] Future studies should describe the types of exercises more elaborately and compare supervised exercises with home exercises to fully understand how to apply exercise therapy for best results.

As patients with TMD pain often experience pain or dysfunction in the cervical spine[19,67] and patients with headache also often experience neck problems[68], it is important to not just look at the masticatory system in patients with TMD and headache, but also include the cervical spine and muscles.[23] Bruxism may also play a role in this three-way association, as temporomandibular disorders, cervical impairment and headaches are all associated with bruxism.[13,19,69,70] When patients are bruxing, not only their masticatory muscles are active but also muscles from the cervical spine.[71] Currently the exact working

mechanism on these four aspects and how they influence each other and treatment outcomes remains unclear. Therefore, more high-quality research is needed to establish the association between TMD, headache and cervical involvement and the effects of treating these complaints separately compared to treating them simultaneously.

Strengths and limitations of the study

There are several strengths in this review. First, this review is the first study to approach the issue of the effect of treating TMD on headache pain intensity. By describing the limitations per study, a clear suggestion for future research can be made. Secondly, all steps within this review have been done by two researchers, blinded to each other's results.

However, the results of this review must be interpreted considering some limitations. First, when interpreting the pooled results, one should consider that these are based on a heterogeneity of interventions, patient populations, and therapists. Furthermore, most included studies scored a high or unclear risk of bias on allocation concealment. A meta-epidemiological study stated that this bias may exaggerate treatment effects.[72] As blinding of participants or therapists in physical intervention studies is near impossible to have, most studies scored poorly on these aspects. Also, the interventions studied in this review could all be given by a physical therapist and are part of the physical therapy modalities, but were sometimes given by undefined therapists[43,44], by a dentist[45], or a mandibular surgeon[46]. Physical therapists are experts in the musculoskeletal field and are equipped to apply interventions to promote movement, reduce pain, restore function and prevent disability, just as the interventions within this review.[73] If these interventions would have been applied to the patients by physical therapists, the outcomes may have been different. Most preferably, a collaboration between different disciplines should be applied in the future for optimal results.[74,75] For the current review, the findings should be interpreted with caution as there was not a physical therapist involved in each study, but contained other disciplines or home exercises, so a full conclusion of the effectiveness of physical therapy cannot be given. Furthermore, this review did not include chiropractic or osteopathic interventions in the search. Even though all three professions work with musculoskeletal complaints and could therefore be applied within the same review, they all require different educational degrees and are therefore not interchangeable. Thus, they were not included in the review, but it may be interesting for future studies to look at the effectiveness of those interventions on headache pain intensity in patients with TMD. Finally, there were only two studies that specified which headache type the patients were diagnosed with.[43,47] As different headache types have different etiologies, treatments may have a different effect on each headache type.[76]

Implications for research

Although it is impossible to blind the therapist in hands-on and counseling studies, intention-to-treat and blinding of subjects are possible but were not used in the included studies. We suggest that future studies should include placebo or sham groups as a comparison so the placebo effect of those therapies can be explored.[77,78] If this is not possible, future studies should compare two distinct interventions to establish the effect of one intervention compared to the other. Furthermore, intention-to-treat analysis should be used more consequently, to reduce bias and increase the quality of methodology and the level of evidence.[34,77] Future studies should also report the headache diagnosis of the patients, as it is very likely that the effect of TMD-treatment on primary headaches is different as compared to the effect on secondary headaches. More research needs to be done to establish the role primary headache may have in the effectiveness of TMD treatment.[13,14,51] Additionally, the treatment protocol needs to be available so physical therapists can apply the treatment methods in the clinical practice when the therapy is effective.

Implications for clinical practice

As multiple factors play an important role in the etiology of both TMD and headache, it is important for therapists to define these factors before starting treatment.[3,13,17,75,79] Because this review has not shown clear evidence for all physical therapy modalities, physical therapists must consider which treatment to apply based on the beforementioned factors. As orofacial physical therapy and cervical manual therapy do appear to be effective to reduce headache pain intensity, a specialized physical therapist should be part of the health care team for the treatment of TMD and headache, although they may not be available in all countries.[47,75,79]

Conclusion

Due to the methodological shortcomings, diversity of interventions and inconsistency of findings, there is currently a very low certainty that there is a non-significant effect of physical therapy for TMD on concomitant headache intensity compared to control interventions.

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Appendix 7.1 – Search strategies

Last performed: August 3, 2020.

Database	Search strategy	Results
Pubmed	((((((((((physical therapy modalities[MeSH Terms]) OR physiotherapy techniques[MeSH Terms]) OR physical therapy[Title/Abstract]) OR manual therapy[MeSH Terms]) OR mobilization[MeSH Terms]) OR exercise[MeSH Terms]) OR manual therapy[Title/Abstract]) OR mobilization therapy[Title/Abstract]) OR exercise[Title/Abstract])))) AND ((((((disorder, temporomandibular[MeSH Terms]) OR disorder, temporomandibular joint[MeSH Terms]) OR craniomandibular disorder[MeSH Terms]) OR temporomandibular dis*[Title/Abstract]) OR craniomandibular dis*[Title/Abstract]))) AND headache	87
PEDro	Title/Abstract: temporomandibular disorder Bodypart: Head / neck Method: clinical trial	52
Cochrane	#1 "temporomandibular disorder":ti,ab,kw or "craniomandibular disorder":ti,ab,kw (Word variations have been searched) #2 "physical therapy":ti,ab,kw or "physiotherapy":ti,ab,kw or "mobilization":ti,ab,kw or "exercise":ti,ab,kw or manual therapy:ti,ab,kw (Word variations have been searched) #3 "headache" (Word variations have been searched) #4 #1 AND #2 AND #3	6

Appendix 7.2 – List and references of excluded articles

The following studies were excluded for reasons listed below:

- Headache pain intensity was not an outcome, or unclear if the pain intensity was specific for the headache (N=25) [1-25];
- The TMD-population was not properly described (N=1)[26];
- The same population was used in multiple studies (N=1)[27];
- The study did not fall under the domain of physical therapy (N=1)[28];
- Not the desired study design (N=3) [29–31].

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8

Chapter 8

Using e-Health in the Physical Therapeutic Care Process for Patients with Temporomandibular Disorders: a Qualitative Study on the Perspective of Physical Therapists and Patients

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Abstract

Background:
Treatment of temporomandibular disorder (TMD) currently consists of a combination of noninvasive therapies and may be supported by e-Health. It is, however, unclear if physical therapists and patients are positive towards the use of e-Health.

Purpose:
To assess the needs, facilitators and barriers of the use of an e-Health application from the perspective of both orofacial physical therapists and patients with TMD.

Methods:
A descriptive qualitative study was performed. Eleven physical therapists and nine patients with TMD were interviewed using a topic guide. Thematic analysis was applied, and findings were ordered according to four themes: acceptance of e-Health, expected utility, usability and convenience.

Results:
Physical therapists identified the need for e-Health as a supporting application to send questionnaires, animated exercises and evaluation tools. Key facilitators for both physical therapists and patients for implementing e-Health included the increase in self-efficacy, support of data collection and personalization of the application. Key barriers are the increase of screen time, the loss of personal contact, not up-to-date information and poor design of the application.

Conclusions:
Physical therapists and patients with TMD are positive towards the use of e-Health, in a blended form with the usual rehabilitation care process for TMD complaints.

Introduction

Up to 15% of the adult population reports pain in the temporomandibular region [1,2]. The cause of TMD is a combination of musculoskeletal and biopsychosocial factors [3–5]. Known risk factors for TMD pain are parafunctional habits, trauma, emotional distress, joint laxity, comorbidity of rheumatic and musculoskeletal disorders, and a poor general health and unhealthy lifestyle [6,7]. TMD can have an extensive impact on quality of life and can lead to work impairment [7,8].

Currently, TMD treatment consists of a combination of noninvasive therapies including physical therapy and splint therapy [2,9]. The American Association for Dental Research (AADR) recommends additional home-based care programs to TMD treatment to educate patients about their illness and how to manage their complaints [10]. Such home-based programs can be delivered through e-Health, which may facilitate the diagnostic process, intervention and follow-up evaluations [11]. E-Health can be described as the application of information and communication technologies across the wide range of activities that are performed in healthcare [11]. Other common terms for e-Health are 'telehealth', 'telemedicine' or 'mobile health'[12]. E-Health can be used as a way to monitor health, communication between patient and healthcare provider and collection of health data [13]. E-Health interventions can substitute or complement traditional face-to-face healthcare delivery [14]. Hence, the potential of e-Health for TMD management is considerable. However, a major issue in e-Health is adherence; just half of the patients fully adhere to e-Health (i.e. observed usage of e-Health compared to the intended usage) [15], which reduces treatment effectiveness. The design of e-Health applications is important for better adherence [15,16]. Furthermore, a lack of acceptance of e-Health by healthcare providers such as physical therapists is a barrier in the implementation of e-Health [17]. For new e-Health initiatives to be successful, it is important to investigate the opportunities and challenges in TMD management.

TMD management is often multidisciplinary, in which a specialized physical therapist plays an important role next to a specialized physician or dentist who determines the medical diagnosis [18]. In the field of oral and maxillofacial surgery, e-Health has already been welcomed to decrease waiting time to see specialists and to provide information and education before and after surgery [19]. From this field, promising results are presented with regard to patients receiving the correct treatment and cost reduction [19,20]. However, it is unknown whether this type of e-Health is effective for patients with TMD who are seen by orofacial physical therapists (OPTs). Additionally, it is unknown whether OPTs would even recommend e-Health to this population.

Therefore, the aim of this study was to assess the needs, facilitators and barriers of an e-Health application included in the healthcare process of patients with TMD, from the perspective of both OPTs and patients with TMD.

Methods

This study has been performed and written according to the Standards for Reporting Qualitative Research (SRQR) [21]. The funders played no role in the design, conduct, or reporting of this study.

Qualitative Approach and Research Paradigm

A descriptive qualitative study design was applied, using open interviews to obtain an in-depth understanding of the perception on the needs, facilitators and barriers with regard to e-Health in the healthcare process of patients with TMD [22].

Participants and Sampling

OPTs were recruited through the registry of the Dutch Society for Orofacial Physical Therapy (NVOF) and individually interviewed in their clinical practice. Interviews were administered between March 2016 and May 2016. Inclusion criteria were: 1) having over three years of working experience as an OPT with minimal a MSc graduation and 2) seeing at least eight patients with TMD per week.

The participating OPTs recruited patients with TMD for the study. When there was no referral from a doctor or dentist, the OPTs screened for the presence of a possible TMD based on the history and physical examination of the patient. Pain in the masticatory system which was aggravated by function or palpation was an indication for a painful TMD, whereas clicking or locking of the joint during function was an indication for a functional TMD. The diagnoses were not confirmed by a dentist or other physician. The individual interviews with the patients were administered between December 2018 and February 2019. Inclusion criteria for patients were: 1) receiving or have received treatment for their TMD (at least three sessions) and 2) being over 18 years of age.

Participants were recruited until saturation was achieved, which was when no new information would be identified from the last two interviews and expected to occur between six and twelve interviews [23,24]. The study was approved by the ethics committee of the University Medical Center Utrecht (OPTs: 15-728/C; patients: 18-703/C). All participants signed informed consent form before the interview.

Interviews

Open face-to-face interviews were conducted with OPTs and patients using pre-defined topic guides (see Appendix 8.1). These topic guides were open to changes when interviews identified new information. All participants were asked about the current situation of TMD management and their experiences, followed by questions about possibilities of using e-Health. The needs, facilitators and barriers were identified through questions like "If e-Health was available, what would make you want to use it and why?" and "What would you need of such an e-Health application?".

Four members of the research team (TvB, HvdM, LdP and CMS) were actively involved in collecting and processing data. The interviews with OPTs were conducted by TvB, a master's student of clinical health sciences and a graduated physical therapist. The interviews with the patients were conducted by LdP, a master's student of musculoskeletal physical therapy and a graduated physical therapist. Both were trained by HvdM, a PhD-student and OPT who received training on qualitative research methods. The topic guide for the OPT interviews was created by TvB and HvdM, the topic guide for the patients by LdP and HvdM (Appendix 8.1), both were validated by CMS who is a senior researcher and OPT. Patients were interviewed at a location of their choice. There were no prior relationships between the researchers and participants.

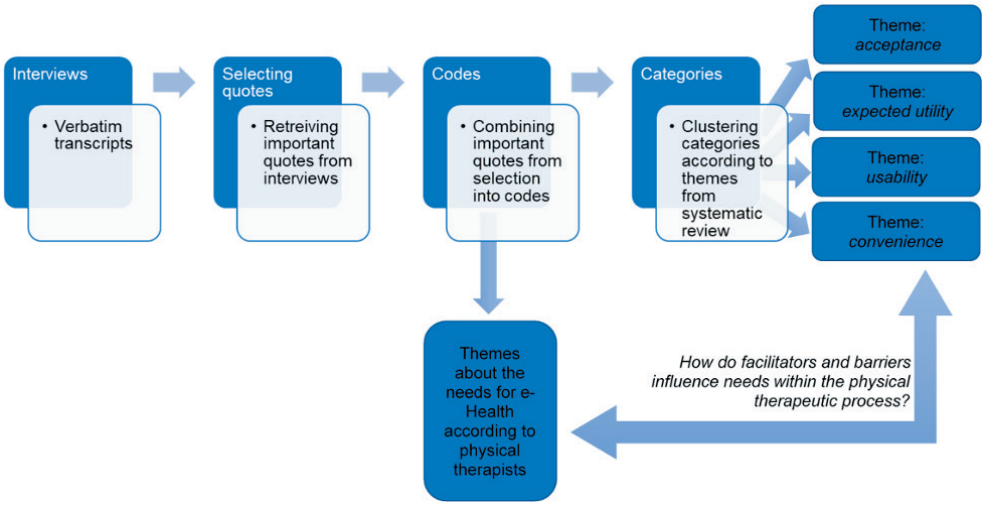

Figure 8.1: Method flow of data analysis.

Data Analysis

Interviews lasted between 30 and 45 minutes and were recorded. The audio files were transcribed verbatim. Anonymized transcripts were imported in the computer program Atlas.ti version 8 for windows (ATLAS.ti Scientific Software Development GmbH) [25].

Data analysis was performed by two researchers independently (TvB & HvdM for the OPTs, LdP & HvdM for patients) and compared after the third and last interview. Data were analysed with a thematic analysis approach [22]. The transcribed interviews were read closely to identify important quotes, to label codes to the data and to generate themes [22]. The identified themes related to needs for e-Health were structured according to the physiotherapeutic care process: diagnostic process, treatment and evaluation. For the facilitators and barriers, categories were identified from codes, which were then structured into themes according to a recent systematic review: 1) acceptance of e-Health, 2) expected utility, 3) usability and 4) convenience [26]. The flow of data analysis is depicted in figure 1. Quotes from the interviews were used to support the themes. All quotes provided in the article were translated into English by HvdM. Quotes by OPTs are marked with OPT_{number} and quotes by patients are marked as Pt_{number}. For every OPT it was indicated if their work experience in the field of TMD was higher than average (+ sign behind the OPT_{number}) or lower than average (- sign), as described in table 1. For every patient, the signs indicated if their age was above (+) or below (-) average as described in table 2.

Table 8.1: Characteristics of the Orofacial Physical therapists (N=11).

Characteristics	OPT participants (N=11)
Age in years, mean (range)	43.1 (28 - 63)
Female, n (%)	7 (63.6)
Work experience in years, mean (range)	21.6 (7 - 40)
Work experience with TMD in years, mean (range)	13.2 (2 – 30)
Primary care setting, n (%)	10 (90.9)
Secondary / tertiary care setting, n (%)	4 (36.4)

OPT: Orofacial Physical Therapist; n: number.

Results

Study Population Characteristics

A total of 11 OPTs participated in the study. The mean age of OPTs was 43.1 years and the majority was female (Table 8.1). Ten OPTs worked, full or in part, in a primary care setting. Mean work experience among participants was 21.6 years and mean work experience specifically for TMD was 13.2 years. For patient participants (Table 8.2), saturation was reached after 9 interviews. The mean age of the patients was 48 years and the majority was female. Five patients had completed their therapy and the majority (78%) went to the OPT because of TMD pain.

Table 8.2: Characteristics of the patient population (N=9).

Characteristic	Patient participants (N=9)
Female, n (%)	8 (89)
Age in years, mean (range)	48 (27 - 68)
Finished treatment, n (%)	5 (56)
Reference to the OPT	
Direct access physical therapy, n (%)	1 (11)
General practitioner, n (%)	3 (33)
Dentist, n (%)	5 (55)
Specialist, n (%)	1 (11)
Treatment setting	
Primary care setting, n (%)	7 (78)
Secondary / tertiary care setting, n (%)	2 (22)
TMD diagnosis	
Myogenic, n (%)	4 (44)
Arthrogenic, n (%)	1 (11)
Myogenic and arthrogenic, n (%)	3 (33)
Surgery, n (%)	1 (11)
Symptoms	
Headache, n (%)	2 (22)
Facial pain, n (%)	5 (55)
Jaw pain, n (%)	7 (78)
Ear pain, n (%)	3 (33)
Pain in the neck/shoulder area, n (%)	2 (22)
Tooth pain, n (%)	1 (11)
Limited mouth opening, n (%)	4 (44)
Trouble eating, n (%)	4 (44)

Needs and Opportunities of e-Health in the Current TMD-treatment

OPTs were asked to describe the current situation of care for TMD patients and what they believe the value of an OPT is in this care process (Figure 8.2). The themes support, efficiency, personal aspects and finances (Figure 8.2) described the needs for e-Health and are ordered in each step of the care process.

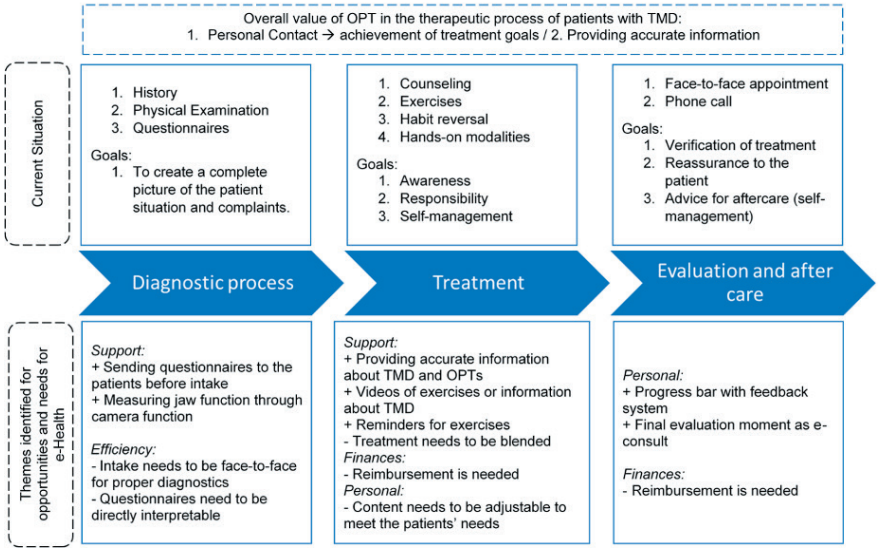

Figure 8.2: Key points of the physical therapeutic process of TMD patients and the needs and possibilities for e-Health according to OPTs.

Diagnostic Process

The diagnostic process is seen as important to understand which factors play a role in origination and preservation of complaints and which factors can be influenced by the OPT. During the diagnostic process, in-depth conversations with the patient are perceived as the basis for formulation of patient-tailored goals. "*A patient tells you their diagnosis*" (OPT09 -). To ***support*** the care process, questionnaires could be sent before the intake assessment, though for ***efficiency*** it is important these questionnaires are directly interpretable.

TMD-treatment

The treatment process is based on the diagnosis, complaints and patient preferences (***personal*** aspects). Counseling is therefore perceived as a crucial aspect of treatment and is applied throughout the entire treatment process. Additionally, exercises, habit reversal and hands-on therapies are applied. All therapies aim at creating awareness of the patient, increase self-efficacy and responsibility of the patient in their own recovery and apply self-management strategies. Vis a vis counseling is seen as essential: "*But I do think that if you do not explain things, you do miss a part of the treatment*" (OPT02 -). E-Health could ***support*** the treatment process through extra information, exercise videos and reminders for exercise but not displace personal contact.

Evaluation

It was emphasized that evaluations are important within the therapeutic process to see how patients do, if they understood the exercises and information that they were given and to reassure them. If the patient is doing well, the final evaluation is often done by phone. "*Well, what I often do with regard to home exercises is to verify that another time to see if it is all going well and eventually, I do see evaluations as treatment as well"* (OPT05 -). There is an opportunity for e-Health to ***support*** this feature, but this would need to get recognized as treatment and be reimbursed as such (***finance***).

Overall Value of the OPT

The overall value of an OPT within the care process for patients with TMD lies in ***personal*** contact. Personal contact between OPT and patient is regarded needed to achieve treatment goals of awareness, responsibility and self-management. Using both physical touch and conversing with patients is seen as important for success. Information can be put in the right context for patients and OPTs can get more in-depth information when they see patients face-to-face. "*I do think that, that is where the strength of the OPT lies, especially in the synchronization between touching and talking*" (OPT06 -).

Facilitators and Barriers for e-Health: Perspective of OPTs

The facilitators and barriers are described according to the structure of the interviews around these themes: 1) acceptance of e-Health: this includes participants' opinion of and experience with e-Health in general; 2) expected utility: which summarizes the participants' expectations of rewards and costs; 3) usability: a widespread term, including description of content of e-Health that participants find useable; and 4) convenience: which focusses on direct interaction with technology [26]. The categories and themes are depicted in table 3.

Table 8.3: Model of the Main Themes including the Key Facilitators and Barriers according to Orofacial Physical Therapists and Patients for the use of e-Health.

Key Facilitators				Key Barriers		
	OPT	Pt		OPT	Pt	
Familiar with e-Health	■	■	**Acceptance of e-Health**	■	■	Technical skills
Going with natural changes	■				■	Downsizing screen time
Prevention	■	■	**Expected Utility**	■	■	Time investment OPT
Self-efficacy	■	■			■	Changes treatment
Motivational	■	■		■	■	Losing personal contact
Insight in process	■	■			■	Fixation
Reliable information processing	■					
Fits TMD treatment	■	■	**Usability**		■	Exercises easy / online
Reminder	■	■			■	Not part of treatment
Information distribution	■	■		■	■	No need for additional information
Moment of use	■	■				Content not ready / up-to-date
Timeline (following progress)		■				
Available app & website	■	■	**Convenience**	■	■	Costs
Clear menu	■	■			■	Advertising
Animated exercises	■	■			■	Social Media
Adjustable	■	■		■	■	Poor design or technology
Personal	■	■			■	Complex profile

OPT: Orofacial Physical therapist; Pt: Patient; TMD: temporomandibular disorder. Green indicates theme identified in interviews with OPTs and blue indicates themes identified in interviews with patients.

Acceptance of e-Health

Identified facilitators were familiarity with e-Health and going with natural changes (i.e. technology is becoming more integrated in society including health care). Some OPTs either developed e-Health initiatives for professional use or tested and evaluated e-Health in their line of work. For example, the NVOF used to have a mobile application for patients to find OPTs throughout the Netherlands and to view videos of exercises which was recommended to their patients by some OPTs. The majority of the OPTs stood positive towards technology to support or improve current healthcare and believed that e-Health will become a part of healthcare. Some OPTs believed the rise of technology in healthcare is unavoidable. "*The way you will work and the way you will give information to the patients and counsel people. Changes are coming, I am sure of that.*" (OPT03 +)

A barrier for acceptance of e-Health the OPTs identified the technical skills needed for e-Health. For some the use of devices or online services is not natural yet: "*But I have to automate myself more for digital things.*" (OPT01 -) This was perceived as a barrier for **efficiency**, which was identified as in the health care process.

Expected Utility of e-Health

Regarding expected utility of e-Health, the following facilitators were identified: prevention, self-efficacy, motivation, insight in treatment process and reliable information processing. e-Health could be helpful as prevention for re-occurring complaints and to decrease treatment frequency and needs. OPTs felt this may lead to an increase in self-efficacy and awareness in patients regarding the management of their complaints. "*I think it [e-Health] can help in the actively involved role of the patient*" (OPT09 -). The positive effects would then mostly be seen in the **support** of the treatment process.

The barriers identified were time investment of the OPT and losing personal contact during the TMD care process as major concern. "*We, of course, never want to lose the essence of our business, and I think that, that is that you also have physical contact*" (OPT09 -).

Usability

Key facilitators regarding usability were compatibility with TMD treatment, reminder functionality, information distribution and moment of use. OPTs mentioned that e-Health is suitable for treatment of TMD. Push notifications and reminders were seen as possibly useful. "*When you can, for example, send a signal to your phone to sometimes get a stimulant of 'oh, what am I doing?'*" (OPT11 +). A timeline or chart to see the progress and goals of the patients was seen as beneficial. Additionally, OPTs were open to a communication source with patients and preferred short messages or a video-chat.

The main barrier reported for usability was regarding the educational content. If the content of an e-Health application was not up-to-date, this could lead to misinformation of the patients.

Convenience

Facilitators for OPTs in using the e-Health application were the availability of an application or website, having a clear menu, having animated exercises and for e-Health to be adjustable and personalized to the patient. Currently most OPTs provide exercises on paper and they see great opportunities in animated videos of exercises, as long as they are of high quality. "*At that way [videos] it is just to create an even better picture of the exercises*" (OPT02 -). Poor design of the application or having to pay a disproportionate amount of money for the application, were identified barriers. "*I think well-working websites is a must, actually. […] It is hard to get to and if you want to show your patient something, it is never easy. So that is why I have so much of my own information and things, but I would think it would be great [if the website was better designed].*" (OPT06 -)

Facilitators and Barriers for e-Health: Perspective of Patients with TMD

The same themes were used as for the OPTs to cluster the facilitators and barriers for patients (Table 8.3). The needs identified by the patients were affiliated to the themes of the perspective on e-Health.

Acceptance of e-Health

The key facilitator for patients to accept e-Health was being familiar with e-Health already. Some patients already use simple apps for their health like a pedometer-app.

Key barriers were the lack of technical skills of the patient and screen time. Some patients did not think highly of their technical skills. "*I am not really the one to look things up online.*" (Pt01). Most of them were positive: "*I think it [e-Health] could work, especially with the jaw, because most work is done when you are* ***not*** *with your physical therapist*" (Pt04 -).

Expected Utility

Prevention, self-efficacy, motivation, insight in the process and reliable information processing were mentioned as facilitators. Patients were positive towards the use of e-Health as they felt it could be helpful to prevent re-occurring complaints and decrease treatment frequency and needs. "*I think it [e-Health] can be very cost-effective for health care, especially for jaw complaints. You can see your OPT less often because you already have your tools with you. I think it's a very good idea" (Pt04 -)*. E-Health could provide motivational support, give insight in the progress of the patient, and provide reliable information to the OPT about complaints patients may have. Moreover, information about OPTs can also be provided. Barriers identified by the patients were time investment of the OPT, changes in

treatment, losing personal contact and fixation on complaints. Patients were concerned about the loss of personal contact between the OPT and patient. "*I like the contact, not just exercises but also the chats, just how you are and give feedback"* (Pt08 +). Additionally, patients were concerned that including e-Health would change their treatment and might create too much fixation on the complaints. "*[…] then you are just too preoccupied with it.*" (Pt09 -)

Usability

The identified facilitators were the compatibility with the TMD treatment, reminder function, information distribution, moment of use and following progress. Patients believed that e-Health is suitable for treatment since exercises for TMD are suitable to their daily routine and can be done anywhere. "*You can grab your phone anywhere, in an instant, if you're somewhere in the waiting room and you think, how was it again, then you can just grab it! You can always do those jaw exercises on the bus or train, because almost no one ever notices" (Pt02 +).* An often-mentioned feature of an e-Health application was being able to receive reminders to do exercises. Patients who had to change their parafunctional behaviour, had trouble to detect and minimize these habits, therefore there is a great need of a reminder: *"And for myself, yes if I notice, I stop it [parafunctional behaviour] right away. But it is very hard to notice that" (Pt05 -). Besides reminders, another* facilitator would be a timeline or chart to see the progress and goals of the patients. A chat function was mentioned, but the patients concluded a 'Frequently Asked Question' section may be sufficient.

Patients identified the following usability barriers: exercise difficulty, separate treatments, and the need for information. When exercises would be deemed too easy and therefore not require support by an app or video, or exercises can be found online (for example on YouTube), patients did not see additional value in an e-Health application. Some also stated that they did not need extra information, as they receive all information they need from their OPT.

Convenience/ Accessibility

Facilitators for patients were the availability of the application or website, having a clear menu, having animated exercises and for the app to be adjustable and personalized to the patient. According to patients, an application should be part of treatment and needs guiding, like blended care. For example, feedback of the therapist is needed to control implementation of the exercises. Animated exercises in an application would help. "*If you have an app for people who have received treatment then it might be convenient if they have their personalized exercises on it.*" (Pt02 +)

Barriers were costs, advertising, social media, poor design or technology and making a complex profile. If an e-Health application would include advertising, having to create a complex profile or attaching it to a social media platform, this would be a barrier for patients to use the application. A poor design of the application or having to pay a disproportionate amount of money for the application, would prevent patients from using the e-Health application as well. *"[…] because I already pay for the physio actually. Then work is taken away again through the app, then I do not think I have to pay for it. Yes, they are just service tasks, they have to organize something else for that. No, I would not pay for that." (Pt06 +)*

Discussion

The key findings of this study are that e-Health would be accepted by OPTs and TMD patients when it is used in a blended form to complement the usual TMD-treatment. The need for blended care is because the greatest value of an OPT was identified to be the personal contact between OPTs and patients. The personal contact helped the patients achieve their goals and receive the right information about their complaints. This personal contact was important throughout the entire care process, from history, diagnostics and treatment. Both OPTs and patients did see opportunities for e-Health within the current TMD care process for additional information, support for exercises, up-to-date information and reminders and feedback to realize behavioural change.

Common facilitators for people to use e-Health are clarity of information, speed of the system, compatibility with one's existing routine, presence of reminders and receiving feedback[26,27]. This was comparable in the current study, where the OPTs were most focused on the clarity of information and the patients on the system and how to use it. TMD-treatment goals consist of increasing self-management and self-efficacy [2], and both OPTs and patients believe e-Health can facilitate this process. This was also found in patients with chronic obstructive pulmonary disease, where an e-Health application for the management of exacerbations was studied [28]. This supports the needs identified in the current study, where OPTs stated that e-Health could help with the support and efficiency of the diagnostic process as well as treatment process, when the application was person-centred and made use of the identified facilitators.

Poor design or technology of an e-Health application was not only mentioned as a barrier in the current study, but was also one of the main barriers found in a systematic review [26]. Additionally, financial costs were a common barrier throughout several populations[26], including the one from the current study. OPTs wanted to receive financial reimbursement (which was also identified as a need), but patients were not willing to pay for the use of an application. At this moment not all health insurance companies reimburse the use of

e-Health, but this could facilitate the implementation of e-Health. The lack of personal contact was the main barrier for OPTs as well as the TMD patients. In the current study, personal contact was considered the biggest value of an OPT in the care process of TMD patients. The option of blended e-Health was perceived as the optimal solution, where e-Health can support certain factors of the TMD-care process. Blended care was also identified as an optimal solution for patients with osteoarthritis, which was just as effective as usual physical therapy [29,30]. In patients with headache, there are tools available for screening and monitoring complaints, which could also be used for blended care [31]. None of the above mentioned studies describe the need for personal contact and how the lack of that may influence the commitment and effectiveness of an e-Health application. Therefore, this needs to be studied in patients with TMD specifically.

Strengths and Limitations

A major strength in the current study is having the perspective of both OPTs and patients, which helps to paint the full picture of when an e-Health application would or would not be used in the TMD care process.

There are some limitations of the current study that need to be considered. Firstly, as saturation was reached after 9 interviews in patients and 11 interviews in OPTs, this may suggest that the interviews did not go in-depth enough in the perspectives of the OPTs and patients. However, sample sizes of this size are common in qualitative research [24,28] and the findings of the current study were comparable to findings of a large systematic review [26]. A second limitation is the fact that the OPTs recruited patients to participate in the study, which may have introduced selection bias. Another limitation could be that the interviews were executed by different people, which may have led to some differences in the way of interviewing. By using a pre-set topic guide (appendix 1), the main topics were covered and the analysis phase confirmed this. Lastly, due to the qualitative research design there are no objectively verifiable results available that can be generalised [32]. Even though quantifying the perspective on something that has not happened yet cannot easily be done, when addressing the experience of an e-Health application in use quantitative data should be collected to increase transparency and external validity.

We concluded that an e-Health application would have added value if barriers and facilitators are taken into account. As there already are e-Health initiatives available, these can be used as starting point to suit the needs of the TMD care process, for instance by adding videos of specific TMD exercises [33]. At least one study described the use of telemedicine for TMD patients. This system shortened waiting time supported diagnostics [20], however, this system did not have all needed elements as the participants from the current study have described in order to use the e-Health application. Therefore, future research needs to focus on developing an e-Health application for TMD patients that fulfils all facilitating

criteria for optimal use. When such an e-Health application is available, the effectiveness should be studied while taking patient satisfaction into consideration. Additionally, as TMD management is preferred to be multidisciplinary[18], future studies should consider the perspective of the specialized dentist or physician towards e-Health in this population as well. Perhaps an integrated e-Health application to not only improve communication with the patient, but also interdisciplinary communication could be benefit [34,35].

Another factor to consider before implementing e-Health in the physical therapeutic TMD care, is the experience of the physical therapist. In the current study, patients have had minimally three sessions of physical therapy and all included therapists are well trained in the field of orofacial complaints including TMD [36]. It is uncertain, however, if the perspectives found in the current study are similar to patients who have not received minimally three sessions, or to physical therapists with a lesser extent of training. Therefore, this design should be replicated in other countries to ensure the validity of the findings.

In conclusion, OPTs and TMD patients are positive towards the use of blended e-Health in the health care process of the TMD complaints, complementary to the usual care. An e-Health application should be easy to use, accessible and contain information about the TMD complaints and animated exercises. Because there is a strong need for personal contact for both OPTs and patients, e-Health should be part of a blended care system rather than replacing physical therapy.

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Declaration of Interest
There is no conflict of interest within this study.

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Appendix 8.1. Summary of Topics mentioned in the Interview Guides for Orofacial Physical Therapists and Patients with Temporomandibular Disorders.

Topic guide for OPT	Topic guide for patients with TMD
Demographics	Demographics
Experiences related to the clinical process of TMD	Experiences related to the clinical process of TMD
(patient subtypes, clinical features, main elements of diagnostic process, main elements of therapy)	*(knowledge about complaints, important elements of received therapy, importance of OPT)*
e-Health; general	e-Health; general
(previous knowledge, digital skills, awareness, definition)	*(previous knowledge, digital skills, awareness, definition)*
e-Health; in TMD care process	e-Health; in TMD care process
(impact on people, impact on relationship with patient, using previous jaw application, needs for e-Health, facilitators to use, barriers for use, content, application, conditions)	*(perspective on how adding e-Health could influence the given therapy, impact on relationship with OPT, facilitators to use, barriers for use, content, application, conditions)*
Any last suggestions or comments	Any last suggestions or comments


9

Chapter 9

The Additional Value of e-Health according to Patients with a Temporomandibular Disorder and Orofacial Physical Therapists: a Mixed Methods Study

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Background:
Physical therapeutic treatment for temporomandibular disorders (TMD) may be supported with e-Health. Especially during the coronavirus lockdown, e-Health was used by many physical therapists. The experiences using e-Health are, however, unclear. In addition, the perspective on the additional value of e-Health, described by orofacial physical therapists (OPTs) and patients with TMD, is currently unknown.

Aim:
To assess the experience and perceived additional value of an e-Health application during the physical therapeutic treatment of patients with TMD.

Methods:
A mixed-methods study was performed. Semi-structured interviews were performed with OPTs and with TMD patients regarding their experience using an e-Health application, Physitrack. The modified telemedicine satisfaction and usefulness questionnaire and pain intensity score before and after treatment were collected from the patients.

Results:
Ten OPTs, of which nine actively used Physitrack, described that the e-Health application can help to provide personalized care to patients with TMD, due to the satisfying content, user-friendliness, accessibility, efficiency, and ability to motivate patients. Ten patients, of which nine ended up using Physitrack, felt that shared decision making before using e-Health was very important. These patients were positive towards the application as it was clear, convenient, and efficient, it helped with reassurance and adherence of the exercises and overall increased self-efficacy. This was mostly built on their experience with the exercise videos, as this feature was most used and seen as most valuable. None of the OPTs or patients used all features of Physitrack.

Conclusion:
OPTs and patients with TMD shared the idea that e-Health is of added value on top of usual physical therapeutic care for TMD complaints.

Introduction

As the coronavirus disease (COVID-19) pandemic settled in the world, many countries experienced one, or multiple, enforced lockdowns. Some patients could still see a physical therapist (PT) if they had an emergency, but most practices were closed for business.[1] Some practices, however, decided to switch to online therapy and to implement e-Health.[1,2]

E-Health can be defined as 'the delivery of personalized health care at a distance through the use of technology (i.e. computers, mobile phones or satellite communications).[3,4] Also before COVID-19, e-Health was increasingly more relevant and applied in physical therapeutic health care.[5–8] Even though there is some evidence that videoconferencing for patients with musculoskeletal disorders show positive effects,[9] high-quality evidence for the effectiveness of e-Health is limited and inconsistent at best.[3] Furthermore, it can be assumed that patients and PTs are sceptical about implementing e-Health.[10,11]

Facilitators to use e-Health are familiarity with, and having adequate digital skills of the end users, perceived usefulness and utility, clarity of information, convenience, and the intrinsic motivation of the end user.[11,12] In a recent study, the facilitators and barriers for the use of e-Health were explored in patients with a temporomandibular disorder (TMD) and specialized, orofacial physical therapists (OPTs).[13] TMDs are health conditions involving the temporomandibular joint, the masticatory muscles and surrounding structures,[14] and they are often treated with a combination of hands-on (i.e. massage, stretching, and mobilization) and hands-off (i.e. exercises, counseling) interventions.[14–16] The main barrier identified for using e-Health in the physical therapeutic care for TMD was the lack of personal (physical) contact.[13] Both patients with TMD and OPTs stated that they were positive towards the use of e-Health in a blended manner, especially in regards to home exercises.[13,17]

One of the available e-Health platforms that can be used for physical therapy and TMD complaints, is Physitrack (Physitrack Limited, London, UK).[18] Physitrack is an online platform that can be accessed through a web page, or through an application on a mobile phone or tablet (PhysiApp). Physitrack has multiple features that can be used: video calls as an online consult, exercise programs including videos, instructions, a reminder function, questionnaires including pain intensity score, and a chat function between patient and OPT.[18] Therapists can decide with their patients which features they would like to use for their patients and fit the Physitrack into their therapy programs.

Previous studies have shown high adherence rates to Physitrack in different patient populations, like patients with a musculoskeletal condition, or patients after an esophagectomy.[19,20] However, no research has been done in patients with TMD.

Additionally, it is unknown how patients with TMD and their OPTs experience the use of e-Health, and if additional value is perceived compared to the usual physical therapeutic TMD care. If patients and health care providers do not expect or perceive an additional value of an e-Health application, they are less likely to implement it successfully and in that case determining effectiveness will not be useful.[21,22] Hence, describing experiences and perceived additional value of both patients and OPTs could help implementation and future research.

Therefore, the aim of this study is to assess the experience and perceived additional value of e-Health, using the Physitrack application, during the physical therapeutic treatment for patients with TMD.

Methods

This manuscript is structured according to the 'Good Reporting of a Mixed Methods Study' (GRAMMS).[23] For the qualitative part, the Standards for Reporting Qualitative Research (SRQR) are followed.[24] The funders of this study and Physitrack played no role in the design, conduct, or reporting of this study.

Study design

A concurrent triangulation mixed methods design was used.[25,26] Here, qualitative and quantitative data were collected from the same population to identify similarities and differences between outcomes sampled in the two methods, and to then present the overall findings. Because the implementation of new interventions, such as e-Health, is not only reliant on effectiveness but also on the perceived additional value, a mixed methods design is most appropriate to explore these aspects.[27,28] In the current study the focus was on the perceived additional value of both OPTs and patients. During the qualitative data analysis, the experience of using Physitrack and the following perceived additional value were discussed during interviews. Furthermore, a questionnaire regarding user-satisfaction was given to the patients for the quantitative data before the interview took place. The data sources and research questions are depicted in Figure 9.1.

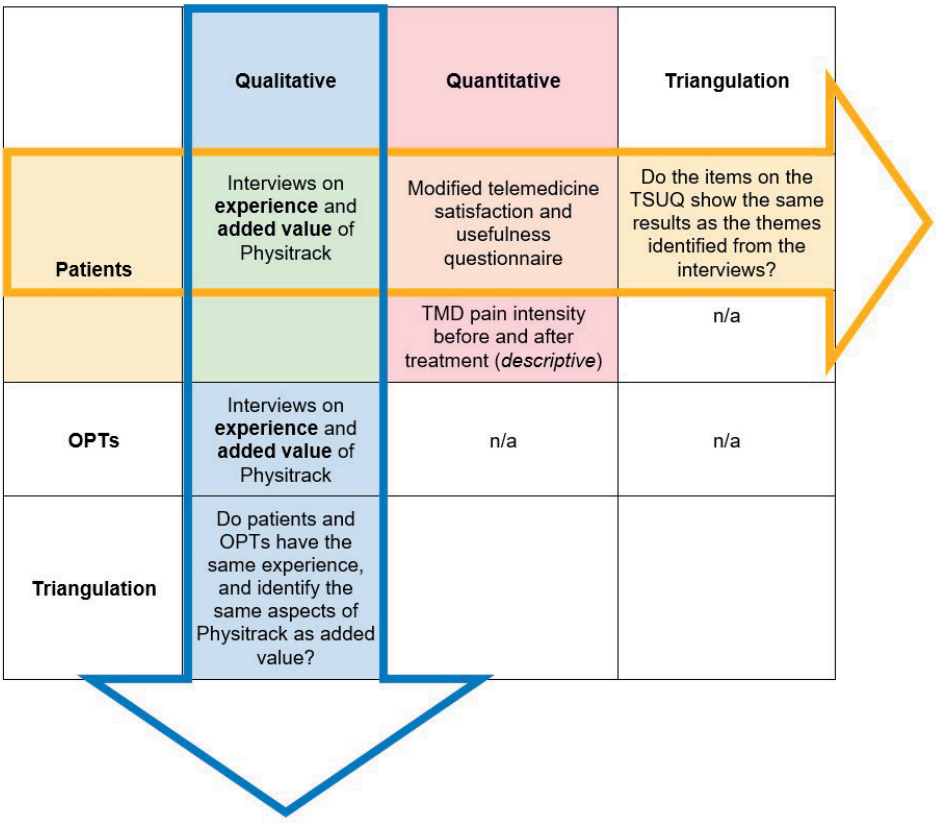

Figure 9.1: Overview of mixed-methods: data sources and research questions.

Study population

For OPTs convenience sampling was applied as OPTs were recruited through previous study participation,[13] a mailing list of the Dutch Society for Orofacial Physical Therapy and LinkedIn. They had to have a master's degree in the specialization Orofacial Physical Therapy, and they needed to have a membership to Physitrack to be included in the study.

For the patients with TMD, snowball sampling was applied, as they were invited by their OPT to participate in this study. Inclusion criteria were: 1) TMD complaint; 2) aged 18 years or older; 3) having had minimally two treatment sessions (face-to-face or online) with their OPT; 4) no serious underlying conditions for the TMD complaints; and 5) being able to communicate in Dutch or English. If the patient was referred to the OPT by a dentist or medical doctor, the information regarding TMD diagnosis and absence of serious underlying pathology was extracted from the referral. In some cases the patient came directly to the OPT without a referral through direct access,[29] and the OPT classified the presence of a TMD based on the history and physical examination of the patient. Pain in the masticatory system that was aggravated by function or palpation was classified as a

myalgia or arthralgia, dependent on the location of the pain. Clicking and locking of the joint were an indication for a disc displacement.

Participants were recruited until saturation of the data was achieved. Saturation was achieved when no new information could be identified from the last two interviews and was expected to occur between six and twelve interviews per group.[30] The study was approved by the Ethics Committee of the Academic Center for Dentistry Amsterdam (201972). All participants signed an informed consent form.

Qualitative data collection: Interviews

Semi-structured interviews were performed with individuals using pre-defined topic guides, asking about experiences with physical therapy in general (for patients), the experience with Physitrack, the perceived additional value of Physitrack, the reason of using Physitrack and future opportunities (for OPTs; see also Appendix 9.1). The topic guides were open to changes when interviews identified new information.

Three members of the research team (HvdM, AD, CMS) were actively involved in collecting and processing the data. One member (MN) had an advisory role regarding the topic guides. The OPTs were interviewed by HvdM, who is an OPT and knew all participating OPTs personally before the interviews. The patients were interviewed by a master's student of orthopedic manual therapy and a graduated physical therapist (AD), who was trained by HvdM. AD did not have any personal relationship with the patients who were interviewed, but they did have knowledge of TMD and the physiotherapeutic methods regarding TMD treatment. Before the interview started, a casual conversation was started to establish a comfortable environment for the participants to tell their story, and to ensure no imbalance in the power relationship was felt.[31] Before the COVID-19 lockdown the interviews were held at a location preferred by the participant, during the COVID-19 pandemic all interviews were done online in a secured environment. The interviews were recorded (audio and video for the online interviews with the OPTs and only audio for the interviews with patients). Then, the interviews were transcribed verbatim and imported in nVivo (QSR International Pty Ltd. Version 12, 2020) for further analysis.

Quantitative data collection: Characteristics and Outcome measures

Information from the OPTs concerned: age, gender, years of work experience in general, years of work experience with TMD patients, type of work setting, and working hours per week.

From the patients' files characteristics of the patients were collected: age, gender, TMD diagnosis, and TMD pain intensity before and after treatment, combined with additional

information on the treatment trajectory: number of (physical) treatment sessions, number of online treatment sessions, and applied functionalities from the Physitrack application.

Furthermore, patients were asked to fill out a modified telemedicine satisfaction and usefulness questionnaire (TSUQ), a 30-item Likert-type questionnaire including three subscales (satisfaction e-Health, satisfaction communication, and usefulness).[20,32] For the first two subscales, the likert scale ranged from 1 ('I agree with the statement') to 5 ('I do not agree with the statement'). The likert scale for usefulness ranged from 1 ('very useful') to 5 ('not useful at all'). The total score ranged from 30 to 150, where lower scores indicate higher agreement, and therefore higher satisfaction and usefulness.[20,32] The modified version of the TSUQ asks patients about their physical therapist instead of doctor or nurse, and refers to e-Health/Physitrack instead of 'telemedicine'.[20] Because the TSUQ was developed for patients, OPTs were not asked to fill out this questionnaire. Due to this, only triangulation between qualitative and quantitative findings could be done for the patients' perspective on the additional value of Physitrack. The TSUQ was filled out before the interview took place.

Qualitative analysis

The analysis process of the interviews was done in a similar fashion for the OPTs (HvdM & CMS) and the patients (AD & HvdM). The interviews were read, and open coding was applied to identify important aspects of the interviews using nVivo (QSR International Pty Ltd. Version 12, 2020). These codes were compared after the third and last interview, checking if consensus between researchers was present. If there was no consensus, the researchers discussed the codes until consensus was met. Then, axial coding was applied to identify themes. Because this process was done separately for patients and OPTs as their topic guide was slightly different, different themes could emerge from the interviews. The themes were compared between patients and OPTs, to see if there was an overlap on certain aspects. Quotes from the interviews were used to support the themes and were translated into English by HvdM. Quotes by patients are marked as Pt_{number} and quotes by OPTs are marked with OPT_{number}. The themes were presented to the OPTs via e-mail, and participants were asked if they identified themselves with these themes, to increase credibility.[33]

Quantitative analysis

Descriptive statistics were used to describe the characteristics of the participants. All outcome measures related to the treatment (pain intensity before and after treatment, number of sessions, use of Physitrack) as well as the TSUQ scores were depicted using descriptive statistics. No further analyses were performed due to a small sample size available.

Triangulation between qualitative and quantitative data

Two types of data triangulation were applied (see Figure 9.1). The first was to compare the qualitative findings of the OPTs with the qualitative findings of the patients regarding to the experience and perceived additional value of Physitrack. Furthermore, the findings of the qualitative outcomes regarding the additional value of Physitrack of the patients were compared to the quantitative outcomes (TSUQ) of the patients to evaluate if the themes identified from the interviews support the findings from the quantitative outcome measures and to establish if there is a convergency or discrepancy in findings.

Results

Participants' characteristics

Ten OPTs participated in the study (see Table 9.1) with a mean age of 34.3 years (male: 80%). All but one OPT worked in a private practice, of which three combined their work with working at a dental department or headache clinic. The mean work experience was 11.5 years, and the mean work experience specifically in the field of TMD was 4.6 years. Characteristics of the OPTs are depicted in Table 9.1.

All OPTs had a subscription for Physitrack, but only nine used one or more features of Physitrack actively. Six OPTs recently started using Physitrack due to COVID-19. The nine OPTs who actively used Physitrack all used the exercise videos, and they all used the video conference call functionality. Other functionalities like tracking progress and adherence, communicating via text message and sending or receiving patient information were not or infrequently used (see also Table 9.3).

Ten patients were recruited by four OPTs. Mean age was 52.3 years, all were female, and the mean number of treatment sessions was 4.9. Characteristics of the patients are depicted in Table 9.2. All but one used Physitrack at least in a part of their treatment course. One patient was unable to install Physitrack and therefore didn't use the application. Five patients were interviewed before the COVID-19 pandemic and the other five were interviewed during the pandemic. Two patients had at least one online session prior to the interview (Table 9.3), and three other patients had an online consult after the interview but during their treatment process (Table 9.2). Of the nine patients using Physitrack, all used the exercise video feature, two had one or more video conference calls with their OPT and two used the reminder and adherence function (see also Table 9.3).

Table 9.1: Basic characteristics Orofacial Physical Therapists.

Characteristic	OPT001	OPT002	OPT003	OPT004	OPT005	OPT006	OPT007	OPT008	OPT009	OPT010
Age (years)	33	39	29	32	41	40	34	29	36	32
Gender	m	m	f	m	m	m	f	m	m	m
Work setting:										
• Private practice	x	x	x	x	x		x	x	x	x
• Dental department	x	x								
• Headache clinic								x		
• Hospital						x				
Work hours per week	36	40	32	28	55	12	28	28	30	32
Working experience (years)										
• Physical therapy	9	15	8	9	19	17	12	6	12	8
• TMD specific	2	9	2	2	7	10	5	1	6	2
Moment of starting with Physitrack										
• Before COVID-19		x	x		x				x	
• During COVID-19	x			x		x	x	x		x
Included patients	y	y	y	n	y	n	n	n	n	n

TMD: temporomandibular disorder; OPT: Orofacial Physical Therapist; m: male; f: female; COVID-19: coronavirus disease 2019; y: yes; n: no.

Table 9.2: Basic characteristics patients with TMD.

Characteristic	pt001	pt002	pt003	pt004	pt005	pt006	pt007	pt008	pt009	pt010
TMD complaint:										
• Myalgia	x	x				x		x	x	
• Anterior disc displacement						x	x			
• Limited mouth opening										
• Other	x	x	x	x	x			x	x	x
Number of treatment sessions*										
• Face-to-face	6	4	3	6	3	4	5	5	3	3
• Online	0	0	3	2	2	1	2	0	0	0
TMD pain intensity (0-10)										
• Before treatment	4	8	4	7	6	5	7	5	3	6
• After treatment	1	0	2	1	1	1	1	1	1	2
Headache pain intensity (0-10)			n/a		n/a	n/a		n/a		
• Before treatment	8	8		8			5		6	3
• After treatment	1	0		7			4		0	3
OPT	OPT05	OPT05	OPT02	OPT02	OPT02	OPT01	OPT03	OPT03	OPT01	OPT02

TMD: temporomandibular disorder; f: female; n/a: not applicable; * number of treatment sessions was collected after the interview.

Table 9.3: Used functions of the Physitrack application prior to the interview.

Participant	Exercise videos	Information	Push-notifications	Pain scores	Video consult	Chat function
			Patients (N=10)			
Pt001	✓					
Pt002	✓					
Pt003	✓	✓	✓	✓		
Pt004	✓		✓	✓		
Pt005	✓					
Pt006	✓				✓	
Pt007						
Pt008	✓					
Pt009	✓				✓	
Pt010	✓					
			Orofacial Physical Therapists (N=10)			
OPT001	✓			✓	✓	✓
OPT002	✓	✓	✓		✓	✓
OPT003	✓				✓	
OPT004	✓			✓	✓	✓
OPT005	✓	✓			✓	
OPT006	✓		✓	✓	✓	
OPT007	✓	✓			✓	
OPT008	✓		✓		✓	
OPT009						
OPT010	✓			✓	✓	✓

Pt: patient; OPT: orofacial physical therapist; n: number of participants.
The grey marked areas indicate the functionalities offered by the OPT, the checkmarks indicate the actual usage of the functionality by the patient.

Based on the research questions and topic guides, there were three major themes present for both OPTs and patient participants: 1) general determinants for success; 2) experience with Physitrack; and 3) additional value of Physitrack. The sub-themes showed some variability between the OPTs and patients (see also Table 9.4 and Figure 9.2).

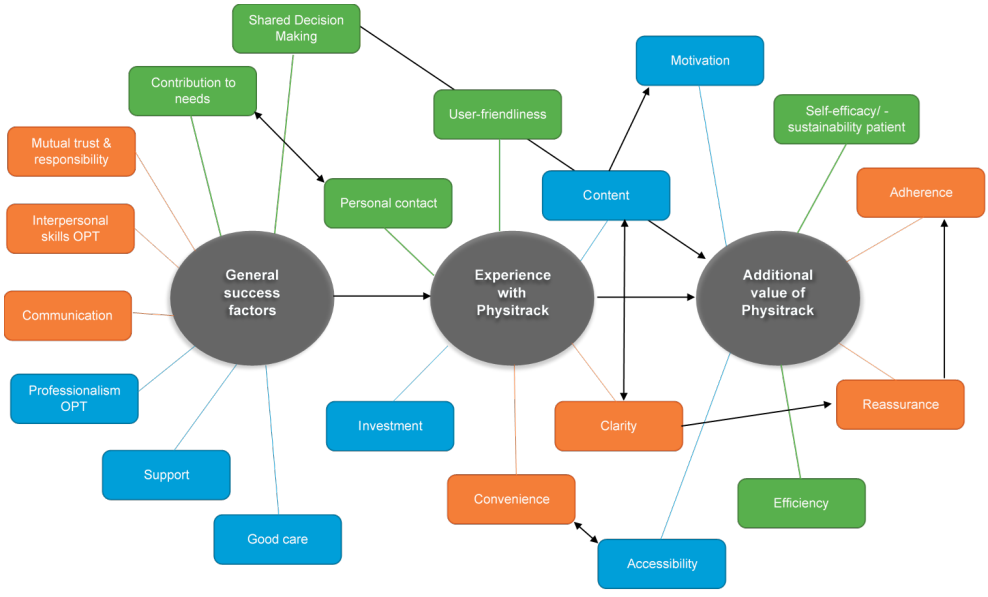

Figure 9.2: Model of interaction between sub-themes identified by orofacial physical therapists and patients. Green: sub-themes identified by both orofacial physical therapists (OPTs) and patients; orange: sub-themes identified by patients; blue: sub-themes identified by OPTs; grey: major themes.

1) Perceived factors of importance for adequate care

The success of orofacial physical therapy in general and the success of using Physitrack was dependent on a few different factors. Most OPTs described that *good care* was important, which for them meant listening to your patient and to provide personalized care. All OPTs stated that patients are responsible for their own recovery: "*I teach you to help yourself" (OPT05)*. Most patients agreed with this statement, stating they understood their own *responsibility* and that *mutual trust* is essential.

Patients felt that the *interpersonal skills* of, and *communication* with their OPT was important for success: "*Well, very enthusiastic [the OPT] and that stimulates me as well" (Pt03)*. Both OPTs and patients described how the *professionalism of the OPT* was an important factor as well, which was also related to the trust that patients had in the therapy. Importantly, the OPTs and patients all felt it was important that the therapy was based on *shared decision making*.

Table 9.4: Overview of themes for both patients and orofacial physical therapists.

Patients *(supportive quotes)*			Orofacial Physical Therapists *(supportive quotes)*
	General determinants for success		
"I think you always need to involve people in their own healing process, what they can do themselves, even if it is only positive thinking, but also dieting and exercises, and well, medication, everything you can do by yourself. Make people think about it and let them work on their own healing" (Pt02)	Professionalism OPT	X	*"Everything depends on the intake, your history-taking. It is how you handle the conversation. It is just that we are health care professionals and we want one thing: to help, help, help. Just listen to what your patient wants!" (OPT02)*
	X Interpersonal skills OPT		
	Good care	X	
	Support	X	
	X Shared decision making	X	
	X Mutual trust & responsibility		
	X Communication		
	X Contribution of needs	X	
	Experience Physitrack		
"But it was very easy, so I had it [PhysiApp] on my phone very quickly, easy to use, so yeah, it was not a lot of trouble for me" (Pt03).	X User-friendliness	X	*"It is a nice coat rack, and then you can hang your own things to it" (OPT06)*
	Investment	X	
	Content	X	*"The videos are fantastic and for people it is really something tangible to see" (OPT07)*
	X Personal contact	X	
	X Convenience		
	X Clarity		
	Additional value Physitrack		
"After two, three days, especially the first week, I could see 'am I doing it right, do I look right, did I do the exercise right', while otherwise I would have phoned the practice like 'I don't remember exactly', or I would have waited till the next appointment"(Pt10)	Motivation	X	*"I do not know if I would think it is worth it, that long trip in the car every time, but then this [Physitrack] is a real solution" (OPT03)*
	X Efficiency	X	
	Accessibility	X	
	X Self-efficacy/ -sustainability patient	X	
	X Adherence		
	X Reassurance		

Especially in the case of applying an e-Health application like Physitrack, this needs to be discussed: "*If I think that it is a patient that would want to use it, I always ask, like, 'I have the possibility to also send this exercise on video', and if I see people feel the need for this, then I always apply it" (OPT10)*. In some cases, OPTs and patients did not see the need for e-Health, and would then decide not to use it. This *contribution of needs* was an important factor of influence on choosing to use an e-Health application, in this case Physitrack. For example, one OPT did not feel the need to use Physitrack during the COVID-19 lockdown, despite having a subscription for the platform: "*I did weekly telephone calls, with the patients, asking how they were doing. And some said they were not managing, then we discussed if they had*

done auto-massage" (OPT09). One of the patients (Pt07) was given access to the program but they had trouble logging on, so they did not use the program, nor felt the need to do so. The patient stated that "*for the jaw I don't see a necessity to learn"* how to use the computer program, as the combination of verbal instructions of the OPT and the printed exercises were sufficient.

2) Experience with Physitrack

The six OPTs who started using Physitrack during the COVID-19 pandemic, chose this platform due to the available *content* and its quality, and the positive experiences of other colleagues in the field. The exercise videos were seen as the most important content aspect of Physitrack, which all but one OPT used as a feature with their patients. Some of the patients said they felt these videos were very clear, and they knew what was expected of them (*clarity*). One OPT stated "*It [video] does slightly stimulate a bit more [to exercise] than yet another piece of paper" (OPT05),* whereas one of the patients did not agree with this: "*I find it easier to have it on paper, because then I can just grab it when I want to and otherwise you have to go to your computer, turn on that thing, that program... well you name it" (Pt07).*

The patients that used Physitrack, were positive towards the *user-friendliness* of the application. Most OPTs agreed but felt that not all features were as smooth as they should be, for instance the video calls were not very easy and did not always work. The video calls were seen as a nice feature that could be used during the lockdown, but not necessarily as a replacement for the physical consult in the future. One OPT stated: "*I am really into body language and that is hard to do through video, I noticed. It is distant, you sit and watch a screen, it is less personal. […] If it is about evaluation, really how are your exercises going, do you think it helps, do you want to adjust your exercise program, are there things you don't understand, check up in between and also final evaluation, those are doable with video, I think" (OPT01)*. One patient even said that they would prefer phone calls over a video call: "*Well I do not really specifically need a face, well at least if I already know the person it is not necessary. Sometimes if you do not know someone then you think 'What do they look like, or what is their expression', but if you already know someone you do not really need it, it can also be a distraction" (Pt05)*. Overall, OPTs and patients were concerned about the *personal contact*. "*Of course, it is nice that you can [practice] yourself, but sometimes you just cannot fix it yourself. And then you can practice as much as you can, but then I just need her [the OPT]"* (*Pt08*). Patients felt that Physitrack was very *convenient*, due to the user-friendliness and clarity, and it opened another door for communication with the OPT. The OPTs experienced this differently, and mostly saw an extra *investment* in time, money, and administration. However, a few OPTs stated that once you have implemented the application and you are used to it, some features are worth this investment: "*Back in the day, I did not see the value to pay for it, because I physically saw patients in the clinic. […] For the video consults I do not*

know, but for the exercise programs I do think it is worth [the costs], because there are more videos, you can easily send the exercises and monitor adherence a bit better" (OPT01).

3) Additional value of Physitrack

When asked what the additional value of Physitrack was on top of the regular therapy possibilities, the overall message of most OPTs and patients was the same: Physitrack can support in increasing *self-efficacy and self-sustainability* of the patient. Some OPTs and patients said that Physitrack was suitable for this, as "*It is always nice that people just have a program to fall back on to go through their exercises properly again" (OPT01).* One patient said that Physitrack helped feeling *reassured* about doing the exercises at home: *"At home one can see exactly how to do the exercises, uh, because it is explained, but yeah when you are at home you think how should I position my head [...] so yes it is convenient to have the app at hand and it is clear in that video how the exercises should be performed exactly [...], I think that's nice, because one forgets it." (Pt01).* Additionally, some patients felt that the tracking feature on Physitrack helped to increase *adherence* to the exercises: "*You are reminded by e-mail, that is nice, because sometimes you have a day, you think 'oh forgotten' and then it pops up. And papers you put aside or in a drawer and then you do not think 'I need to do that now'." (Pt04).* Not every patient shared this idea, as they felt it was their own personal responsibility to do the exercises and an external reminder would not be helpful: "*I don't need it [check boxes] because I think it would take too much time. I look to myself as a measurement instrument. I notice how it helps, so then I continue practicing and I think 'I'm doing it for my own sake, I want to have it cured, get rid of the pain in my jaws'." (Pt10).* One OPT mentioned that not all patients can *motivate* themselves to do their exercises, so Physitrack can help: "*You do not have an excuse not to do it [exercises], you get reminders!" (OPT02)*.

Another added value of Physitrack, was that it enhanced *accessibility* of the specialized OPT for patients, regardless of location in the country. Especially when physical consults were not available, Physitrack was a good alternative. Even though most OPTs and patients still preferred physical consults, some saw opportunities to apply more features of Physitrack in the future: "*I always thought like, you know a video consult does not replace the physical consult. For an intake I am still convinced this is the case but for follow-ups I definitely see a possibility that e-Health will take a larger place than it has so far" (OPT10).* From those who had positive experiences with Physitrack and saw additional value, it was mostly in a blended form where the exercise videos were considered most valuable, especially after proper instruction of the OPT: "*Exactly, it's really clear. I had done the exercise one time at the [OPT's], so in that way you know it a bit like press harder or softer, one tends to press harder than needed, and so [OPT] corrected me like that's not necessary, you don't need to press that much, so do it like the movie, but don't make it too hard, than you strain it too much, so the introduction by [OPT] followed by the video, well, fine!" (Pt10)***.**

Quantitative findings patients

Seven patients came in with pain complaints with a mean of 5.5 ±1.6 points on the NPRS. At the end of their treatment plan, which varied between 3 to 8 sessions, the TMD pain intensity decreased to 1.1 ±0.6. Of the six patients with headache, the headache pain intensity score also decreased over time from 6.3 ±2.1 to 2.5 ±2.7.

The nine patients who used Physitrack have filled out the TSUQ and answered the items which were related to the facilities of Physitrack that they used (See Table 9.5). *User-friendliness* was one of the identified sub-themes from the interviews, which was also recognized in the scores on the TSUQ. Overall, patients were satisfied with the ease of the use of Physitrack (1.9 ±0.4). Patients felt that Physitrack was easy to use, shown by the scores of the ease of using (1.22 ±0.4) and starting to use Physitrack (1.33 ±0.7). This is comparable to the findings of the qualitative data analysis. Patients disagreed most with the statement that their OPT used the information from Physitrack to evaluate with the patient (3.13 ±1.2), whereas this was an important aspect for patients identified under the themes *communication* and *mutual trust & responsibility*.

Three patients did not fill out items of the satisfaction about online consults, as they did not receive online or phone consults. The remaining six patients were not agreeable, nor disagreeable, with the overall satisfaction of the online consults (2.6 ±0.4). They specifically disagreed with the statement that an online consult is just as efficient and satisfactory as a physical consult (4.6 ±0.8), and that online consults are a good way to receive physical therapy (4.2 ±0.8). They agreed with the statement that they missed the physical contact during an online consult (1.7 ±1.0). All of this is comparable to the findings of the interviews, where *personal contact* was seen as very important and this could not always be achieved through online care.

All nine patients agreed on the items regarding the usefulness of Physitrack (1.5 ±0.5); the videos of the exercises were useful (1.0 ±0.0), the overall exercise program (1.3 ±0.5) and the related instructions were useful (1.3 ±0.7). During the interviews, patients also identified the exercise videos and their instructions as most useful. The items with the highest score (i.e. least useful) were regarding the usefulness of the questionnaires (2.7 ±1.3) and the feedback option (2.5 ±1.5). This feature was often unknown to the patient, or not seen as necessary.

Discussion

The key findings of this study show that both patients with TMD and their OPTs are positive towards using an e-Health application (Physitrack) during the treatment sessions, but mostly in a blended form. The exercise videos were considered to be the strongest

additional value of using Physitrack, and online consults (i.e. video calls) were only seen as valuable when physical care is not an option, for instance during the COVID-19 lockdown or in case of long travel distances.

In the current study, there is a discrepancy between what the OPTs stated they offered and what patients used (Table 9.3). Furthermore, patients stated they most valued the exercises, but for some this was the only feature they had used. Patients may not be aware of the possibilities and value of the other features, because they did not use them or knew they existed. The lack of use of different features by the patient, may be due to a few reasons. One may be that the OPT decided which feature to offer to that specific patient, rather than implement the shared decision-making approach where the OPT and patient discuss all options together within the treatment process, and then decide together which features are available and preferred to use. Another possibility is that the OPTs are not yet properly trained in using an e-Health application during their regular physical therapeutic process, leading to incomplete use of all e-Health features. In a study of a population with rheumatoid arthritis, the used e-Health application was also not fully embedded in routine health care.[34] Receiving specific training may lead to full implementation of all the Physitrack features, which could change the perceived additional value of the different features.[35]

Table 9.5: Results of the telemedicine satisfaction and usefulness questionnaire .

		Mean ±SD (range)
Subscale: Satisfaction e-Health / Physitrack (n=8; range 10 - 50)		20.5 ±4.0 (16 – 27)
1.	In general, I am satisfied with physical therapy through e-Health (n=9)	1.4 ±0.5 (1 – 2)
2.	My health is better than it was before I used e-Health (n=9)	2.2 ±1.0 (1 – 4)
3.	I am more involved in my care using e-Health (n=9)	1.6 ±0.5 (1 – 2)
4.	E-Health helps me to better manage my health (n=9)	1.8 ±0.8 (1 – 3)
5.	E-Health helps monitor my health condition (n=9)	2.6 ±1.0 (2 – 5)
6.	My physical therapist uses information from the e-Health application during evaluation moments (n=8)	3.1 ±1.2 (2 – 5)
7.	I follow my physical therapist's advice better since working with e-Health (n=9)	1.8 ±1.0 (1 – 3)
8.	The e-Health system is easy to use (n=9)	1.2 ±0.4 (1 – 2)
9.	I can always trust the e-Health system to work (n=9)	1.8 ±0.8 (1 – 3)
10.	It was easy to learn to use the e-Health system (n=9)	1.3 ±0.7 (1 – 3)
Subscale: Satisfaction communication (n=6; range 11 – 55)		28.8 ±4.0 (23 – 34)
11.	Talking to my physical therapist on the phone, through email or during a video visit is as satisfying as talking in person (n=7)	4.6 ±0.8 (3 – 5)
12.	A physical therapist can get a good understanding of my problem during a video-, phone-, or email conversation (n=7)	3.6 ±1.1 (2 – 5)
13.	My privacy is protected during video-, phone-, or email conversations (n=7)	2.6 ±0.8 (1 – 3)

14.	I can explain my medical problems well enough during a video-, phone-, or email conversation (n=7)	3.1 ±1.3 (1 – 5)
15.	I miss the physical contact during a video-, phone-, or email conversation (n=7)	1.7 ±1.0 (1 – 3)
16.	Video-, phone-, or email conversations are a convenient form of physical therapeutic care delivery for me (n=6)	4.2 ±0.8 (3 – 5)
17.	Video-, phone-, or email conversations save me time (n=6)	2.5 ±1.5 (1 – 5)
18.	Video-, phone-, or email conversations make it easier for me to contact the physical therapist (n=6)	3.2 ±1.2 (2 – 5)
19.	My physical therapist answers my questions (n=6)	1.2 ±0.4 (1 – 2)
20.	My physical therapist deals with my problems adequately (n=6)	1.2 ±0.4 (1 – 2)
21.	My physical therapist engages me in my care (n=6)	1.0 ±0.0 (1 – 1)
Subscale: Usefulness of the e-Health system (n=6; range 9 – 45)		15.8 ±5.0 (9 – 23)
22.	PhysiApp application (n=9)	1.2 ±0.4 (1 – 2)
23.	The exercise program (n=9)	1.3 ±0.5 (1 – 2)
24.	Instructions of the exercises (n=9)	1.3 ±0.7 (1 – 3)
25.	Instruction videos of the exercises (n=9)	1.0 ±0.0 (1 – 1)
26.	Using the pain scores (n=6)	2.2 ±1.6 (1 – 5)
27.	Using the feedback screen (n=6)	2.5 ±1.5 (1 – 5)
28.	The questionnaires (n=7)	2.7 ±1.3 (1 – 5)
29.	Contact with the physical therapist (n=9)	1.1 ±0.3 (1 – 2)
30.	Tracking the progress of the results (n=7)	1.9 ±0.9 (1 – 3)
Total Score TSUQ (n=5; range 30 – 150)		67.4 ±9.4 (56 – 76)

SD: standard deviation; n: number of participants; not all participants filled out each part of the questionnaire and therefore the n differs per item and per subscale. Five out of nine participants filled out every item of the questionnaire. Range of each question (1 through 30) was 1-5.

The current study shows that OPTs and patients feel that an e-health application like Physitrack could support self-efficacy, by giving patients the tools to do things from home in their own time and pace. In patients with impairments in sports, lower limb injuries, or pediatric neurology, the satisfaction of the use of online consults was high, specifically due to the limited travel time and convenience of receiving therapy in a familiar environment.[36] The question that still remains, however, is if e-Health is just as effective, or perhaps even more effective, than only physical consults. In general, e-Health is recommended for musculoskeletal physical therapy,[7] but the (cost-) effectiveness remains unclear for most patient populations.[3,37] Even though the number of participants was low in the current study, the results suggest that the blended form applied by the OPTs (i.e. using Physitrack during the treatment process) was effective to decrease complaints, and increase perceived self-efficacy. Other patient populations show the same results,[38,39] illustrating that e-Health can be a valuable addition to usual physical therapeutic care. However, based on the shared decision-making principle, using e-Health should be discussed with the patient as not every patient may be suitable or open to using the application.

Recently a consensus opinion was published about the appropriateness of e-Health in the management of chronic pain,[40] which could be applicable to patients with chronic TMD. Furthermore, to help physical therapists during this conversation, a special checklist developed for this purpose can be used.[41] This checklist is, however, not yet validated for patients with TMD complaints.

One of the important aspects of the checklist for blended interventions, as well as findings of the current study, show that the motivation of patients to use the e-Health application is important. The motivation of patients is related to the effort required of the patients, the result of this effort and how it influences the needs of the patient. This is similar as what Vroom's expectation theory describes.[42] According to this theory, people are motivated when they expect to complete the task at hand, if this leads to the desired outcome and when it fulfils a need. Figure 9.3 shows the themes and examples from the current study related to the expectation theory. One aspect that is not taken into consideration in this figure, is how therapeutic alliance may play a role in the motivation of the patient to do their exercises or to use e-Health. In the current study, patients identified that the interpersonal skills and the personal connection they had with their OPT was an important factor for adequate care. This may have also influenced their perceived value of e-Health, or other aspects of the therapy. This relationship between the patient and OPT is part of a therapeutic alliance, which may influence the therapeutic adherence.[43] Patients now stated that e-Health helped with adhering to the exercises at home, but this may also be due to this strong therapeutic alliance. In patients with persistent musculoskeletal pain similar results were found where mutual trust, a good relationship between physical therapist and patient, and proper communication were important factors to success.[44] However, there is little known about therapeutic alliance in patients with TMD, so future studies should look into this aspect.[45]

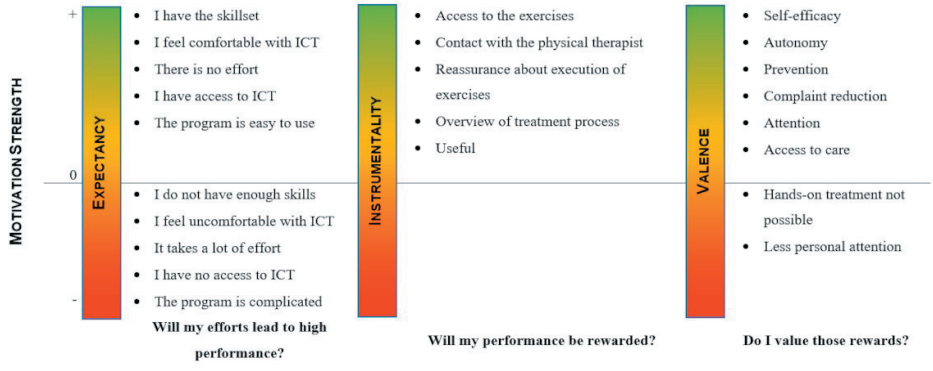

Figure 9.3: Strength of motivation to use Physitrack as patients with temporomandibular disorder related to the expectation theory.

Strengths and limitations

One of the strengths of the current study was the use of a mixed-methods approach allows for a stronger conclusion of the findings.[27] The mixed-methods approach shows the importance of nuance and shared decision making, as outcomes of the TSUQ would sometimes indicate patients were not satisfied with certain aspects of the e-Health system, whereas the interviews showed that it was very context dependent. This approach has been suggested for telehealth studies, because it does shed light on the nuances and differences between quantitative and qualitative findings.[27] In the current study, the TSUQ was filled out before the interview, but the answers were not used during the interview. Having seen the TSUQ before the interview gave patients the time to reflect on their experiences so they could formulate answers better during the interview.

Another strength is having the perspective of both patients and OPTs creates a broader understanding of what the additional value of e-Health, in this study through Physitrack, is during the physical therapeutic care. To determine effectiveness of a blended e-Health intervention, randomized controlled trials are needed. Additionally, future studies should consider looking into successful implementation factors, as the current study showed that not all features of an e-Health application are used in practice and this may bias the end results.

There are a few other aspects that need to be considered. Saturation was reached after 10 interviews in both the patient and OPT population, but in both populations, there was only one deviant case (i.e. someone who did not end up using the Physitrack application). This may have caused a positive bias in the results and not an adequate reflection of the general TMD-patient and OPT population in the Netherlands. Additionally, all patient participants were female. Even though TMD is more prevalent in females,[46] it is also common in men. There may be a difference in perceived value of e-Health, as well as usage, in the different genders.[47] Another limitation is that the OPTs had to have a subscription to Physitrack to be included, which is a form of selection bias as OPTs who have a subscription are more likely to use it and be positive towards the use of it. However, one of the included OPTs had a subscription but still did not use it, which counterbalanced the findings in some way. Additionally, included OPTs recruited patients for the study, which may have led to selection bias of the patients. To decrease the chance of selection bias, OPTs were instructed that all patients with TMD who fulfilled the inclusion criteria were eligible, and they were discouraged to only invite patients who had a successful treatment. Furthermore, not all OPTs recruited patients for the study, meaning some OPTs recruited multiple patients and others none at all. This could decrease the credibility of the triangulation of the qualitative findings of the OPTs and patients. Lastly, Physitrack is an e-Health platform that consists of multiple features, but none of the OPTs used all the features with their patients. Most patients only used between one and three features,

leading to an incomplete view of the program. It could be that OPTs only used some of the features, for instance the video-calling, due to the COVID-19 lockdown which otherwise would not have been used. Most OPTs did state, however, that they are likely to keep using this feature even when the COVID-19 pandemic is not a factor anymore. Based on this study, we can only conclude the perceived value of the used features and not the application as a whole. Future studies should work with a protocol where all features are used in an integrated manner, to see what the value of the entire application is on top of physical therapeutic care for TMD.

Conclusion

Patients with TMD are open to using an e-Health application (Physitrack) during their physical therapy, as long as their OPT discusses the use first and the application is implemented in a blended form. The OPTs use e-Health mostly for the exercise videos and feel that by using e-Health they can provide a personalized care approach which helps their patient increase self-efficacy. None of the participants used the full application.

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Appendix 9.1 – Topic guides for patients and orofacial physical therapists

Topic guide for patients with temporomandibular disorder:

Background information
- Types of complaints (*Why did you visit this physical therapist?*)

Physical therapy
- Experience (*what interventions did you receive, what did you find most important, what was your impression of your PT?*)
- Expectations (*what expectations did you have of yourself and of your PT?*)

Physitrack
- First impression (*what did you think when your PT suggested using Physitrack?*)
- Facilities used (*what components were used during the intervention, what was your experience, what did you use of those offered to you and why*)
- Additional value (*did Physitrack add anything to your values, experience or expectations of the treatment? What other advantages were there with using Physitrack? Were there negative aspects present?*)
- Usability (*was the program easy in use, would you want to add or change anything?*)
- E-health in general (*what is your opinion about e-Health in general?*)
- Use after physical therapy (*would you want to keep using Physitrack when you are done with the PT, and if so, why?*)

Closure
- Anything to add?

Topic guide for orofacial physical therapists:

Background information
- Specialization (*which one and why?*)
- Graduation / experience (*when did you graduate, how long have you seen pts with OFP?*)
- Patient population (*what is your patient population, how many pts with TMD?*)

Before Corona (all interviews were during the corona pandemic)
- Important aspects of TMD treatment (*what was the regular practice, what interventions, what was most important?*)
- Home exercises or instructions (*how did you communicate home exercises or instructions with your patients, did you use paper or an app, was additional information needed?*)

Physitrack
- When and why (*since when are you using physitrack, why e-Health and why physitrack?*)
- First impression (*what was your first impression of physitrack?*)
- User-friendliness (*what can you say about the user-friendliness of physitrack for you as a physio, what did your patients say?*)
- Content (*what content did you use, why, for which populations, why only specific functions, what did you miss, what was good and why?*)
- Additional value (*what was the additional value of physitrack? Why, how?*)
- Influence of physitrack on treatment (*do you think physitrack influences your treatment or treatment outcomes? In what way?*)
- Future use (*do you keep using it after corona, why would you or why wouldn't you?*)

Future of orofacial physical therapy and TMD
- Future OPT (*what will it look like? What do we do?*)
- Role of e-Health (*will e-Health or physitrack play a role in the future? In what way?*)

Closure
- Anything to add?


10

Chapter 10

General Discussion

General discussion

This dissertation is built in the same way a physical diagnostic and therapeutic process is built: starting with patient information and information about the complaints (Part I), continuing into the diagnostic process (Part II), followed by treatment tailored to the patient (Part III).

The general aim of this dissertation is to establish evidence for the different steps in the physical therapeutic process for patients with TMD and headache. This physical therapeutic process starts with the diagnostic process, during which the physical therapist uses their knowledge on the associations between TMD, headaches and other musculoskeletal, personal, or environmental factors, followed by specific measurement instruments to determine a physical therapeutic diagnosis. When there are implications for physical therapy, a tailored treatment plan will follow.

In the introduction we met Femke, a 37-year old woman, who experienced facial pain and headache located in the temporal region of the head. The dentist suggested that Femke should see an orofacial physical therapist for her temporomandibular disorder. Now, let us follow the steps Femke and her physical therapist take together based on the newly gained knowledge from this dissertation.

Association between TMD and headache

When a patient comes to a physical therapist with jaw pain and headache, the physical therapist has an initial hypothesis of what may cause the problems even before the history or examination takes place.[1] This is based on the clinical experience of the physical therapist, but also on knowledge related to the epidemiology and etiology of the complaints. The first section of this dissertation expands on that knowledge. A strong association was found between painful TMD and migraine in a cross-sectional design (**chapter 2**) as well as in a longitudinal study design (**chapter 4**). These findings confirm and extend on earlier cross-sectional studies, which also have shown a strong association between the presence of painful TMD and migraine.[2–4]

Interestingly, in the association between migraine and painful TMD, bruxism was shown to be a confounder (**chapter 2**). Bruxism is defined as a 'repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible'.[5] The significant association between a painful TMD and migraine resolves when corrected for bruxism, meaning bruxism influences both the painful TMD and the migraine. These results confirm earlier findings from a study that focused on the presence of sleep bruxism in patients with a painful TMD. An increased risk of the presence of chronic migraine, episodic migraine and episodic TTH was reported.[4]

There are a few mechanisms that could explain the influence of bruxism on the association between painful TMD and headache, specifically migraine. First, the masticatory muscles involved in bruxing are innervated by the trigeminal nerve, and some authors suggest that the nerve is associated with migraine as well.[6,7] Patients with migraine have a higher reactivity to trigeminal stimuli, so prolonged bruxing could induce autonomic responses such as changes in blood pressure, blood flow or heart rate variability, which then may trigger a migraine attack in this population.[8,9]

A second explanation relates to the finding that, during bruxing, not only the masticatory muscles are involved, but also several muscles around the neck, including the sternocleidomastoid and trapezius muscle, are activated.[10] This neck muscle activity from the upper cervical spine could also sensitize the trigeminal nucleus by activation of the cervical spinal nerves I through III.[11] If this mechanism was the main driver between the association between painful TMD, bruxism and headache, also an association with TTH would be expected. However, no association between painful TMD and TTH seems to be present, whereas the association between TTH and bruxism is debated.[12] Still, the exact mechanism behind the association between painful TMD, bruxism and migraine is still unknown and should be further studied in detail.

Besides bruxism, psychosocial factors were also found to influence the association between TMD and headaches. This finding underlines the importance of assessing TMD complaints, with and without headache, from a biopsychosocial perspective, and not from a pure biomedical one.[13] Somatization, for instance, invalidates the univariate significant association between painful TMD and self-reported headache (**chapter 2**). This psychosocial variable also accounts for 9.0 to 21.3% of the perceived pain intensity and pain-related disability in TMD patients with TTH, as well as headache attributed to TMD (**chapter 3**). In TMD-patients with migraine psychosocial factors have minor influence on pain intensity (explained variance of optimism 14.3%) or pain-related disability (explained variance of depression 10.3%). In TMD patients with TTH and headache attributed to TMD, the psychosocial factors depression, anxiety, somatization, and optimism are more important to take into consideration, as they all were found to significantly contribute to the explained variance of perceived pain intensity and pain-related disability in these populations.

When taking Femke's history, the physical therapist will ask questions specifically about her headache, as Femke's headache may be a migraine headache since this headache is strongly associated with painful TMDs. Additionally, questionnaires about bruxism, depression, anxiety, and other somatic complaints were added to see what influences the relationship between the TMD and headache, as well as the perceived pain intensity and pain-related disability.

There are three initial hypotheses that the physical therapist considers:

Hypothesis 1: Femke has a painful TMD and migraine, and bruxes during the day, which provokes migraine attacks.

Hypothesis 2: Femke has a painful TMD and headache attributed to TMD; both bruxism and psychosocial factors play a role in the etiology of these complaints.

Hypothesis 3: Femke has a painful TMD, migraine, and neck complaints; both bruxism and psychosocial factors play a role in the etiology and prognosis of these complaints.

Hypothesis 4: Femke has a TTH which is precipitated by psychosocial factors.

The third hypothesis considers the influence of the cervical spine. However, as that is out of the scope of the current dissertation, that will not be further discussed in the case of Femke. A fourth hypothesis considers the presence of TTH, which is less likely due to the lack of association between TMD and TTH. But, due to the gender and age of Femke, the physical therapist keeps it in mind during the diagnostic process.

The diagnostic process of TMD and headaches

Figure 10.1 depicts the domains of the International Classification of Functioning, Disability and Health,[14] with specific factors that may contribute to the health condition, in this case TMD and headache. With the information from patient's history, combined with the information gained from the physical examination and questionnaires, the physical therapist forms a physical therapeutic diagnosis. In this diagnosis, the relationship between etiological factors, prognostic factors and the health condition is described for each patient individually.

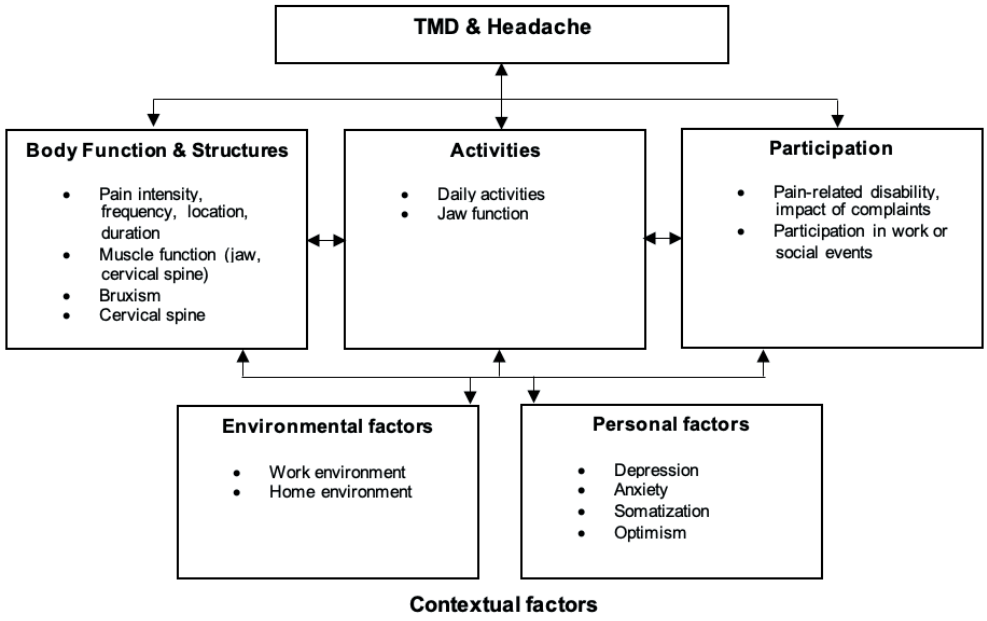

Figure 10.1: Overview of the International Classification of Functioning, Disability and Health,[14] specified towards aspects to take into consideration in patients with TMD and headache.

If a patient visits a physical therapist through direct access (i.e., without a referral from a medical doctor or dentist),[15] the therapist needs to consider which underlying disorder could be responsible for the complaints of the patient, i.e., the health condition. For TMD, the diagnostic criteria (DC/TMD) are available[16] and can be used by trained practitioners, including physical therapists.[17] To quickly screen for the presence of a painful TMD, the TMD pain screener can be used in patients with orofacial pain or headache.[18,19] To diagnose headaches, the International Classification of Headache Disorders, 3rd edition (ICHD-3) is considered the gold standard.[20] The classification of TMD and headache disorders is applied during the history and often confirmed during the clinical examination. To provide practitioners with a screening tool for the presence of the most prevalent types of headache, migraine and TTH, the Headache Screening Questionnaire Dutch Version (HSQ-DV) was developed and validated based on the ICHD-3 criteria (**chapter 5**). To further study the diagnostic accuracy of various measurement instruments for different headache types, a systematic review and meta-analysis was performed (**chapter 6**). This review showed that the HSQ-DV had the best properties to be used to screen for the presence of migraine and TTH. When the patient screens positive on a primary headache, the physical therapist can collaborate with a neurologist for further diagnostics and multidisciplinary treatment.[21]

Having a medical diagnosis does not conclude the diagnostic process of the physical therapist, as this process and the following physical therapeutic diagnosis also includes information on etiology of the complaints and related prognostic factors.[1] Based on previous studies, an important etiological and prognostic factor is dysfunction of the cervical spine. Patients with TMD, headache and with both TMD and headache, show a higher prevalence of mechanical cervical spine dysfunction (e.g., altered movement, decreased range of motion) and a decrease of cervical muscle function.[22–25] To test the cervical muscle function, the cranio-cervical flexion test (CCFT) is recommended. [26,27] The CCFT is a test of neuromotor control, where the isometric endurance of the deep cervical flexors is measured, while also considering their interaction with the superficial cervical flexors.[28] Mechanical and muscular cervical impairment are not only more prevalent in patients with TMD, but also in people who brux.[22] And, based on the findings from this dissertation we know that bruxism is also an important etiological factor to consider in patients with TMD and headache (**chapter 2**). Bruxism can be examined by physical therapists through self-reported information from the patient, intra- and extra-oral inspection, and palpation of the masticatory muscles.[29] Often questionnaires are used to support the self-reporting of bruxism, but the gold standard is a polysomnographic examination.[30–32] During a polysomnographic examination several body functions are monitored while a person sleeps, such as brain activity, muscle activity and heart rhythm.[32] However, this examination is costly in terms of time and finances, so other alternatives are often tried despite not meeting the same diagnostic accuracy as a polysomnogram.[32] For further diagnostics and collaboration during treatment, the physical therapist can refer the patient to a (specialized) dentist.[33] Examples of when a referral to a dentist is indicated are when the patient wakes up with TMD-pain, or when the patient has symptoms that are associated with dental pain.[33]

Besides the association between bruxism, TMD and headache, is awake bruxism also associated with psychosocial factors such as depression and anxiety.[34] These personal factors are also important aspects to consider during the physical therapeutic diagnostic process, as these factors play an important role in the perceived pain intensity and pain-related disability in patients with TMD and headache (**chapter 3**). Generally in health care, many health care providers rely on their clinical impressions of the presence of these factors such as depression, rather than screen for them with more objective criteria.[35,36] The DC/TMD recommends the use of the following questionnaires to screen for these personal factors: depression (Patient Health Questionnaire 9-item [PHQ-9])[37]), somatic complaints [PHQ-15][38]), anxiety (General Anxiety Screener [GAD-7)][39]), and kinesiophobia (Tampa Scale for TMD-related Kinesiophobia; TSK-TMD).[40] Currently it is unknown whether physical therapists use these tools as part of their diagnostic process, and whether they incorporate the outcomes in their clinical decision making for treatment. One of these decisions could be to refer the patient to another health care provider such as a

psychologist. In case of high influence of these psychosocial factors or the presence of psychological trauma, collaboration with a psychologist is indicated.[41]

Femke indicated that she suffers from moderate orofacial pain, rated 5/10 on a VAS scale, (ICF; *body function*) and it gets worse while she is chewing, rated 7/10 (*activities*). She is scared that she might hurt something and make her complaints worse, so she is avoiding chewing tough foods (*personal factors*). Because of this, she cancelled two dinner parties in the last two months (*participation*). Besides kinesiophobia (TKS-TMD), she also screened positive on the presence of anxiety (GAD-7) and multiple somatic complaints (PHQ-15).

Based on the new information from this dissertation, the physical therapist also had Femke fill out the Headache Screening Questionnaire (HSQ) as well as a questionnaire about bruxism. During the physical examination, the physical therapist saw clear signs of bruxism, which was also concluded from the questionnaire. The HSQ showed that there was no TTH present, but Femke fulfilled all criteria for migraine. Furthermore, following the DC/TMD protocol, the physical therapist also found a myalgia of the temporal muscle, as well as a headache attributed to TMD.

For hypotheses 2 – 4, the presence of psychosocial complaints was an important aspect. However, hypothesis 3 regarding the cervical spine will not be discussed in this dissertation, and hypothesis 4 can be rejected as there is no TTH present.

The two remaining hypotheses can both be confirmed with the findings from the diagnostic process:

Hypothesis 1: Femke has a painful TMD and migraine, and bruxes during the day, which provokes migraine attacks.

Hypothesis 2: Femke has a painful TMD and headache attributed to TMD; both bruxism and psychosocial factors play a role in the etiology of these complaints.

Based on this information, the physical therapists and Femke discuss treatment options.

Physical therapy in TMD and headache care

After identification of the disorders, etiological, and prognostic factors, a treatment strategy can be developed. This process involves close collaboration between the patient and the physical therapist. To decrease headache pain intensity, static stretching or orofacial physical therapy combined with cervical manual therapy are the most promising interventions in patients with TMD, according to a systematic review (**chapter 7**). This effect

could be due to the neurophysiological connection between the masticatory system, the upper cervical spine and headache.[11] By applying treatment to the masticatory system or cervical spine, the excitability of second order neurons at the trigeminal nucleus could be decreased and therefore have a positive impact on the headache.[11,42] However, as most included papers of this review did not describe the headache diagnosis of the patients they were studying, no specific recommendations can be made for separate TMD and headache groups.

The longitudinal study described in this dissertation followed TMD patients with different headache types while receiving usual care, in this case multidisciplinary treatment, for their TMD complaints (**chapter 4**). In this prospective longitudinal cohort, a multidisciplinary therapy was applied that included dentistry, physical therapy, counseling by both dentist and physical therapist, and, when indicated, psychology. This is in line with international recommendations on treatment of TMD.[41] In this study, results were stratified for TMD-pain patients with different headache diagnoses. TMD-pain patients with migraine showed a decrease in disability, pain intensity and days with pain for both their TMD complaints as well as their migraine complaints at the 12-week follow-up measurement. This finding is in line with an earlier study that showed TMD treatment to have a positive effect on migraine complaints.[43] In TMD-pain patients with TTH and headache attributed to TMD no concurrent changes of TMD and headaches complaints over time were found (**chapter 4**).

As Femke had a painful TMD, migraine, and headache attributed to TMD, a TMD-focused treatment was provided by a multidisciplinary team including a specialized dentist, orofacial physical therapist and psychologist. Additionally, she was suggested to see a headache specialist for further, additional care.

A TMD-treatment for physical therapists focuses on musculoskeletal signs and symptoms, and, based on clinical reasoning, tailored intervention also containing education and counseling to inform the patients about their complaints (**chapter 8**). During the treatment sessions, physical therapists evaluate the progress and adapt the treatment approach (and formulated hypotheses) when needed. At the end of the treatment process, the physical therapist evaluates the treatment process with the patient after which advice for aftercare is given. Most orofacial physical therapists included in this study stated that this takes place after approximately six treatment sessions, as the overall goal is to promote self-management and self-efficacy of the patient. The value of a specialized orofacial physical therapist is the personal contact with the patient which increases the chance to achieve treatment goals, as well as providing accurate information. In other populations, e-Health has been implemented within physical therapy to increase self-efficacy and this leads to positive results.[44–46] Before implementing e-Health in the TMD care process, key facilitators

and barriers have to be identified for using such an application. After interviewing patients with TMD as well as orofacial physical therapists, key facilitators to use e-Health were familiarity of e-Health in general, increasing self-efficacy, reminder function and the app had to be clear, adjustable and personal (**chapter 8**). Key barriers were lack of technical skills, losing personal contact, no need for additional information, and extra costs. These facilitators and barriers are similar when compared to other populations[47] and can be used to increase the chance of a successful implementation.

Despite orofacial physical therapists being open to use e-Health, before the COVID-19 pandemic there were only a handful of OPTs that had implemented this in their routine care (**chapter 9**). A frequently used e-Health application amongst OPTs was Physitrack®[48], an e-Health application with a web-based platform and an application. Then, when COVID-19 hit and the Netherlands went on lockdown,[49–51] other OPTs also turned to this program as it fulfills the needs of both patients and orofacial physical therapists (**chapters 8,9**). Both patients and OPTs were happy with this possibility, but patients did state that they were most impressed with the skills of their therapist and said an application could never replace that (**chapter 9**). Still, patients felt extra motivated to do their exercises and felt reassured that they were doing their exercises correctly because of the e-Health application. The satisfaction that patients experienced with e-Health was comparable to other populations.[52,53] Nonetheless, both patients with TMD and OPTs preferred a blended approach where e-Health is supportive of the face-to-face care. This blended approach is implemented successfully in other populations, where exercises and swift communication between therapist and patient happened at home through e-Health, combined with evaluation visits in the clinic.[44,45,54–56] In patients with TMD and headache, the exercises and creating awareness could be done through e-Health, for example with Physitrack®[48], but the effectiveness of such blended intervention is yet to be determined.

Femke received extensive counseling by the multidisciplinary team about her complaints and how several factors, including awake clenching, play a role in the etiology and prognosis of these complaints.

The combination of signs of sleep bruxism and migraine led to the dentist to prescribe an oral splint for Femke. At the same time, the physical therapist gave Femke access to an online e-Health application providing different exercises Femke can do on a daily basis and allowing her to report back on how the exercises are going, as well as on the pain complaints. Every few weeks she visits the physical therapists to evaluate, or this evaluation is performed online through a videocall.

After successful treatment, Femke's TMD complaints have decreased, as well as her headache attributed to TMD. She still has migraines, but she reports that the frequency of attacks went down significantly, which has a positive effect on her quality of life.

Methodological considerations

This dissertation is a result of eight studies, each with a different study design, including both qualitative and quantitative approaches, and based on different populations. Because of this, a wide range of research questions, covering various topics related to the physical therapy process, could be answered, but it does bring some methodological considerations. Per study, these considerations are described in the discussion section of the corresponding chapter, but there are some factors to consider when looking at the bigger picture.

The six original studies in this dissertation (**chapters 2,3,4,5,8 and 9**) are all based on clinical populations and data, rather than being controlled studies. One of the advantages to using clinical data is that it is relatable to the patients and daily clinical care. As the data is collected through usual care, it is often comparable to data collected in the clinic, and thus more directly applicable in the real world (i.e., ecological validity) rather than only in scientific studies.[57] This increases the generalizability of the results of this dissertation. The disadvantage of using data from clinical populations is that there is less control on the variables being collected and there may be more missing data. For example, in **chapters 2 and 3**, we had to work with missing data from a retrospective database. If you would have a (controlled) prospective study design, every variable that is needed for the research question could be implemented in the data collection. However, collecting data from a clinical population is very time consuming. So, having a retrospective database with valuable information that reflects the clinical sample is still a solid study design that can answer several questions. Furthermore, it allows (research) questions and information to be collected from a larger sample without adding extra administrative burden to the patients. Some research questions, however, cannot be answered through a retrospective health record study. For instance, in **chapter 4** we applied a prospective, longitudinal design as we needed to observe patients throughout time and the data was not collected through usual care. In this study, it did indeed take a long time to collect data from enough participants and we still had missing data from the clinical population. Collecting data from patient reported outcome measures (PROMs) during usual care has become more integrated, as this information can be used to track progress of patients' complaints over time. This, especially with new technological advancements of online questionnaires and apps, creates an opportunity for doing big data research in clinical populations.[58,59] Based on big data research, new models can be built that would not have been possible with smaller studies.[59,60] The data used in **chapters 2,3 and 4** are from one clinic, and for big data to be applicable collaboration with other clinics, who all collect the same PROMs, should be established. For this, a core outcome set should be established, as described in other clinical populations.[61–64]

The last two chapters (**8 and 9**) discuss e-Health during physical therapeutic care in patients with TMD. Before considering implementing a new therapy such as e-Health, the evidence for e-Health had to be identified, as well as important aspects for patients during their treatment. This is one of the steps for developing and evaluating complex interventions as described by the Medical Research Council (Figure 10.2),[65] and in line with the so-called 'User Centered Design', in which all stakeholders of a system are involved in the development.[66,67] In our case, the application Physitrack® was already developed and found to meet the criteria of the end users, patients and physical therapists, in terms of needs, facilitators and barriers (**chapter 8**). The experiences with the use of Physitrack® and statements of what could be improved based on the interviews from **chapter 9** are shared with Physitrack® anonymously to complete the feedback circle. Now, after completing these steps, in a period where Covid-19 has illustrated the need for online care, we know that both patients and physical therapists are open to use e-Health and see the additional value in using Physitrack® during the TMD-treatment. The next step would be to evaluate the (cost-)effectiveness of blended care.[68]

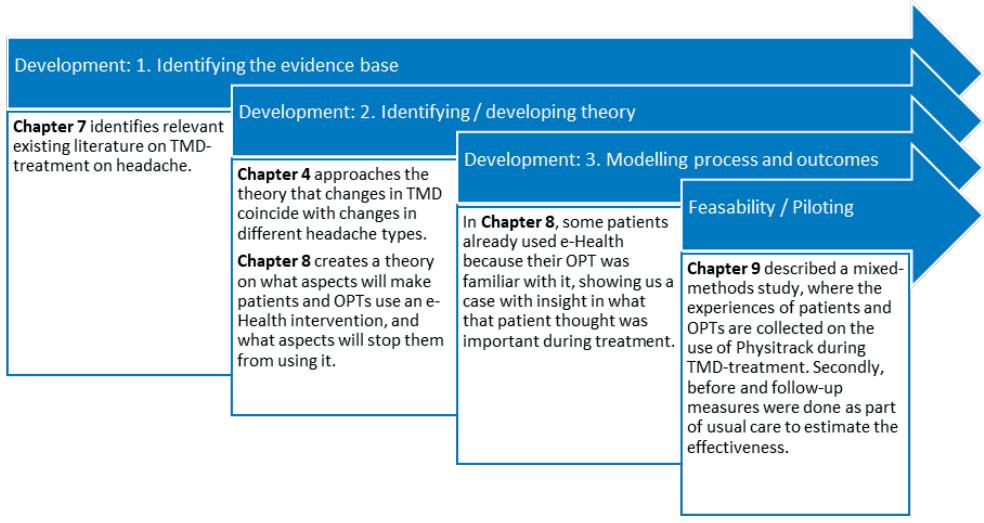

Figure 10.2: The use of e-Health in TMD treatment: the first steps of the Medical Research Council[65] as applied in this dissertation.

Clinical implications

This dissertation is built in the same way a physical therapeutic process is built. Therefore, the results are directly useable in the clinical practice. In Figure 10.3, we demonstrate the steps and considerations that physical therapists can use when a patient with TMD and headache complaints visits their practice. On the left-hand side, knowledge that was already known before the research in this dissertation took place is presented. On the right-hand side, the new insights are shown.

Most importantly we now know that during the history, the physical therapist should not only ask about the jaw and headache complaints, but also about the presence of possible bruxism in patients with migraine (**chapter 2**). Furthermore, psychosocial factors such as depression and anxiety (**chapter 3**) should be explored, specifically in TMD-patients with TTH and headache attributed to TMD. Because a strong association was found between painful TMD and migraine in both a cross-sectional and a longitudinal study, it is important to be able to screen for the presence of migraine, followed by further examination of the prognostic factors related to TMD and migraine. To screen for migraine, the HSQ-DV can be used, as this is a short screening questionnaire developed for this purpose (**chapters 4 and 5**). Most important aspects of TMD-treatment are counseling and exercises (**chapter 8**), and for the latter an e-Health application such as Physitrack® can be used (**chapter 9**). Because patients get visual feedback on their exercises, they feel more confident in doing their exercises, they stay motived to keep doing their exercises and it appears to have a positive effect on their TMD complaints as well.

Even though this dissertation is mostly written from a physical therapeutic perspective, other disciplines can also use the findings of the presented studies. All health care professionals seeing patients with orofacial pain and headache can use the information regarding the association between these two disorders, as well as the diagnostic tool developed to screen for headache. Currently, the HSQ is being used by several health disciplines and is translated into Brazilian Portuguese. If all health care professionals would use validated tools to screen for the presence of migraine and TTH, these disorders may be recognized sooner[69,70] which saves the patient a large healthcare-journey, helps them increase their quality of life by receiving the care they need and it may reduce the socioeconomic burden in the end.

A strong finding of the last two studies of this dissertation (**chapters 8 and 9**) is the perceived value of the orofacial physical therapist as reported by the patients during the interviews. Having enthusiastic specialists who take time to listen to the patient, take them and their complaints seriously and can help them treat their complaints is seen as a big advantage during the TMD care process. Orofacial physical therapists should use this in their communication to other health care specialists and have an active role in the diagnostic and therapeutic process of patients with TMD complaints. Patients and physical therapists stated that even though e-Health could be of additional value, specifically with animated videos of exercises, personal communication and tailoring the treatment process to the patient is most important.

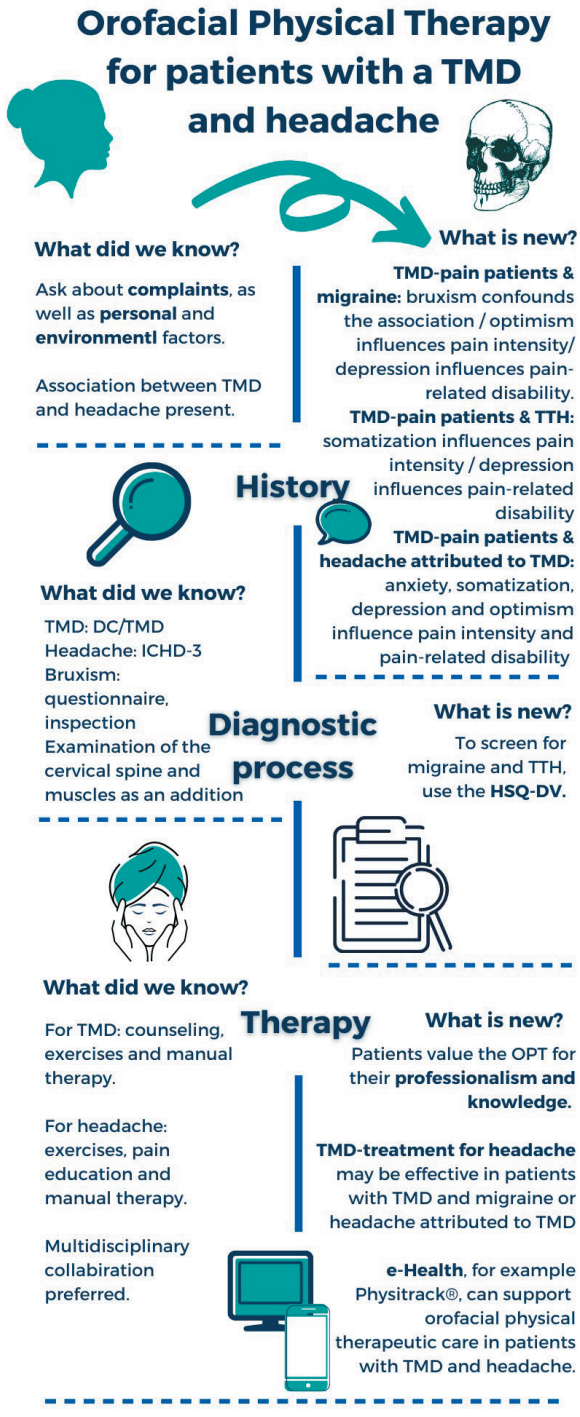

Figure 10.3: Infographic on the new findings of this dissertation in TMD-headache care.

Future directions

Based on the findings of this thesis, a few recommendations for future research can be given, as well as expected directions in the clinical field. There are two interesting questions remaining when we discuss the association between migraine, TTH and (headache attributed to) TMD. First, we and other research groups have found a strong association between migraine and TMD, but the underlying mechanism has not yet been extensively studied. The hypothesis that bruxism may be an aggravating factor that initiates migraine attacks in individuals who have migraine due to a sensitization of the trigeminal system, would be an interesting topic to be studied. This hypothesis looks at the problem starting from the bruxism behavior which may lead to both migraine and TMD. Another viewpoint is the reverse: migraine attacks may stimulate clenching,[71] which then may result in TMD.[72] it would also be interesting to test this hypothesis, preferably in a controlled longitudinal study. Secondly, another question that remains regarding the association between headache and TMD is about the similarities and differences between TTH and headache attributed to TMD. When looking at the clinical features, there are similarities: dull, mild pain, located in the temporal area and often associated with psychological factors. However, there was no association found between TMD and TTH in our studies, nor did the TTH respond to TMD treatment. It would be interesting to know how it is possible to have two headaches that on first glance (clinical features) look a lot alike, yet are completely different headache types. In the International Classification for Orofacial Pain (ICOP), tension-type orofacial pain has been described, but little has been published about this disorder and how it relates to TTH and TMD.[73] Future research should take a closer look at this patient population and describe the different phenotypes and how to tell them apart (i.e., what are the differences) from the clinical features.

To improve (clinical) research, core outcome measure sets are often used.[61] These sets describe outcomes that can be used to determine effectiveness of therapy. For headache, these outcomes are impact of the headache on daily life and headache frequency.[74–76] For TMD, these outcome measures are unknown, and it would be interesting to have these described. Besides the core outcome sets to describe treatment effectiveness, physical therapists use other measurement instruments during their diagnostic process based on the different domains of the ICF. In this thesis only measurement instruments to diagnose headache were included, which leaves the measurement instruments for all the other domains of the ICF, as well as measurement instruments that should be used for patients with TMD to monitor outcomes over time. An overview of the psychometric/clinimetric value of measurements used by physical therapists in patients with TMD[27] and headache[26] would be helpful to improve patient care and clinical research.

Currently, there is not enough knowledge to create an algorithm for patients with TMD and headaches to determine which intervention they should receive. The first step

could be to create a Delphi study in which international specialized physical therapists describe their clinical reasoning process for the treatment plan: which interventions do you apply to which patient, and why? Then, those findings should be tested with patient data. Longitudinal studies where patients receive different therapy modalities are needed in large populations, in order to create such algorithms. The effectiveness of these interventions should then also be tested using a randomized controlled trial design,[77] as the literature shows that the methodological quality of most studies is not good enough to state the effectiveness of most interventions. It would be most useful to study patients with TMD and migraine or headache attributed to TMD as these are strongly related, in contrast to patients with TMD and TTH where the association is lacking.

Furthermore, our study showed that both patients and orofacial physical therapists stated that an e-Health application such as Physitrack® has an added value to the orofacial therapy as usual (**chapter 9**). This is based on limited quantitative data and mostly qualitative data, so it needs to be confirmed with a larger trial. We would recommend using a randomized controlled trial design where the intervention is allowed to change slightly based on changes the company decides to do, to make the results more comparable and applicable to the clinical world. If this is not done, the e-Health application, in the form the trial starts with, may be outdated by the time the trial ends.[78]

It would also be interesting, both in research as well as clinically, to create one e-Health application for multidisciplinary use in health care for TMD and headache patients. As multidisciplinary therapy is strongly recommended for both disorders,[21,41,79] this could enhance the communication between specialists and will keep the patient at the center of their own treatment plan. Aside from being able to access the exercises, which is one of the preferred features of patients with TMD in an e-Health application, the patient should also be able to report back to the specialists regarding how the patient is doing, which allows the team to monitor the patient over time. This has already been studied in patients with cancer, where multidisciplinary e-Health platforms led to improved communication between the health care team, as well as between the patient and specialists.[80] Most ideally, a multidisciplinary e-Health application would be available where the patient can invite their own doctors, allied health professionals and other health care professionals to their own personalized digital environment. Within this environment, all health care providers are able to communicate and collaborate in a personalized treatment plan, which can be adjusted after an online multidisciplinary meeting whenever indicated. So, if the patient has TMD, headaches, or both, they will receive the care they need, which will be centered in their digital environment.

General conclusion

The studies in this dissertation lead to the following conclusions.
First of all, we see that an association between migraine and TMD, both cross-sectionally (**chapter 2**) as well as longitudinally, exists (**chapter 4**). This association is confounded by bruxism and somatic complaints (**chapter 2**). The association between self-reported headache and painful TMD is also confounded by somatic complaints (**chapter 2**). Furthermore, the presence of somatic complaints partly explains the perceived pain intensity and disability in TMD-pain patients with TTH or headache attributed to TMD (**chapter 3**). Other important psychosocial factors to consider when looking at pain intensity and pain-related disability in these populations are anxiety and depression (**chapter 3**).

Furthermore, to screen for the presence of migraine and TTH, therapists can use the Dutch version of the Headache Screening Questionnaire (**chapters 5, 6**).

Moreover, there is evidence that hands-on orofacial physical therapy reduces headache pain intensity (**chapter 7**). For commonly used interventions such as counseling and exercises, this effect was not found. The strength of orofacial physical therapists is that they help patients achieve their goals by personal contact and providing accurate information about the complaints (**chapter 8**). An intake with a patient with TMD complaints is preferred to consist of a physical consult, but the rest of the therapeutic process can be supported by e-Health (**chapters 8,9**). Patients and therapists feel that the animated exercises and reminder function from the e-Health application Physitrack® helps the effectiveness of the orofacial therapy process (**chapter 9**).

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Summary

Temporomandibular Disorders and Headache

Two Pains, One Face

Headache is a common comorbid disorder (75 to 88%) in patients with a temporomandibular disorder (TMD). Patients presenting with both complaints may seek help from a specialized physical therapist, known in the Netherlands as an orofacial physical therapist (OPT). During the clinical reasoning process, the OPT uses their knowledge, clinical expertise, and the story of the patient to determine a physical therapeutic diagnosis and discusses a personalized treatment plan with the patient. Even though evidence for each disorder separately has been described in literature, evidence for the physical therapeutic process regarding patients with both TMD and headache is hardly described. To provide optimal care, it is important for OPTs to understand the association between TMD and headache, how to screen for these disorders during the diagnostic process and what interventions can be used to treat these complaints. The general aim of this dissertation was to establish evidence for the different steps in the physical therapeutic process for patients with TMD and headache, as described above.

Chapter 1 introduces TMD, headaches and the physical therapeutic process. The epidemiology and etiology of TMD and headaches are described. Up to 88% of the patients with a TMD experience headaches, and this co-occurrence may be related to shared etiological factors like age, gender, and the presence of psychosocial factors. Next, the diagnostic process as well as the therapeutic process of the physical therapist in TMD and headache care are described, as well as the role of the physical therapist in multidisciplinary care. Physical therapists are specialized in musculoskeletal disorders and therefore equipped to be part of the multidisciplinary health care team for patients with TMD and headache.

After introducing the core elements of this dissertation in chapter 1, the three main research questions of the dissertation are described:

1. What do we know about the association between TMD and headache and which factors influence this association?
2. What are the measurement instruments that can be used to identify headaches?
3. What effective intervention possibilities are present for patients with TMD and concomitant headache and how are these interventions perceived by this target group?

Chapter 2 describes a retrospective medical file study that investigates the prevalence of headache in patients with TMD, as well as the association between the two diagnostic groups of TMD (painful and functional) and the different headache types (self-reported, migraine and TTH). Additionally, possible confounding factors in these associations which included age, sex, bruxism, stress, depression and the presence of multiple somatic complaints, were identified. Patients with TMD reported having a headache in 67.5% of the cases. Self-reported headache was more prevalent in patients with a painful TMD (82.8%) than in those with a function related TMD (59.3%). Overall, TTH was most prevalent (21.7%), followed by migraine (10.8%) and headache attributed to TMD (5.4%). Furthermore, an association between painful TMD and migraine was found, which was confounded by bruxism and the presence of multiple somatic complaints. The association between painful TMD and self-reported headache, was confounded by the presence of multiple somatic complaints.

Chapter 3 describes the results of a retrospective medical file study and focuses on the influence of several psychosocial factors on the perceived headache pain intensity and perceived pain-related disability in patients with TMD and headache. In patients with headache attributed to TMD headache pain intensity was influenced by multiple psychosocial factors (i.e., depression, somatization, anxiety, and optimism). In contrast, in those with migraine or TTH only one factor (optimism and somatization, respectively) influenced headache pain intensity. In patients with headache attributed to TMD as well as patients with TTH Pain-related disability was influenced by all studied psychosocial factors. In TMD-patients with migraine, pain-related disability was only influenced by depression. This chapter shows that psychosocial factors are important factors to consider in TMD-pain patients with headache, and specifically headache attributed to TMD and TTH.

Chapter 4 describes a longitudinal study where TMD-pain patients with headache are observed during a 12-week period whilst receiving their usual care treatment. For both TMD complaints and headache complaints the outcome measures disability score, pain intensity, days with pain, and days with disability were measured at baseline, and then after four, eight and twelve weeks. This observational study aimed to assess the changes over time in these TMD-complaints, as well as headache complaints, and to describe if these changes were different for TMD compared to headache. During this 12-week period in TMD-pain patients with migraine, the disability, pain intensity and days with pain improved over time in both complaints. For TMD-pain patients with TTH, only decreases in days with pain were found for both the TMD and headache. Interestingly enough, there were no changes over time in TMD-pain patients with headache attributed to TMD. This chapter confirms that there is a strong relationship between painful TMD and migraine.

In order to identify the headaches that may be present, **chapter 5** describes how the Headache Screening Questionnaire was developed, and the validity of the Dutch version was studied. This questionnaire is based on the International Classification of Headache Disorders third edition (ICHD-3) and screens for the presence of (probable) migraine and (probable) TTH. The sensitivity and specificity were 0.89 and 0.54, respectively, for probable migraine, and for probable TTH 0.92 and 0.48, respectively. The high sensitivity makes the HSQ a valid tool to screen for the presence of migraine and TTH.

Chapter 6 concerns a systematic review and meta-analysis, where the diagnostic accuracy of measurement instruments for headache was assessed. Eleven measurement instruments for migraine were identified, of which the ID-migraine was recommended with a moderate level of evidence. Six other measurement instruments assessed both migraine and TTH, of which the HSQ-DV was recommended with a moderate level of evidence. For cervicogenic headache, only the cervical flexion rotation test was identified and supported by a very low level of evidence. This systematic review gives an overview of measurement instruments that can be used to identify different types of headache.

Chapter 7 also concerns a systematic review, but this review assessed the effects of physical therapy for TMD on headache pain intensity. Five studies were identified, of which three studied counselling and exercise versus counselling and/or splint therapy, one studied static stretching versus global stretching, and one studied orofacial and cervical manual therapy versus cervical manual therapy alone. Due to risk of bias, inconsistency, and imprecision there was a very low level of evidence that TMD-treatment is not more effective when compared to any of the control groups. The combination of orofacial and cervical manual therapy was effective in TMD-patients with cervicogenic headache.

Chapter 8 describes the results of a qualitative study on the perspective of physical therapists and patients with TMD regarding the use of e-Health in the physical therapeutic healthcare. Eleven physical therapists and nine patients were interviewed, and questions were asked regarding the physical therapeutic health care process and which role e-Health could play in this process. OPTs and patients described similar facilitators for e-Health, including increase in self-efficacy, motivation, reminder function, animated exercise and personal application possibilities. Patients identified more barriers, especially lack of technical skills, losing personal contact, no need for extra information online, costs, or having to create a complex profile. Overall, OPTs and patients were open to using e-Health as long as it was added to the process in a blended care manner rather than replacing physical therapy.

In **Chapter 9** the results of a mixed methods study are presented. OPTs and patients who had used an e-Health application were interviewed. Out of ten OPTs and ten patients,

one OPT, and one patient chose not to use e-Health as they saw no need to use it. The nine OPTs that did actively use the e-Health application Physitrack reported that the e-Health application can help to provide personalized care to patients with TMD, due to the satisfying content, user-friendliness, accessibility, efficiency, and ability to motivate patients. Patients were positive towards the application as it was clear, convenient, and efficient, it helped with reassurance and adherence of the exercises and overall increased self-efficacy. This was mostly built on their experience with the exercise videos, as this feature was most used and seen as most valuable. Overall, OPTs and patients were mostly positive towards the use of e-Health in a blended form, as predicted in the previous chapter.

Chapter 10 then discusses the most important findings of this dissertation, as well as the methodological considerations and clinical implications. Recommendations for future research are made. This dissertation demonstrates important information OPTs need when they see a patient with TMD and concurrent headache in the clinic, as well as an overview on the latest evidence on diagnostic measurement tools to identify headache. Furthermore, OPTs and patients described that blended e-Health including exercise videos is a positive aspect of the physical therapeutic process.

Nederlandse samenvatting

Temporomandibulaire Disfunctie en Hoofdpijn

Twee Soorten Pijn, Een Gezicht

Hoofdpijn is een veel voorkomende aandoening (75 tot 88%) bij patiënten met temporomandibulaire disfunctie (TMD), oftewel kaakklachten. Patiënten die last hebben van TMD en hoofdpijn kunnen hulp zoeken bij een gespecialiseerde fysiotherapeut. In Nederland is dit de orofaciaal fysiotherapeut. Tijdens het klinisch redeneerproces gebruikt de orofaciaal fysiotherapeut haar/zijn kennis, klinische expertise en het verhaal van de patiënt om tot een fysiotherapeutische diagnose te komen en vervolgens een persoonlijk behandelplan met de patiënt te bespreken. In de wetenschappelijke literatuur wordt veelal aandacht besteed aan TMD of hoofdpijn apart, terwijl er minimale evidentie is voor het fysiotherapeutische zorgproces wanneer deze twee aandoeningen samen voorkomen. Het is belangrijk voor orofaciaal fysiotherapeuten om de relatie tussen TMD en hoofdpijn goed te begrijpen, om te weten hoe men kan screenen op deze aandoeningen tijdens het diagnostisch proces en welke interventies er ingezet kunnen worden om deze klachten te verhelpen. Het overstijgende doel van dit proefschrift is om evidentie te genereren voor de verschillende stappen (diagnostiek en interventie) binnen het fysiotherapeutisch zorgproces bij patiënten met TMD en hoofdpijn.

Hoofdstuk 1 introduceert TMD, hoofdpijn en het fysiotherapeutisch zorgproces. Er wordt beschreven hoe vaak TMD en hoofdpijn voorkomen en welke factoren een rol spelen in het ontstaan van klachten. Tot 88% van de patiënten met TMD ervaart hoofdpijn. Het feit dat deze klachten vaak samen voorkomen, kan gerelateerd zijn aan factoren die bijdragen aan het ontstaan en onderhouden van deze klachten, zoals leeftijd, geslacht en de aanwezigheid van psychosociale factoren. Voorbeelden van deze psychosociale factoren zijn stress, angst en depressie. Verder wordt het fysiotherapeutische diagnostisch- en behandelproces voor TMD en hoofdpijn beschreven, evenals de rol van de fysiotherapeut in het multidisciplinaire zorgproces. Fysiotherapeuten zijn gespecialiseerd in musculoskeletale aandoeningen en zijn daardoor uitermate geschikt om deel te nemen aan een multidisciplinair team binnen de zorg voor patiënten met TMD en hoofdpijn.

Na het introduceren van de kernonderwerpen van dit proefschrift worden tenslotte de drie hoofdvragen van dit proefschrift beschreven:

1. Wat weten we over de relatie tussen TMD en hoofdpijn, en welke factoren beïnvloeden deze relatie?
2. Wat zijn geschikte meetinstrumenten die gebruikt kunnen worden om hoofdpijn te identificeren?

3. Welke effectieve behandelmogelijkheden zijn er voor patiënten met TMD en hoofdpijn, en hoe worden deze interventies ervaren door deze patiëntpopulatie?

In **hoofdstuk 2** wordt de prevalentie van hoofdpijn (zelf-gerapporteerd, migraine, spanningshoofdpijn en hoofdpijn gerelateerd aan TMD) in patiënten met TMD beschreven, evenals de relatie tussen de twee typen TMD (TMD-pijn en functie-gerelateerde TMD) en de verschillende soorten hoofdpijn. Daaropvolgend wordt bekeken welke factoren een vertekenende invloed hebben op de relatie. De factoren die werden bekeken waren leeftijd, geslacht, bruxisme (klemmen/knarsen), stress, depressie en de aanwezigheid van meerdere somatische klachten. In dit retrospectieve medisch-dossieronderzoek had 67,5% van de patiënten met TMD ook zelf-gerapporteerde hoofdpijn. Deze hoofdpijn kwam vaker voor bij patiënten met een pijnlijke TMD (82,8%) dan bij patiënten met een functie-gerelateerde TMD (59,3%). Spanningshoofdpijn kwam het meest voor (21,7%), gevolgd door migraine (10,8%) en hoofdpijn gerelateerd aan TMD (5,4%). Er is verder een relatie gevonden tussen pijnlijke TMD en migraine, welke vertekend werd door bruxisme en de aanwezigheid van meerdere somatische klachten. De relatie tussen pijnlijke TMD en zelf-gerapporteerde hoofdpijn werd vertekend door de aanwezigheid van meerdere somatische klachten.

Hoofdstuk 3 beschrijft de resultaten van een retrospectief medisch-dossieronderzoek en focust op de invloed van diverse psychosociale factoren op de ervaren hoofdpijnintensiteit en ervaren pijn-gerelateerde beperkingen in patiënten met TMD en hoofdpijn. In patiënten met TMD en hoofdpijn gerelateerd aan TMD werd de hoofdpijnintensiteit beïnvloed door meerdere psychosociale factoren: depressie, somatisatie, angst en optimisme. Dit in tegenstelling tot patiënten met TMD en migraine of spanningshoofdpijn, waarbij maar één factor, respectievelijk optimisme en somatisatie, invloed had op hoofdpijnintensiteit. De pijn-gerelateerde beperking werd bij patiënten met TMD en hoofdpijn gerelateerd aan TMD of spanningshoofdpijn, door alle vier de psychosociale factoren beïnvloed terwijl depressie de enige beïnvloedende factor was bij patiënten met TMD en migraine. Dit hoofdstuk laat zien dat psychosociale factoren belangrijke factoren zijn om rekening mee te houden bij patiënten met TMD en hoofdpijn, vooral bij hoofdpijn gerelateerd aan TMD of spanningshoofdpijn.

Hoofdstuk 4 beschrijft een longitudinale studie waarbij patiënten met TMD en hoofdpijn geobserveerd werden gedurende een periode van 12 weken, terwijl ze een standaardbehandeling ontvingen voor hun kaakklachten. De mate van beperking, pijnintensiteit, aantal dagen met pijn en aantal dagen met beperking, werden als uitkomstmaat meegenomen voor zowel de TMD als de hoofdpijnklachten. Deze metingen werden afgenomen tijdens de baseline, daarna na vier, acht en twaalf weken. Dit observationeel onderzoek had als doel om de veranderingen door de tijd van de TMD-klachten en hoofdpijnklachten in kaart te brengen, en vervolgens om te beschrijven of

deze veranderingen verschillen tussen de TMD en hoofdpijn. Bij patiënten met TMD en migraine verbeterde de mate van beperking, pijn intensiteit en dagen met pijn na 12 weken voor zowel de TMD als de hoofdpijn. Bij patiënten met TMD en hoofdpijn gerelateerd aan TMD of spanningshoofdpijn werden geen veranderingen door de tijd gevonden. Dit hoofdstuk bevestigt dat er een sterke relatie is tussen pijnlijke TMD en migraine.

Om een indruk te krijgen van welke vorm van hoofdpijn aanwezig is, is de *Headache Screening Questionnaire* ontwikkeld, en daarna is de Nederlandse variant (HSQ-DV) gevalideerd en beschreven in **hoofdstuk 5**. Deze vragenlijst is gebaseerd op de *International Classification of Headache Disorders* 3e editie (ICHD-3) en screent op de aanwezigheid van (waarschijnlijke) migraine en (waarschijnlijke) spanningshoofdpijn. De sensitiviteit en specificiteit waren respectievelijk 0,89 en 0,54 voor waarschijnlijke migraine, en respectievelijk 0,92 en 0,48 voor waarschijnlijke spanningshoofdpijn. De hoge sensitiviteit maakt dat de HSQ-DV een valide meetinstrument is om te screenen voor de aanwezigheid van (waarschijnlijke) migraine en (waarschijnlijke) spanningshoofdpijn.

Hoofdstuk 6 omvat een systematische review en meta-analyse, waarbij de diagnostische accuratesse van meetinstrumenten voor hoofdpijn onderzocht werd. Er zijn 11 meetinstrumenten gevonden voor migraine, waarvan de ID-migraine aanbevolen wordt voor gebruik, onderbouwd met een matige level van evidentie. Zes andere meetinstrumenten zijn gevonden voor zowel migraine als spanningshoofdpijn. Hiervan wordt de HSQ-DV aanbevolen voor gebruik met een matige level van evidentie. Voor cervicogene hoofdpijn, hoofdpijn vanuit de nek, kwam alleen de cervicale flexie rotatietest naar voren uit de literatuurstudie, waarbij een laag level van evidentie aanwezig is voor dit meetinstrument. Dit systematisch review geeft een overzicht van meetinstrumenten die gebruikt kunnen worden om verschillende vormen van hoofdpijn te identificeren.

Hoofdstuk 7 omvat een systematisch review, dat focust op het effect van TMD-gerichte fysiotherapie op hoofdpijnintensiteit. Vijf studies zijn opgenomen in dit review, waarvan drie studies keken naar counseling en oefentherapie tegenover counseling en/of splint therapie, één studie keek naar statisch rekken tegenover globale lichaamsrektechnieken, en één studie keek naar orofaciale en cervicale manuele therapie tegenover alleen cervicale manuele therapie. Er is uiteindelijk een laag level van evidentie dat TMD-gerichte fysiotherapie niet effectiever is wanneer deze vergeleken wordt met controle-interventies. De combinatie orofaciale en cervicale manuele therapie was effectief wanneer deze vergeleken werd met alleen cervicale manuele therapie bij patiënten met TMD en cervicogene hoofdpijn.

Hoofdstuk 8 beschrijft de resultaten van een kwalitatieve studie waarbij het perspectief van orofaciaal fysiotherapeuten en patiënten met TMD op het gebruik van e-Health in kaart

gebracht is. Elf orofaciaal fysiotherapeuten en negen patiënten met TMD zijn hiervoor geïnterviewd waarbij ze gevraagd werden naar het fysiotherapeutisch zorgproces en de rol die e-Health zou kunnen spelen in dit proces. Orofaciaal fysiotherapeuten en patiënten beschreven vergelijkbare faciliterende factoren voor het gebruik van e-Health, waaronder de toename van zelfredzaamheid, motivatie, een herinnerfunctie voor oefeningen, geanimeerde video's en de mogelijkheid om het programma op de persoon af te stemmen. Patiënten zagen meer barrières om e-Health te gebruiken, met name het gebrek aan technische vaardigheden, het gebrek aan persoonlijk contact, geen behoefte aan extra online-informatie, de kosten of het moeten aanmaken van een complex profiel. Over het algemeen stonden orofaciaal fysiotherapeuten en patiënten met TMD open om e-Health te gebruiken wanneer dit toegevoegd zou worden aan het fysiotherapeutisch proces en geen vervanging zou worden van de fysiotherapie.

In **hoofdstuk 9** worden de resultaten van een "mixed-methods" studie gepresenteerd. Orofaciaal fysiotherapeuten en patiënten met TMD die gebruik hebben gemaakt van e-Health werden hiervoor geïnterviewd over hun ervaringen met het gebruikte programma Physitrack®. Van de tien orofaciaal fysiotherapeuten en tien patiënten hadden één therapeut en één patiënt ervoor gekozen om het e-Health programma niet te gebruiken omdat zij hier geen behoefte aan hadden. De negen orofaciaal fysiotherapeuten die actief het programma Physitrack® gebruikten, beschreven dat het programma kan ondersteunen om persoonlijke zorg te leveren aan patiënten met TMD. Dit kwam door de goede content, gebruiksvriendelijkheid, toegankelijkheid, efficiëntie en de mogelijkheid om patiënten ermee te motiveren. Patiënten waren positief over het programma omdat zij het helder, gemakkelijk en efficiënt vonden en het hen hielp met geruststelling, zelfredzaamheid en het volgen van het toegewezen oefenprogramma. Dit was met name op basis van hun ervaring met de video's van oefeningen, omdat dit onderdeel van Physitrack® het meest frequent gebruikt en meest gewaardeerd werd. Over het algemeen waren orofaciaal fysiotherapeuten en patiënten met TMD positief tegenover het gebruik van e-Health in een aanvullende vorm op fysiotherapie, zoals voorspeld was in het vorige hoofdstuk.

Hoofdstuk 10 bediscussieert vervolgens de belangrijkste bevindingen van dit proefschrift, evenals de methodologische tekortkomingen en klinische implicaties. Aanbevelingen voor toekomstig onderzoek worden gedaan. Dit proefschrift laat belangrijke informatie zien die orofaciaal fysiotherapeuten nodig hebben wanneer zij een patiënt met TMD en hoofdpijn in de praktijk zien, evenals een overzicht van de laatste evidentie voor diagnostische meetinstrumenten voor hoofdpijn. Verder wordt e-Health door orofaciaal fysiotherapeuten en patiënten gezien als een positieve aanvulling op het bestaande zorgproces, waarbij vooral video's van oefeningen een belangrijke rol spelen.

Authors contributions

Chapter 2: The association between headaches and temporomandibular disorders is confounded by bruxism and somatic complaints.

Data acquisition	HvdM
Study concept and design	HvdM, CS, CV
Data analysis and interpretation	HvdM, CS, RE, FL, MNvdS, CV
Manuscript preparation	HvdM, CV
Manuscript editing and review	HvdM, CS, RE, FL, MNvdS, CV

Chapter 3: Psychosocial predictors for pain outcomes in patients with temporomandibular disorders and headaches.

Data acquisition	CT, MvS
Study concept and design	HvdM, CT, CV
Data analysis and interpretation	HvdM, CT, CS, MvS, FL, CV
Manuscript preparation	HvdM, CT, CV
Manuscript editing and review	HvdM, CT, CS, MvS, FL, CV

Chapter 4: The longitudinal course of headache complaints in patients with temporomandibular pain: an observational study.

Data acquisition	HvdM, LC
Study concept and design	HvdM, LC, CV
Data analysis and interpretation	HvdM, LC, CS, RE, MNvdS, CV
Manuscript preparation	HvdM, LC, CV
Manuscript editing and review	HvdM, LC, CS, RE, MNvdS, CV

Chapter 5: Development and psychometric validation of the headache screening questionnaire – Dutch Version.

Data acquisition	HvdM, WM
Study concept and design	HvdM, CV, CS
Data analysis and interpretation	HvdM, CV, RE, WM, MNvdS, CS
Manuscript preparation	HvdM, CS
Manuscript editing and review	HvdM, CV, RE, WM, MNvdS, CS

Chapter 6: The diagnostic accuracy of headache measurement instruments: A systematic review and meta-analysis focusing on headaches associated with musculoskeletal symptoms.

Data acquisition	HvdM, CV, CS
Study concept and design	HvdM, CV, MNvdS, RE, CS
Data analysis and interpretation	HvdM, CV, TV, MNvdS, RE, CS
Manuscript preparation	HvdM, CS
Manuscript editing and review	HvdM, CV, TV, MNvdS, RE, CS

Chapter 7: Effects of physical therapy for temporomandibular disorders on headache pain intensity: A systematic review.

Data acquisition	HvdM, LC, CV, CS
Study concept and design	HvdM, CV, MNvdS, RE, CS
Data analysis and interpretation	HvdM, LC, CV, MNvdS, RE, CS
Manuscript preparation	HvdM, LC, CS
Manuscript editing and review	HvdM, LC, CV, MNvdS, RE, CS

Chapter 8: Using e-Health in the Physical Therapeutic Care Process for Patients with Temporomandibular Disorders: a Qualitative Study on the Perspective of Physical Therapists and Patients.

Data acquisition	HvdM, LdP, TvB
Study concept and design	HvdM, LdP, TvB, MNvdS, CS
Data analysis and interpretation	HvdM, LdP, TvB, CV, MNvdS, RE, CS
Manuscript preparation	HvdM, LdP, TvB, CS
Manuscript editing and review	HvdM, CV, MNvdS, RE, CS

Chapter 9: The Additional Value of e-Health according to Patients with a Temporomandibular Disorder and Orofacial Physical Therapists: a Mixed Methods Study.

Data acquisition	HvdM, AD
Study concept and design	HvdM, AD, MNvdS, CS
Data analysis and interpretation	HvdM, AD, CV, MNvdS, RE, CS
Manuscript preparation	HvdM, AD, CS
Manuscript editing and review	HvdM, CV, MNvdS, RE, CS

Portfolio

Name PhD-student: Hedwig A. van der Meer
PhD period: 2015 – 2021
Name PhD supervisors: prof. dr. C.M. Visscher and prof. dr. R.H.H. Engelbert
Name co-supervisors: dr. C.M. Speksnijder and prof. dr. M.W.G. Nijhuis – van der Sanden

	Year	Workload ECTS
Courses		
Scientific Integrity: online course *Academic Center for Dentistry Amsterdam*	2020	2.0
Academic English: Writing Specialization *Coursera*	2020	1.5
Dentistry for non-dentists *Academic Center for Dentistry Amsterdam*	2018	1.0
Lorimer Moseley Pain Course *NOI Netherlands*	2018	1.0
Basic Course of Clinical Investigators (BROK) *Netherlands Federation of University Medical Centers*	2018	1.0
Systematic Reviews of Diagnostic Accuracy studies *Elevate*	2017	1.5
Qualitative research methods *Radboud University Summer School Nijmegen*	2017	2.0
Basic qualification for didactical skills *Learn Academy Amsterdam*	2015	11.0
Presentations		
Online poster presentation *"Using e-Health in the Physical Therapeutic Care Process for Patients with Temporomandibular Disorders: a Qualitative Study on the Perspective of Physical Therapists and Patients."* at the World Congress on Pain of the IASP	2020	
Invited speaker for online oral lecture *"On the far side of headache diagnosis"*, Watson Headache® Institute International Symposium 'Turning Primary Headache Upside Down'	2020	
Oral presentation *"Temporomandibular Disorders, Headache and Physical Therapy"* at the Danish Headache Center, Copenhagen	2019	
Poster presentation *"Psychosocial predictors for pain outcomes in patients with temporomandibular disorders and headache"* at the IHC, Dublin Ireland	2019	
Invited lecturer for oral lecture series *"The patient with headache"* for the Dutch Society for Manual Therapy, Groningen / Nijmegen / Amsterdam / Rotterdam, the Netherlands	2019	
Poster presentation *"The diagnostic accuracy of headache measurement instruments: a systematic review and meta-analysis focusing on headaches associated with musculoskeletal symptoms"* at the American Academy for Orofacial Pain (AAOP) Scientific Meeting, San Diego USA	2019	
Invited lecturer for workshop and lecture at Academic Center for Dentistry Amsterdam	2018	

Invited speaker for oral lecture *"Headaches and orofacial pain"* for the headache symposium Northern Netherlands, Groningen	2018
Poster presentation *"The effect of musculoskeletal TMD-treatment for temporomandibular disorders on headache: a systematic review."* at the World Congress on Pain of the IASP, Boston USA	2018
Poster presentation *"Does successful TMD-treatment improve concurrent headache complaints in TMD patients?"* at the European Academy for Orofacial Pain and Dysfunction ICOT meeting, London	2018
Poster presentation *"Does successful TMD-treatment improve concurrent headache complaints in TMD patients? Preliminary results"* at the American Academy for Orofacial Pain scientific meeting, Chicago USA	2018
Poster presentation *"Development and psychometric validation of the Headache Screening Questionnaire – Dutch version"* at the World Conference for Physical Therapy, Cape town South Africa	2017
Invited speaker *"Physical Therapy and Headaches"* at the Alumni Event of the Amsterdam University of Applied Sciences.	2017
Poster presentation *"Development and psychometric validation of the Headache Screening Questionnaire – Dutch version"* at the Dutch Society for Manual Therapy congress, Ede Netherlands	2017
Poster presentation *"Development and psychometric validation of the Headache Screening Questionnaire – Dutch version"* at the Royal Dutch Society for Physical Therapy congress, Netherlands	2016
Poster presentation + award for best poster *"The association between headaches and temporomandibular disorders is confounded by bruxism and somatic complaints"* at the Dutch Society for Manual Therapy congress 'Heads Up', Ede Netherlands	2016
Poster presentation + award for best poster *"The association between headaches and temporomandibular disorders is confounded by bruxism and somatic complaints"* at the American Academy for Orofacial Pain scientific meeting, Orlando USA	2016

(Inter)national conferences or visits

Research visit at the Danish Headache Center, Copenhagen, Denmark	2019
International Headache Congress of the International Headache Society (IHS), Dublin Ireland	2019
American Academy for Orofacial Pain (AAOP) Scientific Meeting, San Diego USA	2019
Headache Symposium Northern Netherlands, Groningen	2018
World Congress on Pain of the IASP, Boston USA	2018
European Academy for Orofacial Pain and Dysfunction ICOT meeting, London	2018
American Academy for Orofacial Pain scientific meeting, Chicago USA	2018
World Conference for Physical Therapy, Cape town South Africa	2017
Dutch Society for Manual Therapy congress, Ede Netherlands	2017
Royal Dutch Society for Physical Therapy congress, Netherlands	2016
Dutch Society for Manual Therapy congress 'Heads Up', Ede Netherlands	2016
American Academy for Orofacial Pain scientific meeting, Orlando USA	2016

Teaching

Clinical reasoning, Evidence Based Practice, Practical Physiotherapeutic Skills, Headache, Amsterdam University of Applied Sciences (HvA), Education of Physiotherapy, Amsterdam	2015 – 2021
Temporomandibular Disorders and Headache, University of Applied Sciences Arnhem Nijmegen (HAN), Master program Orofacial Physiotherapy, Nijmegen	2015 – 2020
Temporomandibular Disorders, University of Applied Sciences Rotterdam (HR), Education of Physiotherapy, Rotterdam	2015 – 2020
Face the Head anatomy course, Anatomy Inside, Amsterdam	2017 - 2020
Temporomandibular Disorders, Dutch Institute of Allied Health Care (NPI), Doorn	2020 – 2021
Online guest lecture Temporomandibular disorders and physical therapy, Aarhus Dentistry Program	2020

Supervision

Bachelor thesis students C. van Lingen and M. Sewpersadsingh (dentistry, ACTA) *"Biopsychosociale factoren bij een succesvolle behandeling van migrainepatiënten"*	2021
Master thesis student A. van Doomen (orthopedic manual therapy, HU) *"De motivatie van patiënten met temporomandibulaire klachten voor een eHealth-applicatie"*	2020
Bachelor thesis students D. van Houwelingen and S. Lefferts (dentistry, ACTA) *"Karakteristieken van de patiënt met hoofdpijn t.g.v. temporomandibulaire disfunctie"*	2020
Bachelor thesis student E. Vlasblom (Physiotherapy, HvA) *"Gedragspsychologische interventies voor migraine: een systematische literatuurstudie"*	2020
Bachelor thesis student L. Russo (Physiotherapy, European School of Physiotherapy, HvA) *"Specificity and Sensitivity of Temporomandibular Joint Disorder Diagnostic Pain Questionnaires: a Literature Review"*	2020
Bachelor thesis student C. Kaashoek (Physiotherapy, European School of Physiotherapy, HvA) *"Convergent validity and internal reliability of psychosocial risk factor questionnaires used for TMD patients: a literature review"*	2020
Bachelor thesis students P. van den Hoven and S. van Oene (Physiotherapy, HvA) *"Wetenschap en professionele expertise bij de fysiotherapeutische behandeling van spanningshoofdpijn. Een literatuurstudie en survey-onderzoek"*	2020
Master thesis student L. de Pijper (master musculoskeletal rehabilitation, orofacial physiotherapy, HAN) *"How can e-Health support treatment of TMD? A patient's perspective"*	2019
Master thesis student C. Tol (master musculoskeletal rehabilitation, orofacial physiotherapy, HAN) *"Psychosocial predictors for pain outcomes in patients with temporomandibular disorders and headaches"*	2019
Master thesis student R. Pogosian (master dentistry, ACTA) *"Temporomandibular disorders and headaches"*; winner of thesis award of the Dutch Scientific Society of Dentists (NWVT)	2018
Master thesis student K. Veldt (master dentistry, ACTA) *"Does treatment for temporomandibular disorders also affect headache? Preliminary results"*	2017
Master thesis student T. van Bruxvoort (master clinical health sciences, physical therapy sciences, UU) *"Perspectives of Orofacial Therapists on eHealth initiatives for managing Temporomandibular Disorders: A Needs Assessment"*	2016

Grants

Personal grant from the Science Committee for Physical Therapy (WCF) to spend time abroad (Denmark) for research	2019
Junior travel grant from the International Headache Society to go to the IHC in Dublin, Ireland	2019
Internationalisation grant for PhD-students from the Radboud university medical center Nijmegen	2018
PhD-grant for lecturers from the Netherlands Organisation for Scientific Research	2015

Peer reviewed publications

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Factsheet 'Orofaciale Fysiotherapie & Kaakklachten', Nederlandse Vereniging voor Orofaciale Fysiotherapie (NVOF)

About the author

Hedwig van der Meer was born on October 2nd 1989 in Zoetermeer, the Netherlands. She lived here during primary school, high school (Alfrink College) and her undergraduate study (Amsterdam University of Applied Sciences (HvA)) where she studied physical therapy. She graduated as a physical therapist in 2011, after which she started working as a physical therapist at Corpus Activum in Zoetermeer and as a teacher at the HvA.

In 2013 Hedwig graduated from Utrecht University as a clinical health scientist, and she started her specialization in orofacial pain and headache during her master thesis project. Her master thesis was about the prevalence of headache in patients with temporomandibular disorders, which later would be her first PhD publication (chapter 2). At the end of 2015 she received a personal grant from the Dutch Research Council (NWO) to carry out her PhD at the Academic Center for Dentistry Amsterdam (ACTA) in collaboration with the Amsterdam University of Applied Sciences, the University Medical Center Utrecht and the Radboud University Medical Center Nijmegen.

Hedwig combined her research with clinical work as an orofacial physical therapist at Corpus Activum until 2020. After leaving Corpus Activum, she started working as an orofacial physical therapist at the department of Orofacial Pain and Dysfunction at the ACTA. She stayed as a teacher at the HvA during her PhD, where she was actively involved in writing and teaching the Evidence Based Practice courses. Additionally, Hedwig gave workshops and guest lectures for other educational programs (e.g., lecture on temporomandibular disorders and headache for the master program for Orofacial Physical Therapy at the University of Applied Sciences Arnhem Nijmegen (HAN)). From December 2016 till December 2020, Hedwig was a member of the Scientific Committee for Physical Therapy (WCF), from the Royal Dutch Society for Physiotherapy (KNGF). As a committee member, she represented early career researchers, helped organize several events oriented towards researchers and physical therapists, and was involved in the creation, reviewing, and distribution of research grants.

In 2021, she was part of the curriculum committee that wrote the new master program of Orofacial Physical Therapy at the SOMT University of Physiotherapy, and later she became the head of this master program.

In her spare time, Hedwig loves to run, especially in nature or abroad, go on walks with her dog and family, bake cakes and pies, and watch TV-series at home. She is married to James, and they live together in Zeist as proud parents of Mateo (2021).

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