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Myofascial Pain: Etiological factors and therapeutical methods.

A systematic literature review of the last thirteen years.

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Johannes y Antonia,

Gracias por la inspiración y el permanente apoyo

CONTENTS

ABBREVIATIONS

(A):	Anamnestic Helkimo Index
aB:	Awake Bruxism
ADDwR:	Articular Disc Displacement with Reduction
ADDw/oR:	Articular Disc Displacement without Reduction
BTX:	Botulinum Toxin
CPI:	Characteristic Pain Intensity
CT:	Computerized Tomography
(D):	Clinical Dysfunction Helkimo Index
EMG:	Electromyography
GCPS:	Graded Chronic Pain Scale
GJH:	Generalized Joint Hypermobility
HA:	Hyaluronic Acid
HPA:	Hypothalamic-pituitary-adrenal (axis)
ID:	Internal Derangement
LLLT:	Low Level Laser Therapy
MDD:	Major Depressive Disorder
MIC:	Maximal Intercuspal Position
MMO:	Maximal Mouth Opening
MMP:	Metalloproteinase
MPS:	Myofascial Pain Syndrome
MRI:	Magnetic Resonance Imaging
OHR:	Oral Habit Reversal
PI:	Psychosocial Interventions
RCP:	Retruded Contact Position
REM:	Rapid Eye Movement
RMMA:	Rhythmic Masticatory Muscle Activity
s.:	see
sB:	Sleep Bruxism
SC:	Self Care strategies
SC-co:	Self-Care strategies plus Counseling
SCL-90-R:	Revised Symptom Checklist-90
sEMG:	superficial Electromyography
SF:	Synovial Fluid
TENS:	Transcutaneous Electrical Nerve Stimulation
TMD:	Temporomandibular Dysfunction
TMJ:	Temporomandibular Joint
TrPs:	Trigger Points
UT:	“Usual Treatment”

PREFACE

The multiplicity of definitions for the same clinical situation has been one of the major difficulties to get a consensus in the understanding and management of the orofacial pain. Actually, this concept involves many different entities that differed drastically in terms of the etiological and pathogenical considerations. Dental infections, neuromuscular dysfunctions, multiple syndromes and many other diseases can generate this kind of painful condition.

The orofacial pain is tackled by different medical areas, such as otorhinolaringology, dentistry, head and neck surgery, and orthopedics. The temporomandibular disorders (TMD) represent an important percentage of this condition.

The temporomandibular dysfunctions are a heterogeneous group of signs and symptoms that affect the jaw joint and/or the chewing musculature. They are associated with different expressions of facial pain, headache, and ear alterations (pain, tinnitus, etc.). Due to the unspecific quality of signs and symptoms and the wide variety of clinical expressions, the diagnosis of TMD may be easily conflated with other disorders. This overlap has a high impact on the treatment selection.

Not only different diagnoses in the medical field, but also dissimilar philosophy of treatment evidence the lack of understanding of this pathology. Particularly, the etiology of TMD is still controversial. Currently a multifactorial theory has received a great support among the scientific community. This theory draws the attention to the interaction of psychological, neuromuscular and oral pathogenic factors.

The purpose of this qualitative systematic review of literature was to evaluate the evidence regarding the etiological determinants and treatments of Temporomandibular Disorders collected during a decade of research (1999-2012). Special focus was brought on TMD with myogenous origin.

INTRODUCTION

The present work is divided into five parts. The first part intend to present a definition of temporomandibular disorders, some epidemiological data reported until now, and a narrative review of the possible etiological factors. Further on in the text the multiplicity of therapeutical modalities and their possible mechanisms of action are described. The second part introduced basic concepts of the systematic qualitative analysis.

Subsequently, the third part contains a series of systematic reviews of the randomized clinical studies on TMD treatments published during the last twelve years. The analysis of the same search strategy for patients of myogenous TMD was linked with independent searches for each treatment. For the evaluation of the included studies, the authors applied the Cochrane Collaboration's tool for assessing risk of bias. The therapeutical options gathered from the current international literature presenting at least three current RCTs were categorized into six different groups and tabulated to be analyzed.

Consecutively, the fourth chapter presents a meta-analysis of the current "usual treatment" for TMD based on splint therapy according to the directions of the Cochrane Collaboration for all the available literature published up to now. This systematic review and meta-analysis was conducted with the support of an international research team.

Finally, the last part consists of the discussion of the possible links between the most relevant outcomes and the alleged therapeutical target of the reviewed treatments.

Abstract

Myofacial Pain is the most common form of temporomandibular disorders (TMD), affecting principally women in reproductive age. The etiology of TMD is still controversial. Currently a multifactorial theory has received a great support among the scientific community. This theory draws attention to the interaction of psychological, neuromuscular and oral pathogenic factors. **Objectives**: to describe the possible etiological factors of the Myofacial Pain; and to evaluate the effectiveness of the current treatments for Myofacial Pain. **Materials and methods**: a narrative review of the etiological factors and epidemiological data of Myofacial Pain introduces this work. Thereafter the author presents five systematic reviews of RCTs which have been published during the last thirteen years (1999-2012) for the use of acupuncture, low level laser therapy, drugs, physiotherapeutical interventions, splint therapy, and psychosocial interventions in the treatment of Myofacial Pain. Moreover, the author reports a systematic review and meta-analysis of all the available literature of two modern approaches for the treatment of Myofacial Pain. A comparison between the "usual treatment" based on splint therapy and psychosocial interventions was conducted. **Results:** the author did not find sufficient evidence to support therapies based on one single intervention. However, the condition of the patients with myofacial pain could be treated more effectively with combined treatments. After comparing "usual treatment" with psychosocial interventions, the author observed a tendency of the latter to improve psychological outcomes, whereas the first one was slightly more effective to enhance clinical functional outcomes. In general, a high level of heterogeneity was observed among the included studies of the different systematic reviews. The quality of the studies is susceptible to be improved. **Clinical implications**: the author proposes core outcomes to be implemented within the research on myofacial pain in particular and temporomandibular disorders in general, in order to enable scientifical comparisons between different therapies.

Zusammenfassung

Myofaszialer Schmerz ist die häufigste Form der Temporomandibulären Dysfunktionen (TMD), welcher hauptsächlich bei Frauen im fruchtbaren Alter auftritt. Die Ätiologie der TMD ist noch höchst umstritten. Gegenwärtig findet die multifaktorielle Theorie bei den Experten grosse Unterstützung. Diese Theorie richtet die Aufmerksamkeit auf die Interaktion der psychologischen, neuromuskulären und lokal mündlichen krankheitsverursachenden Faktoren. **Ziele der Studie**: die möglichen ätiologischen Faktoren von Myofaszialem Schmerz zu schildern; und die Wirksamkeit der gegenwärtigen Behandlung von Myofaszialem Schmerz auszuwerten. **Material und Methode**: eine narrative Übersichtsarbeit der Literatur über die ätiologischen Faktoren und epidemiologischen Angaben des Myofaszialen Schmerzes leitet die Arbeit ein. Danach stellt die Autorin fünf systematische Übersichtsarbeiten von RCTs dar, welche innerhalb der letzten dreizehn Jahre (1999-2012) veröffentlicht wurden. Die Themen umfassen Akupunktur, Low-Level-Laser Therapie, Pharmacotherapie, Physiotherapie, Schienentherapie, und pyschosoziale Interventionen gegen Myofaszialer Schmerz. Außerdem berichtet die Autorin von einer systematischen Übersichtsarbeit und Meta-analyse der vorhandenen Literatur von zwei modernen Behandlungsweisen gegen Myofaszialem Schmerz. Es wurde ein Vergleich zwischen der “regulären Behandlung” (usual treatment), welche auf der Schienentherapie basiert, und psychologischen Interventionen durchgeführt. **Ergebnisse:** die Autorin hat nicht genügenden wissenschaftliche Beweise gefunden, um irgendeine einzelne Therapie zu unterstützen. Hingegen sind die kombinierten Behandlungen effektiver um den Zustand der Patienten mit myofaszialem Schmerzen zu verbessern. Nach dem Vergleich von psychologischen Interventionen und der “reguläre Behandlung”, beobachtete die Autorin eine Tendenz der erst gennanten die psychologischen Ergebnisse zu verbessern. Demgegenüber war die „reguläre Behandlung“ bezüglich der klinischen funktionellen Resultate geringfügig wirksamer. Im Allgemeinen wurde eine hohe Heterogenität zwischen den analysierten Studien der verschiedenen systematischen Übersichtsarbeiten beobachtet. Die Qualität der Studien hat noch viel Verbesserungspotenzial. **Klinische Folgerung**: die Autorin schlägt die Nutzung von Kernergebnissen im Kontext der Forschung zu Myofaszialem Schmerz im Speziellen und Temporomandibuläre Dysfunktionen im Allgemeinen vor. Dadurch sollen wissentschaftliche Vergleiche zwischen unterschiedlichen Therapien ermöglicht werden.

PART 1

TEMPOROMANDIBULAR DISORDERS (TMD)

1.1 Definition of Temporomandibular Disorders

This disease was first reported in the 30s under the name of *Costen´s syndrome*, a term that is currently obsolete, however still occasionally used in Otolaryngology. The etiology was certainly unknown, but it was correlated with tinnitus, chronic facial pain and mandibular functional disorders.

Thenceforth several researchers have tried to explain this clinical entity in respect of its pathogenesis and evolution, and have given diverse names in an effort to define it. As a result, the literature compiles many different nomenclatures that are virtually synonymic, e.g. myofacial pain, myofascial pain, craniomandibular disorder, masticatory muscle disorder, myoarthropathy, etc [414]

TMD actually is a complex term that involves different symptomatic definitions which affect the temporomandibular joint and the surrounding structures. It is important to remark that this pathology is considered chronic and self-limiting.

1.2 Anatomical and functional considerations of the Temporomandibular Joint (TMJ). *Disc derangements*.

Four morphofunctional unities of the stomatognathic system are responsible for the oral physiology which implies vital activities such as mastication, deglutition, and respiration-phonation. These unities are the TMJ, the masticatory musculature, occlusion, and periodontium.

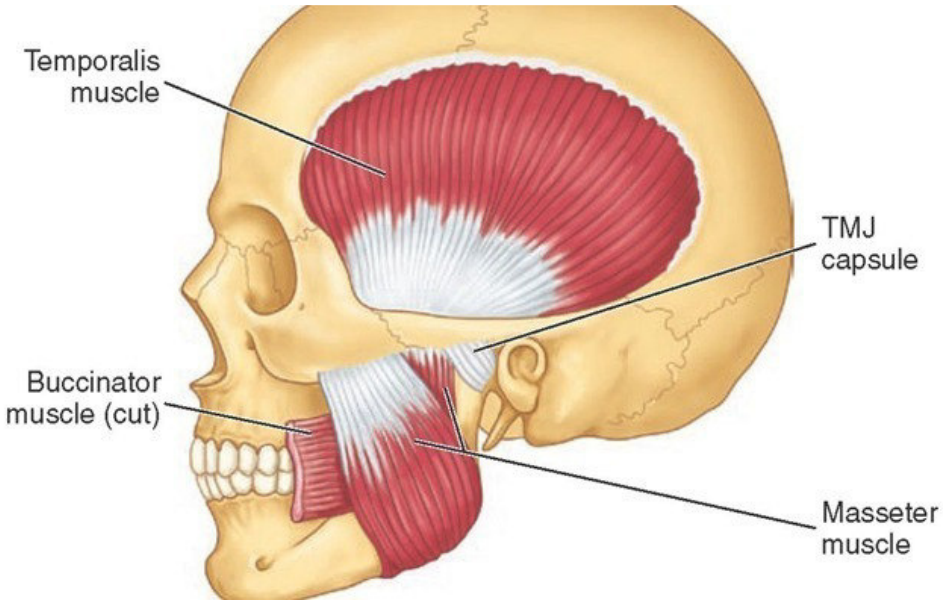

***Figure 1**. Sagittal view from Masseter muscle and Temporalis muscle (what-when-how.com)*

The masticatory musculature comprehends the masseter, lateral and medial pterygoid, and temporalis muscles (fig.1, fig.2). These paired muscles act differently according to the anatomical relations with the skull [s. 598]. The contraction of the temporalis, masseter, and medial pterygoid muscles produce jaw closing, however the chewing forces result principally from the activity of the two latter. The mandibular retrusion follows the contraction of the posterior part of the temporalis muscles; and the protrusive movements are produced by the simultaneous contraction of the lateral pterygoid muscles.

The function of the lateral pterygoid muscle is controversial. It is mostly believed that the inferior head of the lateral pterygoid participates in opening and protrusive jaw movements, while the superior head has been related with positioning of the discus articularis Furthermore, lateral movements are linked to a contralateral contraction of a single pterygoid muscle [77].

Other muscles implied in jaw motion are the suprahyoid muscles; specifically the digastric, mylohyoid, geniohyoid which are jaw depressors. The two latter also contribute to produce retrusion. Additionally, the buccinator muscles protect the cheeks during the chewing activity. Complex functional movements are the consequence of combined coordinated muscle activity.

The pathogenesis of the characteristic muscle pain in TMD patients is an unresolved issue. As well as by other chronic pain conditions, the explanations for muscular pain move around two principal theories, namely the vicious circle,

and the pain adaptation model. Other alternative theories have been put forward; however at the moment questions are still open [565, 444]. The relationship of the neuromuscular component with dental occlusion together with the afferent fibers in the periodontium, and the theories of muscle pain will be discuss further on text linked to the myofacial pain condition.

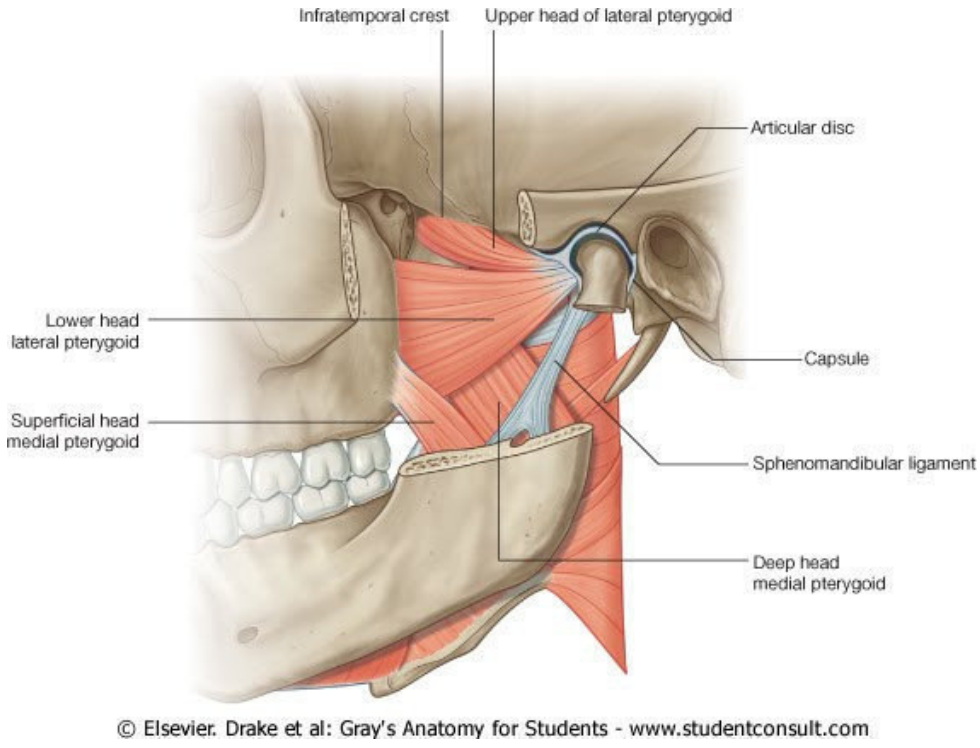

Figure 2. *Sagittal view from Pterygoid muscles, after resection of the ramus mandibularis and zygomatic arch.*

The following text gives brief descriptions of the structural characteristics of the TMJ. It aims to provide the basic context for the comprehension of the next discussion topics as a general reference.

Anatomically, the temporomandibular joint is composed of two articular surfaces and a disc. The mandibular articular surface is called condyle, and the temporal surface comprises the glenoid fossa and the articular eminence. Therefore, the TMJ is a bicondylar joint, which is harmoniously connected by the interposition of the articular disc.

The TMJs are bilateral diarthrodial synovial joints, situated sagittally on both sides of the face. The TMJs are part of the mandibular bone that act simultaneously, and always with the teeth. This interdependence is notorious. The occlusion influences the condylar trajectory, the Bennett movement and the

Bennett angle. Reciprocally, the intercondylar distance influences the occlusal morphology. Specifically, *Olthoff* concluded that the principal determinant of the dynamic occlusal morphology is the mandibular lateral movement range [436].

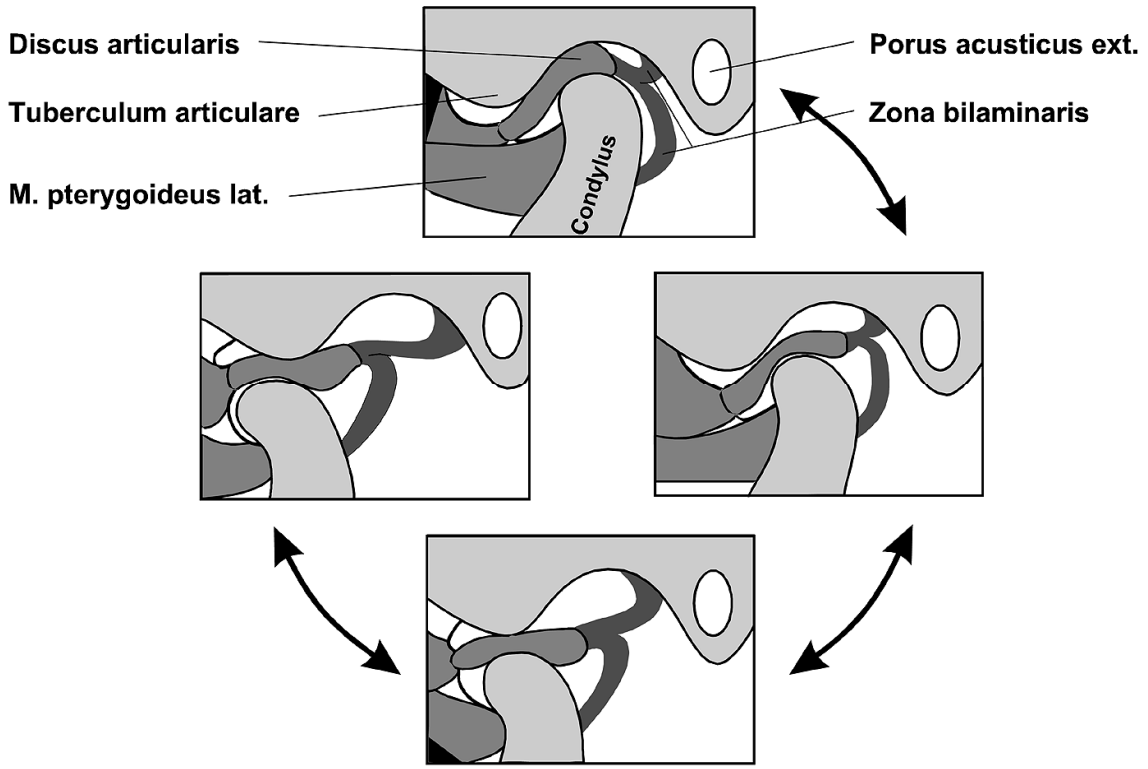

***Figure 3**: Diagram of the kinematic of the TMJ (Fink M et al. Phys Med Rehab Kuror 2001; 11: 221-8)*

The kinematic of the TMJ is complex (fig. 3), due to the manifold combination of movements of translation and rotation. This mechanical performance defines the mandibular system as a six-degree system with a constantly shifting centre of rotation.

Some 3-D computational models and simulators struggle to represent more accurately the complex relationship of the different components of the TMJ [107, 635]; however, the unlikely viscoelasticity of the involved structures has been a great challenge for science, because it modifies the complete calculation regarding the prediction of the jaw movements.

The mandibular kinematics is then widely influenced by the peculiar characteristics of the articular disc that separates the TMJ into two functional compartments. The superior compartment is broader than the inferior one, and participates on the condylar translation; meanwhile inside the inferior compartment the condylar rotation movements are executed.

The articular disc has an exceptional composition intimately related to its function. Histological studies on human discs showed the heterogeneity of this tissue. Interestingly, in contrast to the fibrocartilage of other synovial human joints, the temporomandibular disc is made essentially of fibrous tissue. In fact, the articular disc contains four dissimilar zones, namely anterior, intermediate, posterior, and bilaminar zone.

The anterior zone of compact fibrous tissue, with interwoven fibers that continue the joint capsule, receives the tendon insertion of the lateral pterygoid muscle. The intermediate zone, the working area, is composed of parallel fibrous bundles that contain some cartilaginous islets in the center of the disc; this zone has a low cellular density, is avascular and free from nerve endings.

The posterior zone is a transition area, characterized by a less-compact fibrous tissue with the inclusion of elastic fibers. Finally, the bilaminar zone presents a posterior-superior area of elastic fibers, which are anchored on the tympanosquamous fissure, and are responsible of keeping in contact the articular disc and the mandibular condyle. The posterior-inferior area of the bilaminar zone consists of a venous plexus that acts like a hydraulic bearing during the jaw movements.

Disc derangements

Any deviation in the anatomical position or form of the tissues within the TMJ capsule is considered an internal derangement (ID). The most prevalent articular disorders are the disc displacements with and without reduction, which differ from each other in the capacity to recuperate the initial relation of the articular disc during the mandibular movement.

The finding of clicking sounds represents a pathognomonic sign of the discal reduction. These sounds might appear unique or reciprocal during the condylar translation, depending on the point of time when the condyle is able to recover its relationship with the articular disc.

A disc displacement without reduction may lead to a chronic closed lock (disc displacement without reduction and with limited jaw opening) [500] or an open lock [495]. If that occurs, the disc is lastingly located in an anterior position with

sometimes also a medial or lateral component. The condyle is too far away to relocate the disc over its articular surface, thus altering the jaw function.

Advanced affections of the temporomandibular structures are the arthritis and osteoarthrosis which present patent inflammatory activity into the capsule and some anatomical alterations.

Three different molecular models of the mechanism of TMD based on excessive mechanical stress have been proposed: direct mechanical damage, hypoxia–reperfusion injury, and neurogenic inflammation [387, 259, 558]. These models are rooted on molecular findings in the synovial fluid.

The synovial fluid (SF) is a highly viscous ultrafiltrate of plasma secreted for the synovial membrane. The SF takes action as a nourishment source for the cartilage, and as a cushion and lubricant agent in the upper and lower components of the TMJ [191].

The articular overloading may generate free radicals whether directly under mechanical stress through homolytic fission, or indirectly through hypoxia due to augmented intra-articular pressure [87, 422]. These free radicals may induce a chain of oxidative-reductive reactions modifying the properties of structural molecules surrounded, that also turn into free radicals. Eventually, interactions between altered molecules through covalent bonds may be implicated in the formation of adhesions into the TMJ [143, 518].

The action of free radicals on hyaluronic acid (HA), principal component of the synovial fluid, may reduce the viscosity of the fluid altering its lubricating properties. These changes in the composition of the SF may be implicated in producing major adherence of the articular disc and therefore the development of disc derangements [605, 422].

On the other hand, other authors point out a pathogenic effect in ID of chronic neurogenic inflammation. High levels of inflammatory mediators in synovial fluid samples were found in severe cases of TMD linked to disease progression [103, 420]. Moreover, one study reported high levels of aggrecanase in synovial fluid of TMD patients, a metalloproteinase (MMP) which degrades the proteoglycan aggrecan present in the articular cartilage [627]. Besides, levels of MMP-2 and MMP-9 were increased in fluid samples of patients with articular disc displacement without reduction (ADDw/oR) compared to articular disc displacement with reduction (ADDwR), suggesting an active destruction process

[553]. These MMPs seems to be increased also in osteoathritic TMJ [552, 628]. In spite of the role of the MMPs remains unclear, the above mentioned molecules may be useful as markers of TMD.

Additionally, some authors even reported the presence of bacteria some antibodies against mycobateria in the synovial fluids, which meaning is unknown [543, 295,10].

Taking together, there is a lack of comprehension about the potential link among the mentioned stages of TMD, and there is no evidence to assume a linear progress.

1.3 Epidemiology of TMD

1.3.1 Epidemiological studies

The prevalence of TMD in the general population over age 18 fluctuates around 10%, with a major percentage of affected women in the reproductive age [566]. However, the prevalence data vary significantly according to the different diagnostic criteria of TMD and the characteristics of dissimilar populations [334]. Table 1 presents several epidemiological population-based studies of general and young samples.

De Kanter [282] published in 1993 a meta-analysis of TMD prevalence including studies from 1974. The results were expressed in percentages of symptom free individuals according to two parameters: anamnestic (A_0) and clinical dysfunction (D_0) Helkimo Index. This meta-analysis found an overall rate of 70% (23 studies, n=15,559) anamnestic symptom free A_0 subjects, and 56% (22 studies, n=16,820) clinically no dysfunctional D_0 subjects in randomized samples. It is noteworthy that many critical methodological observations of the included studies were stressed: 75% of the studies did not state a definition of TMD, 50% of the articles did not specify the dentition, and assessments varied widely (TMD ranged from 6-93% using interviews and from 0-93% using clinical examination).

According to the 3rd German Oral Health Study in 1999, the prevalence of painful TMD in a German population (n=2022) was 4.6% for patients between 35 and 44 years old, and 4.7% for patients aged 65-74yrs [571].

Table 1. Epidemiological studies in non-patient population					
Author	**Sample N (women/men)**	**Population and Diagnostic tool (DT)**	**Age (yrs)**	**Total of TMD symptoms/ diagnosis (%)***	**Epidemiological findings**
***Gonçalves et al.* 2010 [221]**	1230 (633/ 597)	Stratified sampling Brazil DT: questionnaire (telephone survey)	Range: 15-65	At least one symptom of TMD was present in 39.2% of the sample	Most prevalent symptoms were: TMJ sounds (23.7%), and masticatory muscle pain (15.4%). This study found an increased prevalence of TMD symptoms in individuals with headache compared with those without headache
***Janal et al.* 2008 [265]**	782 (only women)	Random sample positive screened for a chronic pain disorder, or as demographic control USA DT: RDC/TMD	Range:18-69+	10.5% (95% confidence limit (CL)=8.5-13.0) were women with myofacial-TMD	Women in the age group under 50yrs showed 11.9% of myofacial-TMD prevalence, while the same condition was found in 7.9% of the women over 50yrs.
***Isong et al.* 2008 [262]**	30,978 (17,498/ 13,480)	Representative sample USA DT:validated questionnarie	18+	Overall prevalence of TMD: 4,6%	Among the gender groups, the prevalence of TMD was 6.3% for women, and 2.8 for men Ethnic composition: 20,389 non Hispanic whites, and 4,179 non-Hispanic blacks. Non-Hispanic white women presented slightly higher prevalence compared to non-Hispanic black women (6.7% vs 5.1%)
***Rutkiewicz et al.* 2006**	6,335 (3,466/	79% of a national representative sample	30+	38% of subjects presented at least one TMD sign	TMD signs were significantly more prevalent for women than men (P<0.001)

[483]	2,869)	Finland DT: clinical examination			
***Bevilaqua-Grosso et al.* 2006** **[73]**	109 (95/14)	University students, Brazil. DT:questionnaire by Fonseca	Mean: 21.61±1.91 Range: 18-27	87% (43.2% mild TMD; 34.8% moderate, 9.2% severe TMD)	Affected women from the TMD sample: 43.15% mild TMD, 37.89% moderate TMD, 10.52%severe TMD Affected men from the TMD sample: 5.50% mild TMD, 1.83%moderate TMD, 0% severe TMD
***Plesh et al.* 2005** **[452]**	887 (only women)	Cohort of young women USA DT: RDC/TMD	Range: 19-23	13% of Caucasians and 6% of African American reported facial pain in the last 6 months.	Ethnic composition: 411 Caucasian women, and 419 African American women. From the 61 TMD diagnosed women: 80% presented myofacial pain (group I), 33% disc displacements (group II), 48% group III. For each diagnosis, the majority were Caucasians.
***Nilsson et al.* 2005** **[418]**	28,899 (13,843/ 15,056)	Random sample in a Swedish county Sweden DT: question-naire	Range: 12-19	4,2% reported TMD pain	Higher prevalence among girls than among boys (6.0% vs 2.7%; P<0.001); and in the cities compared to rural zones (4.4% vs 3.9%; P<0.05)
***Casanova-Rosado et al.* 2006** **[98]**	506 (274/ 232)	University students Mexico DT: RDC/TMD	Mean: 17.2 ±2.7 Range: 14-25	41.6% showed grade of TMD	Among the TMD diagnosis were found: 15.6% disc displacement with reduction; 10.9%myofacial pain, 12%disc displacement without reduction (6.1% without and 5.9% with limited opening); 0% diagnosis group III. Women exhibited higher prevalence of TMD than men (52.9% vs 37.9%)

***Gesch et al.* 2004 [209]**	4,289 (2,180/ 2,109)	Random sample Germany DT: clinical examination	Range:20-81	24.9% joint sounds; 12% muscular tenderness; 6.1% TMJ tenderness under pressure 11.1% restricted mandibular mobility (1.2% with pain)	For all the clinical outcomes, the prevalence among women was higher than for men. (i.e. masticatory muscle tenderness, TMJ sounds, deviation and deflection, and pain upon palpation or during jaw movement)
***Miyake et al.* 2004 [396]**	3,557 (1,041/ 2,516)	University students Japan DT: questionnaire	Mean: 20.4 ±2.1 Range 18-26	41.7% reported TMJ noise, 16.0% TMJ pain, and 16.3% impaired mouth opening	This study suggests a relationship between TMD symptoms and parafunctional activities.
***Rantala et al.* 2003 [457]**	241 (125/ 116)	Employees of a Finish company Finland DT: RDC/TMD	Mean: 46±7 Range: 30-55	27% diagnosis of TMD	Among TMD diagnosed subjects: 13.3% Myofacial pain (group I); 15.8% disc displacement (group II); 1.2% arthralgia (group IIIa), 0.4% osteoarthritis (group IIIb), 2.4% osteoarthrosis (group IIIc)
***Hirsch et al.* 2002 [252]**	525 (291/ 234)	Random sample of population Germany DT: RDC/TMD	Range: 20-60	9% (36% aging 20-29 40% aging 50+yrs)	Sex ratio women/men of TMD diagnosed population 5:1
***Sönmez et al.* 2001 [533]**	394 (194/ 200)	Random sample of public school Turkey DT:questionnaire and clinical examination	Range:9-14	62.4% (67.58% of 182 children with mixed dentition, 58.01% of 212 children with permanent dentition)	Prevalence of TMD symptoms in mixed dentition: 67.50% girls, and 67.64% boys. Prevalence of TMD symptoms in permanent dentition: 60.52% girls and 55.1% permanent dentition
***Goulet et al.* 1995**	897 (497/ 400)	Random sample of French speakers	Range:18 and over	30%(confidence interval CI=26.9%-33%) reporting overall	Sex ratio for frequent TMD symptoms: 2 women:1man

[224]		Canada DT: TMD screening questionnaire (telephone survey)		presence of jaw pain, and 7%(CI=5.1%-8.8%) reporting frequent jaw pain	In the different age groups, the prevalence for jaw pain in women/men was: 18-34: 8.7%w / 3.5%m 35-54: 10.4%w / 6.8%m 55+: 9.7%w / 3.3%m
***Kanter, de et al.* 1993** **[282]**	3,468 (1,815/ 1,653)	Representative sample, nationwide survey Netherlands DT: Helkimo Index	Range:15-74	21.5% of Dutch population perceived some dysfunction 44.4%presented clinical signs and symptoms of TMD	16.6% mild self-reported symptoms, 4.9% moderate self-reported symptoms in adults 41.6% clinical mild dysfunction, 2.8% moderate to severe dysfunction. For both, anamnestic and clinical indices, women showed significantly more frequent and more severe dysfunction than men.
***Korff, von et al.* 1988** **[303]**	1,016 (593/ 423)	Representative sample from health maintenance organization USA DT:questionnaire (mail) on facial pain	Range:18-65+	17% of the subjects reported facial pain in the prior 6 months	From the sample, 15% of women reported facial pain (11% in the age group 18-24yrs., 18% in age group 25-44yrs.,12% in age group 45-64yrs., and 2% in age group 65+yrs. The prevalence of facial pain for men was 8% (7% in age group 18-24y, 10% in age group 25-44y, 8% in age group 45-64y, and 0% in age group 65+y)
***Szentpétery et al.* 1986** **[549]**	600 (315/ 285)	Random sample Hungary. DT: Helkimo Index	Mean: 40.7 Range:12-85	20.6% reported symptoms related to anamnestic dysfunction Index (15,3% A_I, 5.3% A_{II}), and 79.8%presented clinical signs and symptoms of TMD (72.3% D_I, 7.0% D_{II}, 0.5% D_{III})	Sex ratio woman to man was 3.1:1 for anamnestic findings. Also a significant overrepresentation was found for clinical findings, particularly pain on palpation among masticatory muscles

In a survey applied to patients with orofacial pain in dental services of the German county Rhein-Sieg, 40.2% patients were diagnosed with TMD, 18.2% with headache-syndromes related to facial pain, and 17% with atypical odontalgia [614]. Data of studies conducted on individuals seeking treatment are summarized in the table 2.

The most frequently symptoms observed in a retrospective sample of patients seeking treatment for TMD in USA were 79.3% headaches, 75.0% TMJ, and 82.4% ear problems [113].

Macfarlane reported that 46% of adults suffering orofacial pain seek treatment in United Kingdom [353], while *Locker* observed 40% seek treatment in a random Canadian sample [348]. For the same condition, the rate was only 20.3% in a sample of the Chinese population [374].

Rates of seeking treatment for TMD vary in Western countries between 3%-7% [92]. Even lower figures seek treatment for TMD were found in Turkey (12.2%) [413] and China (0.6%) [453].

1.3.2 Need for treatment

Carlsson concluded in a systematic review of epidemiologic studies that the presence of signs and symptoms do not correlate with the treatment need, which is estimated at about 5%. This estimation matches the seek treatment rate for TMD in adult population (3%-7%) [92].

In a meta-analysis, *Al-Jundi* calculated the need treatment rate at 15.6% in general adults. Interestingly, the estimations were higher for studies that were based on clinical TMD signs than studies measured in self-report outcomes [33, 34].

De Kanter estimated the need for treatment at 3.1% for the Dutch population [282], and *Rugh* made an estimation of 5% for the population in USA [485]. Need for treatment in Germany was estimated by *Micheelis* at 3.2% for adults aged 35-44, and 2.7% for the age group 65-74 yrs. [384], thus the German epidemiological data of TMD are reportedly similar to those of other Caucasian populations.

Table 2. Epidemiological studies of individuals seeking treatment					
Author	**Sample N (women/ men)**	**Population and Diagnostic tool (DT)**	**Age (yrs)**	**TMD symptoms/ diagnosis (%) ***	**Epidemiological findings**
***Winocur et al.* 2009 [612]**	298 (232/ 66)	Jewish subjects seeking treatment at Orofacial Pain Clinic, Tel Aviv University Israel DT: RDC/TMD	18+	Axis I: 65% MP (group I), 38% DD (Group II), 18% Ar, OAis or OA (group III, 11%, 5% and 2% respectively) Axis II: 20% severe depression, 35% somatization	Pain was reported in 82% of the patients, with a Graded Chronic Pain score of 0 only in 8% of the sample. The disability score was 30.0 ±30.2, Sex ratio women/men 3.5:1
***Lee et al.* 2008 [330]**	87 (77/ 10	Southern Chinese subjects seeking treatment at Dental Hospital China DT: RDC/TMD	Mean: 39.3 ±12.8	Axis I: 57.5% MP (group I); 42.5%and 47.1% DD (Group IIright and left TMJ respectively); 19.5% and 23.0% Ar, OAis or OA (group III, righr and left TMJ respectively) Axis II: 42.5% moderate/sev-ere depression; 59.7% moderate/ severe somatization	15% presented psychosocial dysfunction measured by Graded Chronic Pain Scale
***Akhter et al.* 2007 [26]**	236 (72/ 164)	Subjects seeking treatment at Dental College Bangladesh DT: RDC/TMD	18+	12.9% MP only; 3.1% DD only; 7.9% joint pain only (Ar, OAis or OA); 6.9% MP+DD; 8.1% MP+joint pain; 1.3% DD+joint pain; 5.2% MP+DD+joint pain	236 (45.4%) out of 520 persons seeking treatment in Dental School were diagnosed with TMD. This study correlated RDC/TMD diagnosis with psychological stress, concluding that MP is more common among patients under stressful events.
***Manfredini et al.* 2006 [362]**	377 (276/ 101)	Italian subjects seeking treatment at Section of Prosthetic Dentistry, University of Pisa Italy	Range: 38.8 +-15,7	Axis I: 38.2% MP (group I), 52.3% DD (Group II), 52.6% group III (Ar: 17.5% right TMJ and 16.2 left TMJ; OAis: 12.7% right TMJ and 10.9 TMJ; OA: 11.7% right TMJ and 12.5% left TMJ)	Sex ratio women/men of the total sample 2.6:1, with a significant difference in sex ratio for group I 6:1($P<0.05$)

		DT: RDC/TMD			
***Anastassaki et al.* 2004 [40]**	2,721 out of 3,149 (2,330/ 819)	Retrospec-tive data from the Department of Stomato-gnathic Physiology Sweden DT: clinical examination	Mean: 42 Range: 9-90	29% DD; 19%tension- type headache; 18% myoarthralgia 14% Ar; 11%myalgia; 10% OA in TMJ; 6% unspecified orofacial pain; 4% rheumatic disease of TMJ	This study gathe together data from 1995 to 2002
***Wirz et al.* 2003 [614]**	985 (658/ 327)	Subjects seeking treatment at ambulatory institutions Germany DT: not specified	Range:0-70+ 81.1% in range 20-60, 3.55% no data	40.3% were diagnosed with TMD (29.1% myogenous TMD, 9.9 % arthrogenous TMD, 1.2% TMD -not specified-)	Among 985 patients with chronic orofacial pain, 635 were treated, 11.3% of those received splint therapy, 15.7% received a drug therapy, and 15.6% received phisiotherapy
***Yap et al.* 2003 [625]**	191 (138/ 53)	Patients at National Dental Center Singapore DT: RDC/TMD	Mean: 33.6 ±9.3	31.4% group I (13%MP, and 18%MP with limited opening); 30.8% group II (15.1%DD left TMJ, 15.7% DD right TMJ): 25.6% group III (12.6%left TMJ,13.0%right TMJ)	This study compared Asian sample with a Swedish (n=82) and American (n=261) Sex ratios women to men were: 3.1:1in the Asian, 3.6:1 in Swedish and 5:1in the American cohorts.
• MP= myofacial pain; DD=disc displacement; Ar=arthritis; OAis=osteoarthritis: OA=osteoarthrosis					

1.3.3 Gender and age effect

Hirsch reported that the prevalence of TMD in adult women in Germany outnumbers men by approximately five times [252]. *Zwijnenburg* observed that only 3.6% in a German sample were interested in TMD treatment, and 68% of those were women [639]. Several other studies in Germany stated that three quarters (about 75%) of the individuals seeking treatment for TMD were female [142, 509].

Several population studies over the world estimated the sex ratio women/men to be around 2:1 (s. table 1). The high prevalence among women is more accentuated in samples of individuals seeking treatment (s.table 2).

The over-representation of feminine sex is an important unresolved question, because it may be related to the pathogenesis of TMD. Three principal hypothetical causes have been argued: **hormonal, behavioural,** and **genetic**.

The observation of epidemiological information has directed some research to the possible effects of **sexual hormones** like estrogens [335, 602, 281] and relaxin [603]. Estrogens may have a direct influence on the structural reorganization of the TMJ [202, 603]. Estrogen receptors were detected in cells of the synovial membrane and articular disc, suggesting a target action on these tissues [423]. *Henry* disagreed with that report showing a total absence of estrogen-binding sites in 28 samples of posterior bilaminar zone obtained from TMD patients post-surgical disc repositioning [244].

Besides, it is believed that estrogens may be related to the pain transmission. The estrogens may have a modulating role on the pain pathways, especially in association with inflammatory processes, whether altering the expression of some neuropeptides and neurotransmitters, or increasing the excitability of TMJ afferents [393, 599, 603, 620].

On the other hand, the possible differential **behavioural factors** between sexes include psychological profiles (e.g. stress-related disorders and depression) and the relationship with medical services.

Just as other chronic pain syndromes like fibromyalgia and chronic fatigue, TMD seems to be linked to stress. It expresses physiological effects through the activation of the hypothalamic-pituitary-adrenal (HPA) axis [204]. Higher levels of cortisol in TMD patients (30 to 50% more than healthy patients) may be a consequence of the HPA axis hyperactivation [306]. The initial analgesic effect of

cortisol in acute pain may develop into hyperalgesia under prolonged exposure to stress [319]. The HPA axis dysregulation has been reported for several psychiatric conditions (e.g. depression, post-traumatic stress among others), whose molecular mechanism is gender-related. Presumably, women are more vulnerable to stress-related disorders due to hormonal regulation of the HPA axis and LC-norepinephrine system [62].

Along the same line, depression maximizes the perceived pain impact and influences the illness conviction in headache and orofacial pain [128]. Depression is probably a consequence of permanent pain or may be an underlying factor in depressive conditions after pain episodes [190]. Both hypotheses are compatible with the diathesis-stress model proposed by *Bank* and *Kerns*, which explain that the nature of psychological stressors (disability, aversive sensory and distressful emotional dimension of pain, among others) related to chronic pain may predispose to depression [140]. Therefore, the higher female prevalence of depression is relevant [293].

About the relationship with healthcare, it has been reported that women consult more frequently and are more persistent in seeking treatment [187, 493]. This behavior may be related to the reasons for consultation. Some authors indicate that women are more sensitive to clinical and experimental pain [494, 127].

Moreover, several epidemiological studies assert that women reported more subjective complaints than men [108]. *Green* and *Pope* in a longitudinal study (n=2603) observed that women experienced more symptoms than men, although they reported a similar health status. They concluded that attitudinal and behavioral factors, and not health knowledge, determine gender differences in careseeking [226]. Contrarily, critical viewpoints have emerged against these epidemiological findings, suggesting methodological artifacts may explain the reported sex differences [456, 473].

In a review of literature from 1998 to 2008, no evidence was found in favour of a sex-differentiated pain threshold for experimental cold or heat pain, however women declared less tolerance to pain. Concerning induced muscle pain, the authors did not find any conclusive support to distinguish pain patterns between men and women [456]. Neither studies on endo- or exogenous estrogens, nor neuronal sensitization experiments submitted sufficient evidence to demonstrate distinct pain patterns for women. However, coping style factors (specifically catastrophizing, masculinity-femininity, and adaptive coping

strategies) were associated to dissimilar experience of pain, whereas depression and anxiety were weak or inconsistently correlated with sex differences regarding pain sensitivity [455].

Fillingim summarized several studies that point out the socio-cultural meaning of pain linked to the role gender. Interestingly, femininity and masculinity were found predictors of pain tolerance, although modifiable by expectations of pain [188, 615]. These gender stereotypes were strongly linked to gender differences in pain sensitivity and not to personality trait scales [28].

An alternative explanation is that women are effectively more prone to morbidities due to additional risk factors, or due to the combination of sex-specific pain mechanisms treated under homogenous medical interventions [228].

Finally, many of the **genetic** investigations focus on the factors mentioned above, exploring polymorphism of receptors, and psychological differences between genders. Other research lines are focusing on the inflammatory process. In a review of literature, *Oakley* and *Vieira* summarized the current focus of research on genes for individual variations in pain perception, gender and ethnicity, proinflammatory cytokines, female hormones, breakdown of the extracellular matrix, and syndromic forms of TMD. In respect to gender, estrogen-related genes (e.g. COMT and CYP19A1) and pain receptor-related genes may be considered potential distinctive factors [426]. For example, *Kang* remarked on the polymorphism of the estrogen receptor suggesting that certain haplotypes may be related to major pain susceptibility in female TMD patients compared to healthy women [281].

Despite these epidemiological observations, the prevalence of TMD decreases for both sexes with advanced age. *Riley* and *Gilbert* found that gender differences for pain ratings were not significant in a cohort of orofacial pain patients older than 65 years old in contrast to a younger cohort [472].

Some anatomical changes due to aging in the temporomandibular joint include increased content of calcium and loss of viscoelastic properties of the temporomandibular disk [554], and higher prevalence of osseous changes like osteosclerosis, flattening, osteophytes and bone erosion [151, 31]. These factors may be related with the high prevalence of TMJ sounds in geriatric patients [258, 439, 507], despite this sign of TMD in this age group use to be symptomless. Contrarily, other study conducted in Finland (n=6,335) showed that from those presenting at least one symptom of TMD (n=2442) after clinical oral health

examination, older groups exhibited more frequent signs of TMD (joint sounds, crepitation and muscle pain) [483]. It is noticeable that epidemiological data differs according to the measured outcomes [334].

Unell reported a 4% higher incidence of temporomandibular pain in women compared to men within a cohort of 50-year-old population who were followed up ten years later [581]. In an initial report, this cohort exhibited gender differences with women reporting more frequently TMJ pain and TMJ sounds, while men having greater problems with chewing and jaw opening [269]. In other study in the same geographical area, the age group of 50 years presented higher TMD prevalence than other age group composed of 60-year-old individuals. Apparently those changes in the general TMD prevalence begin around the 50 years old. It is hypothesized that the decrease of TMD prevalence in the elderly may be associated to a lower report of pain, either for anatomical adaptive changes or for a decreased sensitivity in old patients. *De Boever*, however, found higher subjective pain ratings for the age group of 50 to 70 years compared to a younger group of 20 to 30 years old [80]. This contradictory data points out the need to distinguish between the physiological and psychological dimensions of pain when outcomes are chosen for a clinical trial.

It is also remarkable that gender is not a differential factor in children. In a sample of 394 Turkish children (age=9-14), *Sönmez* observed a significantly higher prevalence of TMD symptoms in children with mixed dentition than those with permanent dentition, but no differences between sexes [533]. Neither Jordanian (n=2157, age range=3-15) [277], nor Finnish (n=483, age range=6-8) [595], nor Israeli (n=244, age range=5-12) [170] children showed gender differences in the prevalence of TMD. In a Chinese study of children and adolescents, sex differences were found either (n=3105, age range=3-19) [137]. However, *Tecco* reported a significantly higher prevalence of myofacial pain in Italian girls (n=1134, age range=5-15) [555].

Taking together, in this section several factors probably associated with the pathogenesis of TMD were exposed by means of explaining the prevalence of TMD markedly linked to women of a reproductive age.

1.3.4 Risk factors for TMD

In an attempt to define epidemiological characteristics of this pathology, many local and general conditions have been studied concerning TMD patients. Suspected risk factors comprehend anatomical factors of the stomatognathic system, some syndromes and psychological problems, and epidemiological factors.

Among the orofacial structural risk factors, those most investigated are the altered dental occlusion, and the joint hypermobility. Severe occlusal alterations like open bite and large overjet have been considered as risk factors for TMD [442, 573, 441, 506]. Nonetheless, after adjusting data to age and gender of 3033 German children, *Hirsch* did not find an increased odd ratio for TMJ sounds compared to children with normal values of overjet and overbite [254]. Controversies about the role of occlusal and other structural factors in TMD will be discussed further below.

According to the occlusionist current of thought, orthodontic treatments have been questioned as they modify the occlusal relationship. Concerning pathological signs of TMD, speculations about negative effects of the extraction of premolars and certain orthodontic appliances have been gradually rejected. Actually, there is no evidence of increased risk of developing TMDs associated with any current orthodontic, orthognathic device or procedure [526, 294, 331, 44, 85, 222].

Some authors suggest that condylar asymmetry, associated to potential negative occlusal factors or bruxism causes a predisposition to develop TMD [392, 622, 600, 299]. However, no sufficient evidence supports this statement.

Generalized joint hypermobility (GJH) [253, 116, 292, 139] and the experience of whiplash injuries have been related to the TMD etiology [300]. GJH, also known as generalized joint laxity and loose ligaments condition, is a hereditary syndrome characterized by increased mobility of the body joints [609]. On the other hand, the whiplash syndrome emerges as a result of a trauma (normally a car accident) which alters the jaw-neck function [174]. Both syndromes affect the neuromuscular component of the TMJ. Nonetheless, evidence neither backs up GJH nor whiplash syndrome sufficiently as risk factors [144, 183, 287, 486, 609]. Probably they define conditions with high vulnerability to develop a secondary TMD. Currently some authors put forward the whiplash syndrome as a totally

independent condition. This position assumes that the high prevalence of TMD in patients who suffered whiplash injuries may be an expression of widespread chronic pain disorder and psychological problems arising from the accident [597, 469].

Psychosocial aspects play a role among risk factors. Apparently, a lower socioeconomic status would favor the appearance of orofacial pain [471]. *Johansson* identified a higher risk of TMD pain in blue collar workers compared to other three more comfortable categories of the Socio-Economic Index [271]. In Netherlands, TMD non-native non-Western patients were characterized with lower levels of education, income and incidence of employment than TMD patients born in countries with high socioeconomic and cultural standards. *Van der Meulen* concluded that psychological factors such stress, depression, disability, and somatization define the ethnic background of TMD patients, even regardless of socioeconomic status [583].

In the interpretation of data from diverse ethnic populations is important to consider cultural reasons, including religion and language influence, which may modify experimenting and reporting pain [555, 41, 267, 168]. A global sight of the ethnicity impact is difficult to infer. Only few studies managed simultaneously data from patients of different countries, while in some countries the different ethnic groups involved sociodemographic variables which include minority problems or sociocultural issues. Comparing samples, *Lee* found diagnoses and psychological findings similarly distributed within patients of Asian and Western countries, except that Asian patients yielded higher prevalence of myofacial pain with limited jaw opening [330, 625]. One comparative study between Arab and Jewish Israeli detected differences in psychological outcomes, namely depression, somatization and anxiety which scored significantly higher for Arab women [467]. On the other hand, Caucasians in California, USA, reported more TMD symptoms than African Americans in a young female cohort, but no significant differences were found with respect to RDC/TMD Axis I diagnose [452]. Also in the USA, non-Hispanic Whites reported more TMD symptoms in a national survey. Within this group, the prevalence decreases as it gets older. Interestingly non-Hispanic Blacks showed an inverse relationship of prevalence to age [262].

In summary, excluding gender and sex (s. section above), scientists explore the significance of a variety of controversial risk factors that should be taken into

account when designing and analyzing epidemiological information about TMD. The influence of oral parafunctional activities will be discussed in the following text.

1.3.5 Bruxism and other parafunctions

Bruxism (Br) can be regarded as a parafunctional activity. It refers to teeth-clenching, grinding, gritting, clicking and gnashing in a subconscious state; in other words, it is an unintentional habit [432]. According to a recent consensus, "Bruxism is a repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible. Bruxism has two distinct circadian manifestations: it can occur during sleep (indicated as sleep bruxism) or during wakefulness (indicated as awake bruxism)" [346]. The exact influence of Br over the stomathognatic system is still controversial, particularly regarding the etiology of TMD. Many authors linked it to hyperactivity of the masticatory muscles and altered psychological factors.

The diagnosis and the variables of the multifactorial etiology of bruxism are not yet consensual [347]. Several intrinsic characteristics of this habit complicate an accurate diagnosis and the comprehension of its clinical significance, for instance, the unawareness of the patient.

Bruxism is ubiquitous in individuals with and without temporomandibular pain, therefore some researchers interpreted this habit as a remaining evolutive behaviour facing threatening situations [284, 527], Interestingly, the stress-induced bruxism activity in rats have shown an attenuating effect on the activation of the autonomic nervous system during stress exposure [496].

85% to 90% of the population reported grinding at least once in their lifetime [442], indicating that bruxism does not always represent a pathology. However, some individuals maintain this bruxism activity for long periods of time developing clinical consequences such as muscle tenderness, increased muscle tonus, hypertrophy among others.

Experimental grinding and clenching induce muscle soreness and pain-related TMD at short-term in a fraction of healthy individuals [50, 213, 179]. The experimental conditions however are not always representative of the clinical situation. In healthy individuals, after continuous muscular contraction of the masseter muscle follows a desensitization of the vasodilatory system [24].

Interestingly, the masseter muscle in myofacial pain patients apparently experiences an edematous condition [49].

Other researchers claim that the direction of grinding is relevant to induce higher EMG values in the temporalis of healthy subjects. Concentric and not eccentric grinding displayed higher temporalis EMG activity than clenching patterns [234]. This result becomes relevant as a predictor of pathogenesis for the case that higher EMG activity is linked to muscle tenderness due to local hyperactivity.

Okeson pointed out the strong bruxism forces as aggravating or maintaining agent of TMD. *Okeson* estimated that parafunctional forces applied during Br can be theoretically up to three times stronger than the functional activity [432]. The horizontal component of these parafunctional forces may act damaging teeth [502, 559].

Recent reports estimated the overall prevalence of Br around 30% going down with rising age. While some authors identified no gender differences, others found a masculine trend [110, 380,,603]. Previous reports on prevalence are highly variable depending on diverse assessment systems and definitions of Br [149].

The activity patterns make a distinction between nocturnal or sleep Br (sBr) and diurnal or awake Br (aBr). The sBr is considered a sleep related movement disorder conforming to the International Classification of Sleep Disorders [39]. According to this classification, grinding of teeth during sleep at least weekly was reported by 8.2% of a representative sample (n=13,057) from three countries (United Kingdom, Germany and Italy) revealed by a telephone survey. Out of this population, 4.4% met criteria of sBr diagnosis, showing no gender differences and a higher prevalence between 19 and 44 years old [428].

A great activity of the chewing musculature during non-rapid eye movement (non-REM) phases characterizes sBr. Normally during these episodes occurs a particular movement pattern called rhythmic masticatory muscle activity (RMMA). It consists of a co-contraction of the jaw-opening and jaw-closing muscles followed by salivation and swallowing [320]. This pattern was observed two to twelve times per hour in sleep bruxers, while just once per hour during sleep in young subjects without sBr [322]. EMG of bruxers compared to non-bruxer persons display not only more bursts per episodes, but also larger EMG amplitudes and shorter duration [324]. Consequently, polysomnographic diagnostic criteria for sBr comprehend: at least 2 bruxism episodes with grinding

sounds, over 4 Br episodes per hour of sleep and/or more than 25 bursts per hour, and/or more than 6RMMA bursts per episode [323].

The high prevalence of RMMA in bruxers suggests a central neural regulation over the movements of masticatory muscles. In this regard, some authors designate a mainly central etiology to this parasomnia. Therefore sBr may represent an exaggerated RMMA. This activity may be related to general sleep body movements [58, 130]. Others suggest that this high RMMA may be an aftermath of microarousals, which are recurrent brief awakenings of 3 to 15 seconds that occur together with ascending heart rate and muscle tone [320, 290, 324, 289, 288]. Others believe that bruxism activity may be triggered by the influence of the dopaminergic system and the cortex during sleep [421].

Several studies put forward other factors that may be involved in the pathophysiology of bruxism, for instance, some psychological factors and local factors related with the dental occlusion. Bruxers exhibite higher prevalence of some psychological disturbances, like anxiety and stress, when compared to control subjects [363, 410, 17, 97, 231, 527]. On the other hand, some peripheral stimuli coming from orofacial receptors may also influence the maintenance of bruxism. However, their role seems to be secondary [for review: 291]. Furthermore, various factors have been overestimated, such as a supposedly augmented alertness in bruxers [360] or the presence malocclusions [590].

The current predominant view of bruxism highlights the role of central mechanisms as compared to the peripheral regulation [for review: 347]. The bruxism generator model, proposed by *Lobbezoo*, results then from the integration of diverse hypotheses, emphasizing the possible interaction between RMMA activity and multiple modifier factors in concordance with a multifactorial etiology of sBr [347].

The etiological determinants of awake bruxism are even more controversial. Several methodological demanding tasks defy the researchers [for review: 322]. The observation of aBr signs is very laborious, except for the cases of secondary Br in patients with neurological diseases or medication effects. The use of normal EMG registers faces many obstacles when clinicians intend not to alter the normal habits of the patients. Moreover, EMG signals do not distinguish Br from daily activity, or between clenching and grinding. In an EMG study, 12 denture wearers were asked to carry out some functional tasks in an attempt to prove differential jaw muscular activity in a suspected subgroup of bruxers. Suspected

bruxers exhibited transitory events of raised activity (10% Maximal Voluntary Clenching) only for this group in the masseter muscle when performing silent reading. In spite of all the other tasks not being meaningfully different, this increased activity may give orientation on bruxism diagnosis [450]. Ordinarily aBr is defined as the awareness of jaw clenching [322].

In addition, diurnal bruxers are mainly not cognizant of this parafunctional activity. *Glaros* proffer three possible explanations for this awareness, i.e., imprecise meaning of the terminology related to clenching in clinical or laboratory tests makes difficult the communication between clinician and patients; or the patients are not completely able to interpret accurately the masticatory muscles perception; or bruxism represents an adjunctive behaviour [212].

An unanswered question therefore arises when comparing diurnal and nocturnal bruxism: are they different expressions of the same condition or are they completely separate entities? Many authors set apart aBr from sBr. Some clinical factors between those conditions differ notoriously. For example, it is widely believed that stress and anxiety are risk factors of awake Br [322, 586]; contrarily, diaries collecting data of anger and stress failed to show a correlation with sleep Br [322]. However, aBr and SBr can be present simultaneously in some patients and have been allegedly reported as mutually predictor of each other [613]. In a trial with three categories of bruxer patients and a control group, awake bruxers patients were significantly dissimilar to sleep bruxers in level of anxiety and somatization. Furthermore sleep bruxers differed also significantly with the awake-sleep bruxers in every psychological outcome of the SCL-90-R. However the group of awake bruxers did not show significant differences compared to the group of awake-sleep bruxers except for the positive symptom distress index [64].

The current research about aBr principally relies on self-reported information. It is striking that the majority of those patients are not aware of their bruxism activity. In contrast, sleep bruxers stated 74% awareness of their parafunctional activity [479].

Regarding the relationship between Bruxism and TMD, contradictory literature has been published. In a 20-years follow-up of a cohort (n=402) from childhood to 25-35 years old, the prevalence of Br rose significantly each consecutive decade. The reports of grinding and clenching were related to jaw fatigue;

however, these outcomes exhibited an important fluctuation during the study [162]. In an adolescent Japanese sample, TMJ clicking was related to severe sBr defined by the occurrence of over 125 events per night [408].

Among 437 Finnish workers, a positive association was found between bruxism and orofacial pain using the RDC/TMD Axis II [16]. In another study, Br was the strongest predictor for both pain and dysfunction for people aged between 50-60 years [270]. Moreover, in a representative German sample (n=4310, age range=20-81), *Gesch* found a significant association between reports of frequent clenching and TMD symptoms [210].

Conversely, *Schierz* did not find an increased risk for TMD in adults aged 35-44 years old using anterior tooth wear as indicator of bruxism [498]. Also measuring Br by tooth wear, no relation was found between overall wear turnover and the number of muscular tender points [462]. These previous results may be questioned, due to the clinical significance of toothwear as an indicator of active Br. Critical views on the toothwear measurements include the impossibility of recognize the physiological from pathological forms, the moment of its incidence and its relation with active Br, and the unproven relation between wear facets and reports of Br [3, 366, 323, 307, 448, 589].

On the other hand, the suggested hyperactivity of the masticatory muscles has not been categorically linked to pain. *Rompré* described a sBr subgroup at high risk of developing painful symptoms, although they exhibited low frequencies of bruxism activity [479].

In a polysomnographic study, patients with sBr showed associations neither with TMD nor with muscle pain on palpation [424]. In other study with TMD patients, self-reported Br was not correlated with muscle pain on palpation. Actually no bruxers reported a significant greater number of painful joint sites than individuals who were aware of occasional or frequent bruxism activity [448].

Taken together, many authors indicate bruxism activity as risk factor for TMD [591, 354, 181], although no consensus has been reached. Challenges to resolve this topic are the confusing information of multiple studies using different definitions of TMD and bruxism; the difficulties of self-report in a transient and subconscious condition; and the validity of polemic outcomes such as tooth wear.

Further specific studies relating bruxism and myofacial pain (MP) will be analyzed in the corresponding section of MP.

1.4 Etiological theories of TMD

In spite of the multiplicity of studies in TMD, a complete comprehension of neither the causes, nor even the pathogenesis of the TMD has been elucidated. In an historical appraisal, the rationale turned from a localist mechanicist theory into a multifactorial model. In the following text a narrative review is presented of some factors which have been associated with the etiology of TMD. Many of those are essential parts of etiological theories, and some of them were lately considered as risk factors of TMD. For didactical reasons, these items are categorized into spatial-anatomical, neuromuscular and psychosocial factors, however many of them are intrinsically related with more than one category and eventually constitute the current multifactorial theory of TMD.

1.4.1 Structural factors

When the first report of TMD was published - at that time it was called Costen's Syndrome - the same author attempted to define its etiology. Erroneously *Costen* attributed to jaw impacts over the glenoid fossa the appearance of otologic symptoms [115]; however, the concept that an abnormal anatomical relationship between jaw and skull prevailed over a half century of research in TMD.

Thereafter, in Dentistry a preponderant role was assigned to the dental occlusal factors. From the orthodontic concept of a normal occlusion emerged the proposal that occlusal disharmonies were possible causes for TMD, namely the presence of occlusal interferences, discrepancies between the maximal intercuspal position (MIC) and the retruded contact position (RCP) greater than 4 mm., and loss of occlusal support, among others. This mechanicist approach as a unique etiological factor has been gradually ruled out by many researchers [106, 506]. Regardless, occlusal factors may have effects on TMD, which are poorly understood.

In fact, only weak evidence supports a relationship between occlusal interferences or premature contacts and the incidence of TMD [111].

Some authors propound that mediotrusive (balancing or non-working) interferences may modify the jaw kinematics, establishing a harmful lever arm with the fulcrum placed on the occlusal interference. As a result, the ipsilateral

molars would be located above the occlusal plane, causing compression of the ipsilateral TMJ. Contrarily to this expected effect, artificial mediotrusive contacts created on the teeth of healthy persons have shown to reduce the upward jaw movement during clenching [512, 57]. Still more, *Pahkala* declared a protective effect of balancing contacts, as the risk of clicking was reduced for persons with mediotrusive contacts in a follow-up from childhood to the age of 19 years of a cohort (n=49) [442]. On the other hand, *Fujii* did not find any association between the location of occlusal interferences and the symptomatic side of TMD patients [201]. Even, in a comprehensive literature review, *Marklund* and *Wänman* found no sufficient evidence to support any effect at all of mediotrusive interferences [367].

Experimental changes in the occlusal scheme, placing artificial mediotrusive and laterotrusive (working) interferences simulating different situations are a frequent design to study occlusal interferences. Artificial occlusal interferences in rats induced hyperalgesia which was correlated with the height of the interference. This hyperalgesia continued to exist even after the removal of the artificial interference [91]. On the contrary, artificial occlusal disturbances did not induce symptoms of TMD in a group of healthy women. After the collocation of the artificial interferences, the EMG activity in masseter muscles dropped throughout the first two days. Since the third day, the EMG activity increased gradually to reach the baseline levels of EMG activity. These observations indicated a normal ability of the stomatognathic system to adapt to occlusal disturbances in humans [385]. Actually, *Le Bell* indicated that the effect of artificial occlusal interferences depends on previous experience of TMD [325, 326].

Other occlusionist concepts have been explored searching associations with TMD. For instance, it has been claimed, that loss of occlusal support has detrimental effects on jaw stability, then predisposing to TMD. However, in a population study (n=483) symptoms of TMD did not correlate with loss of occlusal support. Indeed, the mean number of lost occlusal units was greater for participants without TMD than for those with TMD (1vs.3) [109]. In other study, partial denture wearers showed a higher prevalence of TMD signs when compared to complete denture wearers. Although 70% of these partial denture wearers exhibited occlusal alterations, no specific causes were identified that could explain this higher prevalence [32]. It is possible, that important occlusal alterations originating from the tooth loss, for example supraeruptions, are more

relevant than the condition of partial edentoulism itself. In one study, patients with posterior tooth loss having at least one occluding reference, presented a high prevalence of retruded contact position (RCP) contacts. These were associated to dental supraeruption [118]. On the other hand, RCP contacts were positively linked to higher risk of TMJ clicking in a group of young adults [100].

Regarding slides between MIC and RCP, *Pullinger* found a higher relative risk of intracapsular TMD with occlusal slides larger than 4mm [454]. However, in other study, this measurement was only weakly associated with disc displacement [106]. On the other hand, *Marklund* and *Wänman* reported a higher risk of persistent signs of TMD in patients with a lateral slide in centric greater than 1 mm [368]. Lateral slides between RCP and the intercuspal contact position (ICP) were also correlated with TMJ sounds in a 20-year follow-up of 320 Swedish individuals [354].

Up to now however, it is not possible to conclude any relation between occlusal factors and the pathogenesis of Br or TMD [111, 278, 208, 570].

Along the same line, other spatial-anatomical factors have been studied in respect of the etiology of TMD, specifically, the condylar relationship with the skull.

The natural variety of the condylar anatomy among healthy subjects defies any notion of abnormality. *Kurita* observed in a retrospective study that a reduced condylar horizontal size was related to internal derangement (ID) [312]. However, this relation may also be viable conversely, i.e. that architectural changes in the condyle may be a consequence of ID. Different relations of the mandibular condyle concentricity with the mandibular fossa in rest position and during displacements of the articular disc are usually observed [566]. One study reported a correlation between TMD and the condylar axis position measured a condylar position indicator. They inferred that this condylar position was related with occlusal factors, and therefore they declared a relationship between occlusion and TMD [119]. Sharp criticism against the relevance of the condylar position indicator has sparked after this publication [227, 332]. Currently, there is a lack of clinical validity of this kind of jaw devices as diagnostic tool. In addition, the disc position measured using arthrograms, was not linked to any evaluated occlusal factor (cuspid-protected occlusion, balancing-side contacts, deflective occlusion, horizontal and vertical overlap, among others) [476].

Finally, some authors surmise a link between condylar asymmetry and craniomandibular disorders. In one study, patients with more than 10% of condylar asymmetry showed higher pain ratings [299]. However this author failed to present evidence using no reliable outcomes and a scarce control group.

1.4.2 Neuromuscular factors

Early explanations of the muscular pain in TMD patients appealed to the Hilton's law related to an inflamed TMJ [422]. It must be considered, however that some expressions of TMD do display neither muscular pain nor clinical inflammation, and the functional jaw limitations can be originated from a disc derangement.

Intense research on neuromuscular mechanisms brought out two principal concepts, namely vicious cycle theory, and pain adaptation model. These theories endeavor to elucidate the pathogenesis of muscular pain and justify complementary therapies for pain. In respect of TMD, these and other alternative theories are briefly reviewed in this section.

The first attempts to explain muscle pain were grounded in negative effects of muscular hyperactivity, muscle spasm and overwork. The vicious cycle theory proposes that the body, facing persistent pain reacts with more pain, mutually reinforced by muscular hyperactivity. This muscle hyperactivity that is caused by some abnormal anatomical or behavioural stimuli produces dysfunction and pain, which in turn perpetuates the cycle maintaining the muscle hyperactivity [564]. In spite of this concept - closer to being considered a hypothesis, and not truly a theory - also known as the pain-spasm-pain or tension-spasm theory has been frequently recurred within literature to explain multiple musculoskeletal conditions, including TMD [383].

Bruxism has been considered a cause of muscle hyperactivity, and therefore a possible etiologic agent of TMD (s. "Bruxism as risk factor"). Nonetheless no sufficient clinical or epidemiological evidence supports this relationship [for reviews: 546, 454]. The bruxism activity does not modify substantially the daily muscle activity and is not always accompanied by pain. Actually, the maximal voluntary clenching of bruxers and not bruxers did not differ significantly [114]. In other EMG study on healthy volunteers, conducting a sustained tooth-clenching at

low intensity induced a reduction in the jaw opening. The subjects in this study denoted principally fatigue and not pain in relation with these EMG changes [545]. The fundaments of the vicious cycle theory have been gradually refuted over the time due to inconsistencies with EMG and neurobiological data [412, 540, 502, 514, 547].

As an alternative to the vicious cycle theory, *Lund* and *Stohler* developed the pain-adaptation model [349, 485]. This model is based on the protective reaction of the muscular groups exposed to persistent pain which may be dawn from a broad variety of different causes, but not hyperactivity. In case of pain, the neuromuscular regulation mechanisms command a reduction in the muscular activity on the agonist muscles, while coordinately to increase it on the antagonist muscles [349]. As a result, the force and the range of velocity of mandibular movements are reduced. This adaptation system has also been observed in patients with muscle tension headache, fibromyalgia, chronic lower back pain, and post exercise muscle soreness [566].

Several EMG studies point out the protective adaptation of the muscles when experiencing pain. In order to study this topic, simulation models of clinical pain have been satisfactorily conducted in humans by the infusion of hypertonic saline (HS) or inflammatory agents [485]. *Wang* observed that HS-induced muscle pain in masseter muscles of healthy volunteers reduced their maximum bite force and the respective EMG activity [601].

Studies showing increased amplitude of jaw-jerk reflex due to pain are in accordance to the pain adaptation model [588]. This reflex, also known as stretch or masseteric reflex has been related with the maintenance of the jaw posture [389]. It is noticeable that the jaw stretching reflex induced by glutamate injections was found more painful in women, and moreover glutamate facilitated the jaw jerk reflex in men but not in women [89]. Gender differences in the report of experimental pain indicate greater sensitivity of women [188]; however these differences are more usual in long lasting, but not in short-lasting experiments.

In spite of this, the pain adaptation model is not applicable to every situation [514]. The direct application of agonists of NMDA receptors or irritant chemicals (mustard oil) in the TMJ induced an increased EMG activity of the masticatory muscles. The authors suggested a nociceptive reflex activity of the jaw muscles [633, 88].

The possible action of central mechanisms in muscular pain is mentioned in recent studies to explain the observed changes in EMG of the masticatory muscles suffering chronic pain. In a study of EMG activity on masseter and temporalis muscles, patients with myofacial and neuropathic pain presented more EMG activity at rest position than patients with disc derangement and healthy individuals. Particularly the fact that this higher EMG activity was bilateral, independently of the location and number of painful sides, suggests that muscle activity in these patients was not a result of hyperactivity, but probably of an adaptive reaction of central origin. Other observations reinforce this tentative statement, e.g. that not only myogenous but also neuropathic pain was related to higher levels of rest EMG activity, and that bilateral myofacial pain showed higher EMG activity than the unilateral condition. Furthermore, the masseteric reflex presented bilaterally lower amplitude for these patients in comparison to healthy volunteers, although the amplitude also decreased for the group of non-symptomatic disc displacement. This fact again alludes to a central regulation [78].

In other study, healthy patients reacted to hypertonic saline solution-evoked pain reducing the muscular activity of the ipsilateral masseter during a chewing task in agonistic phase, but also decreasing the EMG activity of the contralateral side, suggesting a strain dependent phenomena or a central regulation [569].

How the muscular activity of masticatory muscles may induce the disc derangement is another question unsolved. Anatomical continuity of pterygoideos lateralis muscle with articular disc has been observed [133] bringing up a possible pathogenic role. An anatomical variant of pterigoid lateralis directly and only inserted on the disc was related to greater prevalence of disc derangements [372], and moreover, this muscle showed the highest activation during different experimental clenching tasks [504]. However, it is noteworthy that disc derangements appear frequently in asymptomatic persons, therefore not always related to TMD diagnosis [551].

Finally, some studies highlight the influence of the craniocervical postural relationship on the condylar position [429]. Nonetheless only controversial data support postural behaviors being predisposed to TMD. In a systematic review, neither myofacial pain nor disc derangements were conclusively related to head posture. The number and quality of the detected studies was scarce [434]. In

myofacial oral pain patients, the experimental forwarded position of the head exhibited greater measurements of unassisted jaw opening [315]. This forwarded position may be related to an adaptive posture [435]. *Komiyama* observed improvements on myofacial pain patients when applied a postural behavioral therapy, however the results were only comparable to the effects of cognitive behavioral therapy [302].

Experimental neck pain was not associated with tonic increases in jaw EMG activity; on the contrary jaw muscle pain can be linked to increases in neck EMG activity with the head and jaw at rest [548]. Furthermore, under physiotherapeutical examination, TMD patients showed more lifted shoulders compared to healthy volunteers, however this finding was not related to TMD severity [405]. Other studies did not determine any relation between body posture and TMJ signs [406, 596, 371]. As a conclusion, some postural differences observed between patients with TMD and healthy volunteers did not clarify the direction of causality and cannot claim clinical significance [487, 470, 261].

Pain and Neuropathic mechanisms

One important theory of pain is implicated in the current management of TMD. The gate-control theory by *Melzack* and *Wall* conceive the pain as particular pathways under reciprocal control of the CNS which are susceptible to modifications when altering stimuli [381; for review: 397]. Discussions further lead to the neuromatrix theory where the multidimensionality of pain would be explained by the interaction of “neurosignatures” patterns with their associated central zones in a genetically determined “neuromatrix”, which is susceptible to modifications through sensory inputs [382]. Pain messages directed to the brain are subjugated by the feasibility to continue their electrical wave to the superior CNS through the “gates” into the spinal cord. These gates are principally inhibitory agents that prevent this information from getting to the brain; as a consequence the stimuli are imperceptible. Different sensory nerve fibers can be activated to “close the gate” overriding the painful stimuli and neutralizing or diminishing its effects, as for example in thermal receptors excited by heating using thermal packs after muscle injury. It is remarkable that this modification of pain perception can be achieved by central regulation through descending impulses implicating psychological, cognitive and attentional factors.

Therefore, multiple therapeutical alternatives supported on this theory attempt to generate new stimulis aiming to block the painful interpretation at CNS level, for instance, acupuncture, transcutaneous electrical nerve stimulation, and some physiotherapies (cold and heat packs, massages, etc.)

Neuropathic mechanisms may be related with the pathophysiology of TMD. Although these mechanisms are not the primary concern of this review, the author introduced some concepts to better offer a global context for this condition.

A possible explanation for the transition of acute TMD into chronicity may be the central and/or peripheral sensitization. Neuronal hyperexcitability and sensitization of nociceptive trigeminal or spinal neurons in the medullary dorsal horn and other areas of central somatosensory pathways may be a consequence of prolonged noxious stimuli from body periphery. Although the exact neuropathic mechanisms involved remain unknown, it is suspected that this peripheral sensitization can be related to phenotypic changes of C-fibers, traumatic lesion of afferent fibers, ectopic impulses, or a cascade of events entangling N-methil-D-aspartate (NMDA) receptors. Probably these mechanisms perform together to induce central sensitization. However, central sensitization is able to occur also independently from peripheral stimuli when descending systems modulate pain expression.

Woda proposed a unified concept of idiopathic orofacial pain including TMD, atypical facial pain, stomatodynia, and atypical odontalgia, based on similar neuropathic mechanisms unleashed by the presence of certain risk factors. Hormones for example would act inversely as a risk factor for some of these conditions, i.e., highest prevalence for TMD are observed during reproductive ages of women; on the contrary, menopause and post-menopausal periods are often related with the other above mentioned conditions [617].

Some investigations focused on the neurological conditions of the TMD patients have not identified any evidence of central hyperactivity of the motor cortex or the reticular formation. Notwithstanding, some authors claim that the function of somatosensory system in temporomandibular pain patients is disturbed [358, 503, 514].

1.4.3 Psychosocial factors

Important works on TMD have recently highlighted the influence of altered psychological or emotional states on the prognosis and also probably the etiology of TMD. Although this relationship has not been clarified, there exists a huge support regarding the influence of depression, somatization and anxiety on the clinical manifestation of TMD.

At the end of the 70s, *Engel* started to promote the concept of biopsychosocial model, which is certainly ambiguous [172]. Principally it declares the interdependence between the psychological, social and biological components of an individual to recover and maintain health. This model has been extrapolated to chronic pain, and specifically also to TMD.

This principle illustrates some of the extensive research at the University of Washington. During the past two decades they put on the table the necessity to consider psychological parameters in the treatment of TMD. First in 1992, *Dworkin* published the Research Diagnostic Criteria (RDC/TMD) which includes one clinical dental axis and other psychological axis [158] (s. Diagnostic indexes and classification systems).

Using the Graded Chronic Pain (GCP) scale, the patients with lower scores of pain, and others with higher levels were separately subjected to two parallel randomized controlled trials (RCTs) comparing the efficacy of cognitive behavioral treatments (CBT) and the "standard" therapy [155, 159]. This GCP questionnaire combines the reports of the characteristic pain intensity (CPI) and the pain disability index. Thus it represents a multidimensional representation of pain. Lower scores I and II-low indicate no grave psychosocial impact of pain in the life of the patient. On the contrary, grades II-high, III and IV correspond to serious pain-related disabilities [156]. This latter psychological disposition interferes in the prognosis of the treatment and suggests a distinctive treatment for different types of patients according to the psychological distress level.

Actually, there is no evidence to elucidate if those psychological conditions are etiological factors or if they represent a consequence of chronic pain. Likewise, this feature concerned many other clinical chronic pain conditions, for instance chronic back pain, and fibromyalgia. Nonetheless the psychological profile between different figures of chronic pain seems not to be identical [161].

In order to study the comorbidity of major depressive disorder (MDD) and chronic pain, familial data of 107 myofacial pain patients were set over against 54 control probands. The authors tested three hypothetical situations to explain this relationship, namely chronic pain causes MDD, chronic pain is a variant of MDD, or this relationship is a methodological artifact on the selection of patients. Only the percentage of psychological affected first degree relatives of patients with myofacial pain and early onset of MDD differed with statistical meaning compared to the control group. This observation supports depression being run as a consequence of extended chronic pain conditions [148]. In other articles, these authors rejected the familial aggregation for myofacial pain after comparing familial antecedents through telephone interviews to relatives of 106 myofacial pain patients and 118 control persons without history of this condition [459]. These results contradict the alternative hypothesis that chronic pain originated from MDD when considering that depression do aggregate into families.

On the other hand, TMD is the most frequent non-odontogenic orofacial pain; however, it is not the only condition related with psychological disturbances. Idiopathic orofacial pain including atypical facial pain, stomatodynia (also called burning mouth syndrome), and atypical odontalgia, shares some subjective symptoms with TMD. For all of these conditions, psychological problems are frequently reported [616, 76, 499, 342]. One sample of about thousand chronic facial pain patients characterized by a highest prevalence for TMD (40.3%) showed that 22.7% presented a comorbid psychosomatic condition, and 3.6% psychiatric diagnoses [614].

In a study of 95 patients with myofacial pain and atypical facial pain divided into two groups according to initial self-reports of pain, psychosocial isolation and more adverse self-rated psychological status was significantly higher for patients reporting more pain. Moreover, these high initial scores of pain (VAS>5) were positively predicted by a low educational status [230]. In another study, TMD patients and atypical odontalgia patients coincided in displaying moderate to severe scores of depression, and severe levels of somatization [56]. It was suggested that teeth grinding and facial trauma are expressions of somatization, because the common incidence in patients with chronic orofacial pain and patients with idiopathic syndromes [15].

The comorbidity of TMD and psychological disturbance occurs very often, showing some patterns outlining the profiles of myogenous and arthrogenous diagnoses, and chronicity. In a population study, patients with acute TMD rated 47% anxiety disorders and 12% depression, in contrast with patients suffering chronic TMD who reported 12% depression and 34% anxiety [412, 205].

Among the patients of TMD, those suffering myogenous conditions state even more psychological imbalances. Patients with myogenic TMD present more depression and somatization than arthrogenous [412, 507, 243]. In a sample of 258 TMD patients, level of depression represented an intermediate score between the “normal” population, and both general medical outpatients and psychiatric inpatients. The depression scores of the myogenous group were higher than scores of the group with disc derangement, showing a higher share of males for lower scores, while higher scores were mainly women [53]. In another trial with 154 TMD patients, 19.5% exhibited severe depression, and 18.2% severe scores of somatization. Among these patients, those with disc derangement showed significantly lower levels of depression and somatization than those reporting combined muscular and articular symptoms [101]. Moreover, patients diagnosed with myofacial pain yielded higher decline in their oral health related-quality of life compared to patients with disc displacement and healthy volunteers [465].

Other psychological aspects highlight the complexity of the TMD patients. Concerning coping abilities, patients with dysfunctional and interpersonally distressed coping profiles exhibited higher levels of pain intensity, depression, and somatization compared to adaptive copers. According to these data, dysfunctional and distressed patients are at higher risk of developing myofacial pain, and myofacial pain combined with disc derangement, but not disc derangement only [173].

In addition, apparently stressful life events may influence the psychological profile of the TMD patients. TMD patients relative to somatoform orofacial pain and a control group, experienced personally or witnessed, before and after the age 16 years, significantly more accidents combined with illness, and more painful dental treatments [164]. Physical abuse in the historial of TMD patients was associated with higher levels of pain and depression when compared to no abuse and sexual abuse antecedents. Moreover, anxiety was significantly higher for patients who were under exposure to physical abuse than for patients

not reporting abuse, but the difference was not significant when compared to persons who suffered sexual abuse [90].

Anxiety has been associated to symptomatic evaluation of TMD in adolescents, and correlated specifically with muscle tenderness. Adolescents with a greater number of subjective pains showed increased levels of depression and anxiety [81].

In a study conducted in India within adults, other stressful events appear to be linked to TMD. These stressful events include financial stress, self-health related stress, and stress related death of a relative for myofacial pain and combined muscular and articular TMD, while job stress is a common factor for these forms of TMD and also for disc derangement [26].

A trial within a community-based female twin pairs showed that patients after experiencing post-traumatic stress disorders were more prone to suffer TMD [11].

From the high prevalence of psychological disturbances emerges the idea of multidisciplinary teams for the treatment of patients suffering chronic facial pain [198]. It is believed that the control of psychological factors will determine the success of the treatment [505].

1.5 Diagnosis of Temporomandibular Disorders

1.5.1 Diagnosis of TMD

Headaches, orofacial pain (chewing musculature, temporomandibular joint, or both), ear affections (tinnitus), and alterations of jaw biomechanics (limitation or deviation of the mandibular trajectory) are characteristical signs and symptoms of TMD that can appear in multiple combinations. The most prevalent sign and symptoms reported in a sample of patients seeking treatment were pain during chewing and during jaw opening-closing, cephalalgia in occipital and temporal area, and TMJ pain [522].

Anamnesis and clinical examination, static and dynamic functional analysis are the conventional procedures for an initial diagnosis. However, the selection of the emphasis in the diagnosis phase depends on the knowledge and beliefs of each clinician.

According to *Freesmeyer* [196], clinicians can distinguish three principal clinical findings during the initial diagnosis of TMD, namely occlusal, myogenous and arthrogenous which determine the corresponding typology of TMD.

Although the clinical significance of occlusal disturbances is controversial (s. etiological factors), clinicians use to record a detailed analysis of occlusal contacts, with attention to interferences and several malocclusions. Among other occlusal findings are attrition, abrasion, gingival recession, and other tooth substance loss. The identification of the mentioned signs is believed to represent a long-term effect of parafunctional habits such as bruxism. Nevertheless this relation is not absolute and do not denote active progression of TMD. Not every bruxer generates a TMD, nor is every TMD patient affected by a bruxism habit.

These dental and periodontal signs are to be identified during the clinical observation and static analysis of the dental occlusion. The inquiry for frequency and awareness of parafunctional habits is relevant in the anamnesis, even more than the only presence of dental facets, which have a cumulative trait. In a systematic review on attrition and abfraction, the relationship between facets and TMD were inconsistent. Four studies found no correlation; one study reported a negative correlation; and finally, four studies showed positive correlations, although one of them was restricted to some groups of TMD. Very different methodology and attrition scales prevent a conclusion on any recommendation for the TMD management [589]. Currently, the evaluation of facets lacks standardization; some references about its clinical diagnostic validity were discussed previously in the text.

Myogenic findings include muscular spasm, muscle pain, with particular attention on trigger points. The muscular symptoms are related to fatigue and muscle pain. A decisive diagnostic sign is the clinical finding of trigger points in the taut bands of masticatory muscles. Up to now, the only valid diagnostic technique for trigger points is the clinical palpation of the muscular fibers. For TMD diagnosis a standardization of muscle palpation is recommended using an algometer [593].

Figure 4: *electromyographic assessment.*

The electromyography (EMG) on masticatory muscles (fig. 4) has been widely utilized in experimental studies; nonetheless its usefulness for clinical diagnosis is open to discussion. Muscle pain can disclose minimal EMG activity, and often the timing and intensity of EMG records do not correlate with the pain intensity.

The arthrogenic findings comprise the internal derangement of the articular disc, displacement of the TMJ, and anatomic modifications of the articular disc and condyle. These findings are diagnosed through the detection of TMJ sounds such as clicking, popping, grating sounds; the anamnesis for TMJ locking and catching; and using medical image techniques, specifically the Magnetic Resonance Imaging (MRI).

Regarding the dynamic examination of the patient, the most relevant sign for TMD is the functional alteration of the mandibular kinematic. The functional analysis of the jaw trajectory is a routine examination for dental diagnosis.

Passive or assisted and active or non-assisted measurements of the jaw opening, the range of lateral and protrusive excursive movements, and the tracing of the opening-closing are registered in the clinical records. The simplest jaw motion examination consists of linear measurements of the distance between the incisal edge of the superior and inferior incisors during jaw opening using a millimeter ruler, or alternatively a vernier caliper. Normal ranges of mouth opening are considered to be between 40mm and 70 mm. *Naeije* measured a mean 51.3±7.1 mm of maximal mouth opening (MMO) in healthy volunteers without significant age or gender effects [407].

The temporomandibular opening index (TOI) aims to measure the mouth opening independent of anatomical references, which according to the authors obviates the gonial angle and ramus length as well as gender and race influence [400]. *Miller* [390, 391] introduced the TOI as a diagnostic technique to distinguish arthrogenous from myogenous TMD, stressing its technical simplicity. TOI is calculated as the centuple of the division between the negative and positive difference of the maximum voluntary mouth opening (MVMO) and the passive opening, both measured utilizing a modified Bowley gauge:

$$(TOI) \quad = \frac{Passive\ Opening - MVMO}{Passive\ Opening + MVMO}\ x\ 100$$

Sari et al. [492] found sufficient effectiveness of TOI for the evaluation of mouth opening in children, irrespective of gender and TMD symptoms. However, no sufficient evidence allows comparing TOI with the classical linear measurement in terms of their clinical relevance in the TMD diagnosis.

The development of diagnostic tests for a disease with a wide spectrum of clinical expressions and unknown etiology is a serious challenge for scientists.

In Germany, the German Society of Oral Health (Deutsche Gesellschaft für Zahn- Mund, und Kieferheilkunde, DGZMK) recommends the application of the Clinical Functional Evaluation (Klinischen Funktionsstatus, s. appendix 1 [643]) in order to diagnose TMD. This specific medical chart compiles the most important diagnostic criteria according to the German Society of Diagnostic and Treatment of TMD (Deutsche Gesellschaft für Funktionsdiagnostik und –therapie, DGFDT). It is widely used by German professionals, and complemented with the form for manual structural analysis (Manuellen Strukturanalyse, appendix 2 [643]) which summarize findings related to mandibular kinematic.

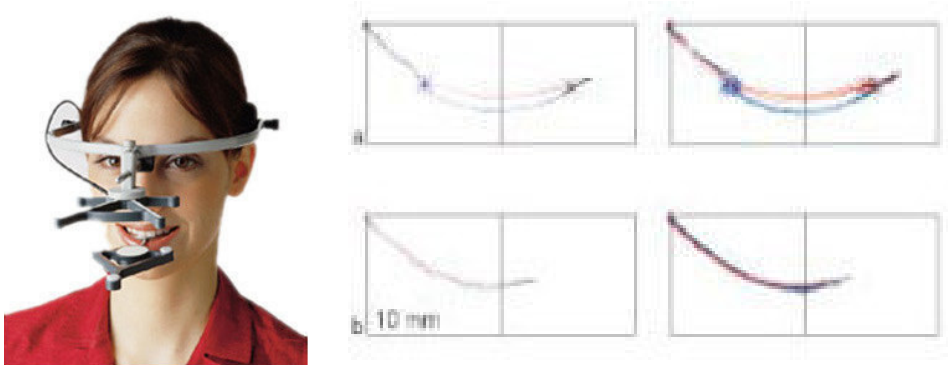

Figure 5: *jaw tracking device ARCUS Digma (left).*
Typical example of condylar movement in a patient with disc displacement (right) [61]

Other methods and instruments to analyze the mandibular kinematic include jaw electronical tracking devices (fig.5) [255, 61], electromyography (EMG), muscle stimulator systems, radiographic imaging, sonography, mandibular excursiometer, and termography among others [126]. Again, the clinical relevance is highly debatable.

Pain is the pathognomonic symptom of TMD and the principal reason for seeking treatment. At least three months of persistent pain in rest position or activity is mandatory for the diagnosis of TMD, which is considered a chronic disease. Knowledge acquired through neuroscience allows including a multidimensional appreciation of pain. The Visual Analogue Scale (VAS) and Numerical Rating Scale (NRS) for quantity estimations, and the McGill Pain Questionnaire and Multidimensional Pain Inventory (MPI) for quality appreciation of pain are examples of valid instruments to measure pain.

One important instrument to determine a multidimensional representation of pain level is the Graded Chronic Pain Scale (GCPS) [304]. This questionnaire combines the reports of the characteristic pain intensity (CPI) (mean of the actual, usual, and worst reported pain) and the pain disability or interference index. Lower scores I and II-low indicate no grave psychosocial impact of pain in the life of the patient. On the contrary, grades II-high, III and IV correspond to serious pain-related disabilities [156].

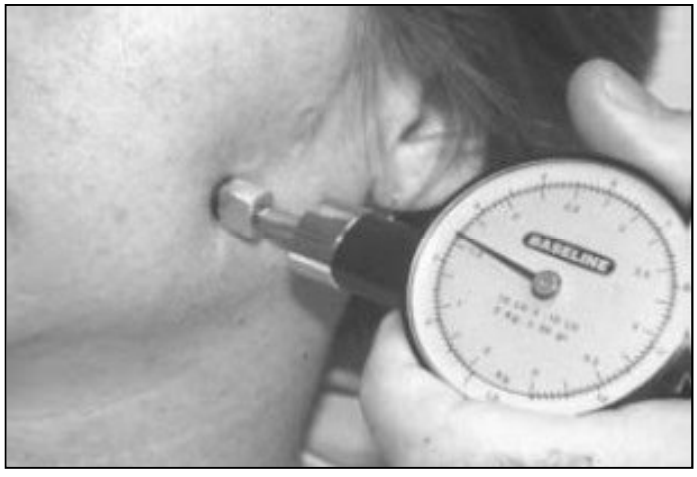

***Figure 6**: Pressure algometer to measure Pressure Pain Threshold [219]*

In clinical studies, other common measure of pain is the Pressure Pain Threshold (PPT), defined as the minimum force applied which induces pain using an algometer (fig. 6). Although it is believed PPT is less contingent on the

subjectivity of pain reporting, consecutive records in healthy patients show it is not free of such fluctuations [195].

Finally, the psychological aspects must be included in an integral approach of TMD. Psychological tests to measure depression, catastrophizing, mood, coping abilities, etc, have been often added in current studies. For example the Beck Depression Inventory Mean (BDI) and the Revised Symptom Checklist-90 (SCL-90-R) represent well known tests that had to be earlier validated for the specific population in study and are now used in combination with clinical dental examination (s. RDC/TMD). In Germany, the Hospital Anxiety and Depression Scale (HADS) [530] is recommended by the DGFDT to incorporate in the diagnostic phase, however not in the first consultation.

Additionally, for the cases of arthrogenous TMD, medical imaging is widely indicated as complementary examination. Techniques for TMJ imaging with reportedly diagnostic validity include computerized tomography (CT) [250, 327], magnetic resonance imaging (MRI) [45, 70, 388], ultrasonography [557, 582], radiography [251] and cephalometric analysis [20]. Reliable criteria have been developed for the use of CT to assess osteoarthritis, and for the use of MRI to detect the disc position and to diagnose effusion [19]. Nevertheless, imaging findings do not correlate always with the clinical findings [63, 171]. Therefore the latter are mandatory in the diagnosis of TMD

Differential diagnosis and clinical overlap

Due to the unspecific quality of signs and symptoms and the wide variety of clinical expressions, TMD may be overlapped with other disorders. Differential diagnoses are necessary for signs and symptoms also present in many other conditions like headache (chronic headache, tension-type headache, rhinosinus related-headache [216, 544,, 67, 521]), otalgia and tinnitus (primary otologic [105, 464, 445]), toothaches (pulpitic symptoms [296, 427]), facial pain (trigeminal neuralgia, atypical facial pain [102, 56, 245, 535]) muscular tenderness (chronic fatigue syndrome, fibromyalgia [220, 1]), articular pain and/or sounds (primary and secondary inflammatory articular disorders [82]).

After clinical examination, 230 TMD patients reported two zones of major complaint, i.e, masticatory muscles (68.26%) and TMJ (31.74%). 85% of these patients reported referred pain. Pain originated in the temporomandibular area

can project symptoms on extensive cranial zones including periorbital and cervical regions. Inversely, reflective pain has been reported in the craniofacial area upon palpation of cervical and shoulder muscles [619]. This zone of pain referral is also common with some frequent comorbid conditions.

Concerning frequent comorbid conditions for myofacial oral pain, two conditions are recurrent, namely fibromyalgia and chronic tension headache. Fibromyalgia can be regarded as a comorbid condition that could modify the myofacial pain condition. It is a chronic syndrome characterized by hyperalgesia and allodynia. The diagnosis is based on the painful reaction on the palpation of 11 out of 18 specific tender points. As with other psychosomatic conditions, the relation with TMD is not really understood [461].

One of the most persistent and confounding symptoms is the headache, because probably one may be intrinsically linked to the incidence of the other. Chronic tension headache is the most common type of headache. It has been postulated that an increased activity of the pericranial muscles may be responsible for painful periods. However, similar to TMD, current understanding of pain leads to pathophysiological mechanisms pointing out the central sensitization. *Fernández-de-las-Peñas et al*. described that 80% of 20 patients with unilateral migraine presented simultaneously ipsilateral myofacial trigger points. Thus myofacial disorders might initiate or to perpetuate the migraine [182]. It is noticeable, the important overlap of muscular symptoms in headache with TMD, namely temporalis, sternocleidomastoid amongst others.

In a dental examination, toothache is an important referred pain that must be included in the differential diagnosis with endodontic pathologies [427, 178]. In a sample of 230 TMD patients 11% have complained about toothaches [619].

This clinical overlap has a high impact on the treatment selection. Patients of TMD usually visit other different specialists before resorting to a dentist trained in TMD. In a retrospective study with 300 (256 women/44 men) patients seeking care from a private practice in USA, the patients reported having consulted 3.92 practitioners (range 1-26) concerning craniofacial and temporomandibular pain [515].

Disambiguation of the term Myofacial Pain

The myofascial pain syndrome (MPS) is a widespread pathology affecting the muscular tissues. The clinical characteristics are muscle stiffness and fatigue, and the pathognomonic sign is the presence of trigger points [194].

The trigger points (TrPs) are localized spots, hyperirritable, clinically palpable as a firm nodule. These areas, also called taut bands, consisting of hypercontracted extrafusal muscle fibres, which under TrPs palpation generate widen, radiating, aching pain [606]. To the present, the unique diagnostic method for trigger point is the manual palpation. Many other diagnostic techniques showed no correlation with the clinical findings, i.e. the ultrasonographic images [336], EMG, pressure algometers, thermography, etc.

The etiology of MPS is unknown; hence the uncertain approach of the medical team. Even the term of MPS is not the extent of the polemic. The recognition of this syndrome as a unique entity has been discussed [443]. Currently, the differential diagnosis embraces many non-specific musculoskeletal disorders such as fibromyalgia, fibrositis, bursitis, tendonitis, hypermobility syndromes, and fasciitis [66]. Coincidentally, these musculoskeletal diseases are more frequent in women [384].

Some general characteristics approximate the terms of myofacial oral pain and MPS, namely the presence of trigger points and some comorbid conditions. However, for the MPS there are apparently no local factors associated with it, as in the case of the myofacial oral pain since TMD can be linked to the kinematic of the temporomandibular joint, either causally or consequently [161].

In Dentistry, the myofacial pain is included as a sub-diagnosis of TMD. Discussions about the terminology continue being a topic for the experts [273]. Considering the misunderstanding produced by the ambiguity of the term, *Crockett* proposed to use myofacial instead of myofascial pain to describe the localization and not the tissue affected by this condition, and therefore to clarify the diagnosis [122]. The author agrees with this concept within the text.

Myofacial pain can be regarded as pain of muscle origin, associated with localized areas of tenderness to muscle palpation. According to the RDC/TMD, myofacial pain corresponds to muscle disorders subcategorized into two clinical groups differentiated for the mandibular opening ability (fig.4). They consider limited opening when the patient presents a measurement of the symptomless

unassisted mandibular opening <40mm, and the later assisted jaw opening reaches 5mm or less of maximal abduction.

1.5.2 Diagnostic indexes and classification systems

Helkimo Index [242] is one of the first indexes developed to diagnose the clinical conditions in TMD. This Index comprises an anamnestic and a clinical dysfunction sub-indexes. The anamnestic evaluation is based on three categories: no anamnestic dysfunction, mild symptoms, and severe symptoms; depending on the information given by the patients. Moreover, *Helkimo* defined four clinical dysfunctional degrees: 0 no dysfunction, I mild dysfunction, II moderate dysfunction, and III severe dysfunction. The parameters of clinical evaluation are five principal signs, namely, functional impairment of the TMJ, impairment of the jaw range movement, muscle pain, TMJ pain, and pain during mandibular movements. The Helkimo Index was designed especially for epidemiological surveys. Despite the attempts for its improvement, this index is currently less in demand, but not completely ruled out [69, 46, 580].

In 1986 *Fricton* and *Schiffman* put to press the Craniomandibular Index which comprises two subindexes, for instance Dysfunction and Palpation [200, 446]. The dysfunction index consists of measurements of the jaw motion, and register of TMJ sounds. The palpation index records pain at 22 points of extra- and intraoral muscles, including also some neck muscles, and TMJ upon digital pressure of 1lb per square inch. The principal goal is to measure therapeutical effects in clinical studies. Some items about jaw mobility and joint sounds showed poor reliability, although the aggregate scores by summing individual binary scored items were found highly reliable in a sample of non-patients. In other words, this index achieved agreement only in general but not in specific diagnoses [239].

The usage of a standardized classification system can reduce the confusion within the literature, helping to concentrate the dental research on the etiology of TMD, and to appeal against the superposing diagnose with other medical disciplines.

Up to now diverse classification systems and biometric procedures have been proposed. Amongst them a few are still valid and have been applied in some research articles within the last 13 years. The Wilkes' classification defines the

severity of disc displacement into five stages from asymptomatic until arthritic changes in the TMJ [529, 433, 401]. It is however not befitting to identify myogenous conditions.

At present two widely used classifications are the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) and the classification by the American Academy of Orofacial Pain (AAOP). The latter sort the patients into two groups depending on the clinical origin of the pain, namely myogenous (muscle-related TMD), and arthrogenous (joint-related TMD). The myogenous condition embraces myofacial pain, myositis, myospasm, contracture and neoplasia. The arthrogenous group consists of developmental or acquired disorders, articular disc disorders, inflammatory-immune disorders and infections, osteoarthritis, condylar dislocation, ankylosis and fracture.

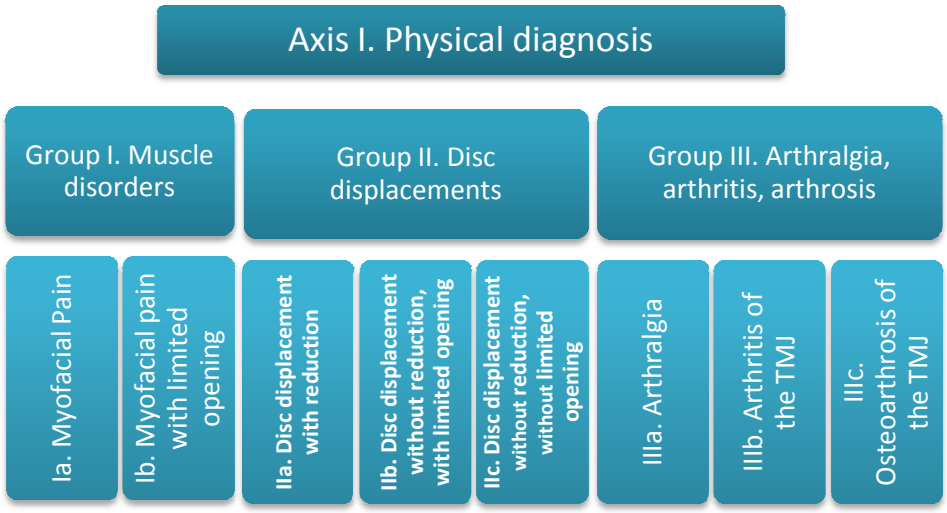

***Figure 7:**. RDC/TMD Axis I.*

The classification of Research Diagnostic Criteria for TMD (RDC/TMD) has been proposed in 1992 by *Dworkin et al*. It consists of two axes which resume the physical and psychological findings (fig.7 and fig.8).

The physical axis classified the patients in three principal groups: muscle disorders, disc displacements, and arthrogenous TMD. The behavioral axis evaluates the psychosocial dimension of pain and the psychological status of the patient.

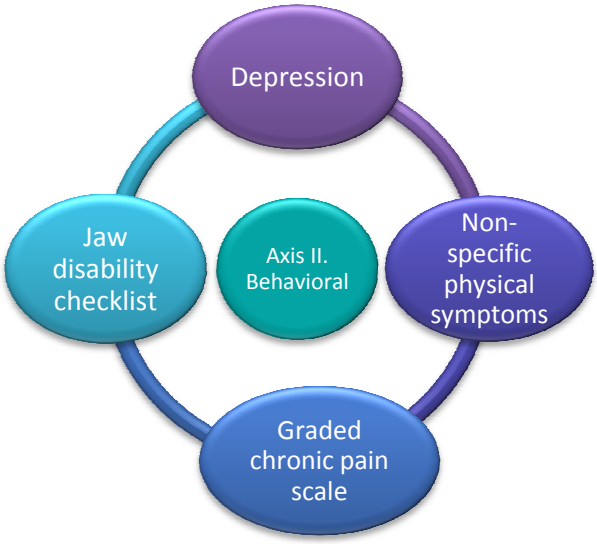

Figure 8: *RDC/TMD Axis II*

Currently the RDC/TMD is internationally recognized and available in 20 languages [260, 362, 612, 284, 274]. The translation and validation of this tool allows the unification of the criteria and facilitates the comparison of research results with other countries. Medical imaging matched the osseous diagnosis and disc displacement group [19, 364].

Nonetheless, the RDC/TMD figured out diagnoses oriented to the investigation of TMD and it is not really easy to implement in clinical practice. In order to improve the clinical applicability, the International RDC/TMD Consortium Network developed a new version, called the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). This version simplified some diagnostic procedures [431]. Other authors proposed shorter versions of the RDC/TMD [466]. In conclusion, the last decision to prefer one classification system over others depends on the clinical approach chosen by the attending professional, and especially on his/her own beliefs on how to treat TMD.

1.6 Therapeutics for TMD: reversible and irreversible treatments

Multiple possibilities have been proposed regarding the treatment of TMD. According to the maintenance of the integrity of the anatomical tissues, they are divided into reversible and irreversible therapies. Currently recognized standards of treatment for TMD prioritize reversible interventions over invasive

ones. A first diagnosed patient should be treated by conservative and reversible therapies, such as patient education, medication, intraoral splints and behavioural treatments with different results. In failure case, it should be elected the modification of the anatomical environmental through surgery or other irreversible option such as occlusal adjustment.

1.6.1 Conservative treatments

The schemes of multimodal therapies can include drugs, physiotherapy, acupuncture, Transcutaneous Electrical Neural Stimulation (TENS) etc., which are aimed to the pacification of the neuromuscular system. These treatments are normally accompanied by a dental intervention focused on the recuperation of mandibular stability. Nowadays the “usual treatment” for TMD is based on the fabrication of an oral appliance by a dentist. Many other therapeutical options have been proposed as unique intervention, but the current opinion tends to a multidisciplinary approach.

In the third part of this dissertation, the author presents a series of systematic reviews of the most frequently reported conservative treatments for myofacial pain during the last 13 years: acupuncture, low level laser therapy, pharmacological therapy, physiotherapy (jaw exercises), splint therapy and psychological interventions.

Furthermore, in the fourth chapter the results of a meta-analysis of the actual “usual treatment” for myofacial pain are reported. This meta-analysis was conducted over all the published literature until now. This “usual treatment” consists of the combination of splint therapy, self-care strategies and a pain palliative. This approach is common to other forms of TMD; however, the principal interest of this research is to evaluate the efficacy of conservative therapies for myogenous TMD (s. Part 3 and Part 4).

Other alternative treatments, mostly associated with physiotherapeutic techniques using devices and specific psychosocial interventions, were scarcely reported during the last decade (1999-2012). Nonetheless a few RCT were published in the next topics during the mentioned period, which are here briefly commented upon.

- **Transcutaneous Electrical Neural Stimulation (TENS)** (fig. 9) is the application of electrical stimulation to the skin conventionally used to induce analgesia [528]. TENS acts transmitting a continuous current, which is applied over the skin to activate nerve terminals for two different ranges (50-150 Hz for A-β terminals, and 1-10 Hz for A-δ and C terminals). The recommendation regarding the use of TENS as an instrument to reduce the pain level is to apply it in combination with physical exercises, at a treatment dose of over 60 min [286]. This symptomatic effect can be increased with the sensation of the self-control of the patient through self administration as the current TENS models are mobile. These models consist of two-channel systems, which have the advantage of stimulating two sites simultaneously, ideally with different impulses.

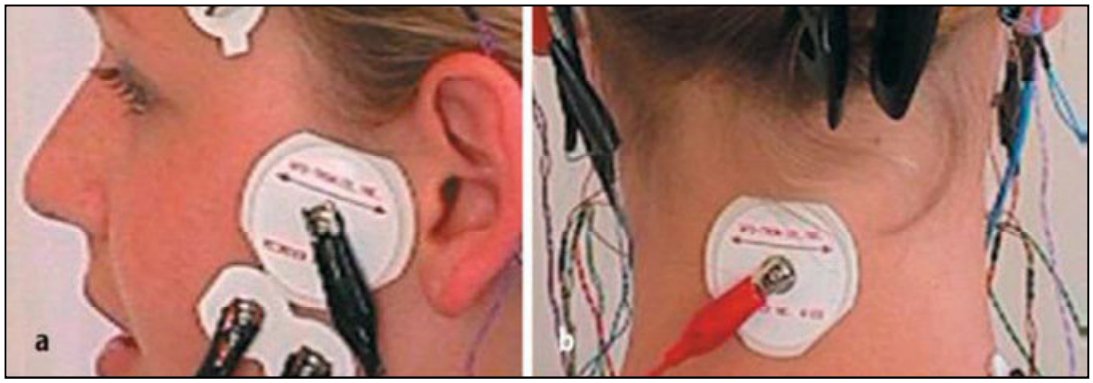

Figure 9: *Electrodes position in TENS therapy [256]*

Regarding the treatment of TMD, some researchers have demonstrated the effectiveness of TENS on pain. *Rodrigues et al.* reported the relief of pain after applying the therapy of TENS for 45 minutes, although the electromyographic activity has not been modified [478]. *Nuñez et al*. observed that TENS is effective improving the mouth opening of TMD patients, however less effective than Low-Level Laser Therapy [425].

- Another therapeutic approach is the **EMG-biofeedback**, which is based on the self-regulation of the muscular activity through graphical methods. These visualizations intend to promote the consciousness of the patients about their own physiological activity. Possible mechanisms of action of the EMG-biofeedback include the reduction of muscle activity, enhancement of the interception, and/or the strengthen of copying abilities [305]. These different

expected effects explain the fact that biofeedback can be regarded as a psychosocial intervention although it acts on the muscular component. In the case of EMG-biofeedback for TMD, the electrical signal is mostly represented as a graphic visual which describes the muscular contraction-relaxation phases.

***Figure 10**. Biofeedback devices Grindcare® (left), Bruxismustrainer MyoStab-E® (right)*

The EMG-biofeedback can be implemented using clinical monitors or giving the patients a portable device. The portable devices enhance the experience of the patient allowing a flexible use, for instance nocturnal feedback at home (fig.10). Many of these devices send out a bip sound or electrical biofeedback stimulus when the activity of the masticatory muscles increases (e.g. Bruxismustrainer MyoStaeb-E®, MyoTrac™ sEMG, Calmset Thought Technology)
In a meta-analysis, *Crider* and *Glaros* identified the EMG-Biofeedback to be efficient enough to manage TMD. Among the included clinical trials, 69% of the patients treated with EMG were successfully evaluated, against a 35% of improvement in the control cases [120].

- Some other references take account of the use of **ultrasound** [584], and **radiofrequency** [72, 30]. Scarce evidence is available for these techniques introduced by physiotherapists, which tackle principally symptomatology.

1.6.2 Continuative treatments

In cases of recurrent or relapsing symptomatology or therapy failure, the continuative therapies include occlusal adjustment, orthodontics and surgical interventions.

The two first options are intrinsically related to the occlusal relationships as etiological component. Both are currently discredited for the TMD treatment.
Other more invasive alternatives encompass pharmacological infiltrations (e.g. intraarticular injections of glucocorticoids, intramuscular injections of local anesthetic on trigger points, and injections of Botox), and surgical interventions, including arthrocentesis and implantation of temporomandibular prosthetic devices with controversial clinical consequences.
The most prevalent continuative therapies in the literature between the years 1999 and 2012 are listed below:

- Considering the occlusal factor as the principal one, some dentists indicate the technique of **occlusal adjustment**, which consists of the mechanical elimination of possible interferences or premature contacts (fig.11). *Kirveskari* and *Jämsä* observed that a systematic occlusal adjustment reduced the incidence of "spontaneous" treatment request by female patients with head and cervicobrachial pain [298]. However these results may reflect a greater awareness of the TMD condition.

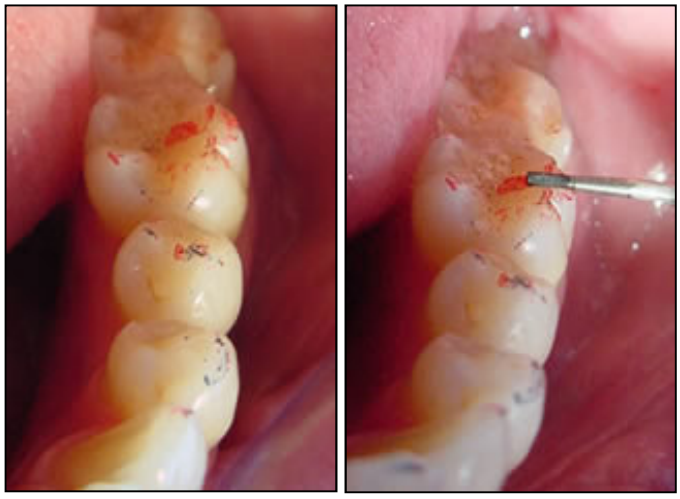

Figure 11: *Occlusal markings using marking paper to identify occlusal contacts (left). Occlusal adjustment (right)* [641]

In a non-controlled clinical study, *Torii* and *Chiwatta* reported improvement in TMD patients after applying occlusal adjustment using a muscular reference position called bite-plate induced occlusal position [561]. These results are difficult to interpret due to the unproved importance of this mentioned muscular

position, which is allegedly related with disc displacements by the same authors [560].

Moreover, results of a systematic review concluded a lack of evidence to support this therapy [301]. Currently, this method is barely applied due to the irreversible lose of dental structure.

- Similar to the occlusal adjustment, **orthodontics** for treating TMD has not proved any efficacy. In a study of 20 TMD patients, the authors reported improvement after using a Function Generating Bite, a device with double action as orthodontic corrector and occlusal appliance. However the design of the study included an inoperative control group of healthy patients and the results were not correctly interpreted [99]. According to a systematic review, up to 2010 there was no any publication of successful orthodontic treatment for TMD [351].

- The **arthrocentesis** (fig.12) is a minimal invasive surgical technique aimed to relieve pain and to improve the articular dynamic. Initially was proposed to release the articular disc and to remove adhesions between this structure and the mandibular fossa, such as closed lock of the temporomandibular joint [35] and arthritis.

The arthrocentesis is a valid and effective therapy in patients who have experimented failed conservative treatments for arthrogenous temporomandibular dysfunctions, especially disc displacement without reduction, but also it has been applied for disc displacements with reduction.

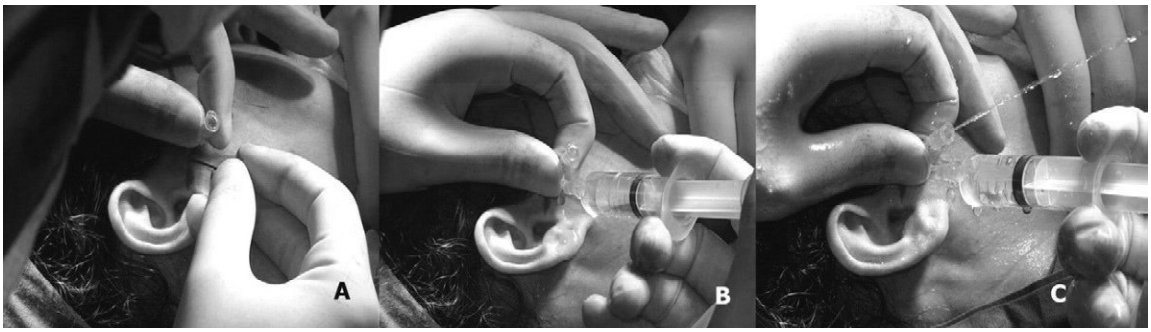

Figure 12: *Patient during arthrocentesis [146]*

For the superior joint space a needle is inserted 10 mm anterior to the tragus and 0,5mm below an imaginary line that unite the tragus with external ocular

angle. A second needle is located 20 mm anterior to the tragus and 1 mm. below the mentioned line. In this way, it is constructed a tract that allows the liquid irrigation of the intracapsular structures.

Some authors modified the original technique first described by *Nitzan* in 1991 in order to improve the efficacy or simplify the treatment of chronic closed lock; for example, using of a single needle for arthrocentesis [229]. Others suggested that the application of a higher hydraulic pressure can produce more effectiveness of arthrocentesis, particularly for severe adhesions [35]. Up to now the reported success rates of arthrocentesis are very auspicious for treatments of disc displacements without reduction [84].

Another therapeutical option for advanced cases of TMD is the **intra-articular infiltration of drugs**, such as morphine [638], corticoids, ethanolamine, hyaluronate, etc.

- **Arthroscopy** (fig.13) is a less-invasive surgical technique aimed to release the locked temporomandibular joint, first introduced in middle 70's. It is indicated for recalcitrant cases, in particular for chronic closed lock, which has been unsuccessfully treated with arthrocentesis [145].

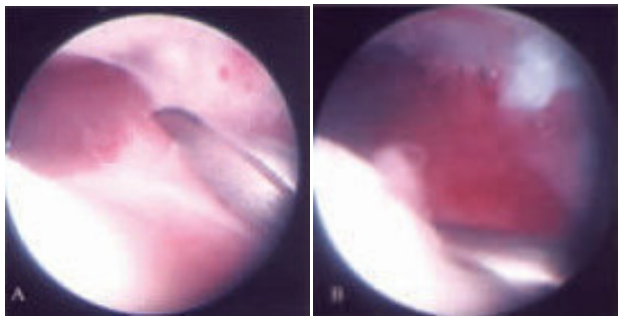

Figure 13: *Arthroscopic lysis: the adhesion was cut using a needle (left), and fibers were removed after arthroscopic lysis (right) [637]*

Positive results of this intervention have been informed in 86.7% for internal derangement of the articular disc [529]. Other study reported a long-term effective for patients treated with arthroscopic lavage and lysis in a follow-up study for 2-10 years [534]. One study reported no significant differences between arthroscopic lysis and lavage, and operative arthroscopy for the treatment of chronic closed lock [223]

The arthroscopy provides immediate pain relief, but it should be considered as a part of a multidisciplinary therapy, because its effect is principally symptomatic.

- For severe cases of TMD, different techniques of **invasive surgery** are usually indicated. Nonetheless, the results are highly variable. In 1979 *McCarty* first published a surgical technique for the **repositioning of the articular disc** of the TMJ [373]. Different techniques to achieve this goal have been developed (fig.14).

In a 20-year follow-up study of disk repositioning surgery, *Abramowicz* and *Dolwick* registered a 77% of pain reduction in comparison to the pre-interventional condition, and 94% of the patients declared an improvement in their quality of life. It is remarkable that half of the patients in this sample were still wearing splints 20 years after the surgery [7].

Despite the high success rate reported, this open surgery is nowadays an infrequently choice for TMD treatment, due to the general preference for less invasive therapies.

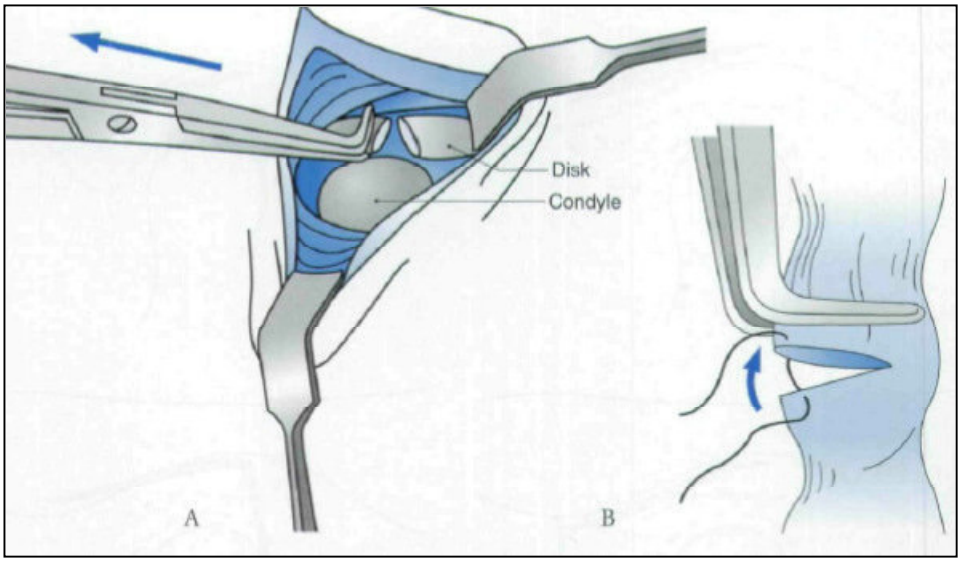

Figure 14: *one technique of disk repositioning achieved through a full-thickness excision of the posterior attachment. Sutures on posterior and lateral margins are responsible of the retention of the disc position [241].*

Other technique is the disc retrofixation - that was shown to be ineffective at least in 30% of cases, fact that tends not to be advisable for TMD treatment [266]. Even more invasive is the **TMJ implantation surgery** - that has been polemic

and partially rejected. Dramatic results were described with respect to the failure of alloplastic temporomandibular joint implants [8].

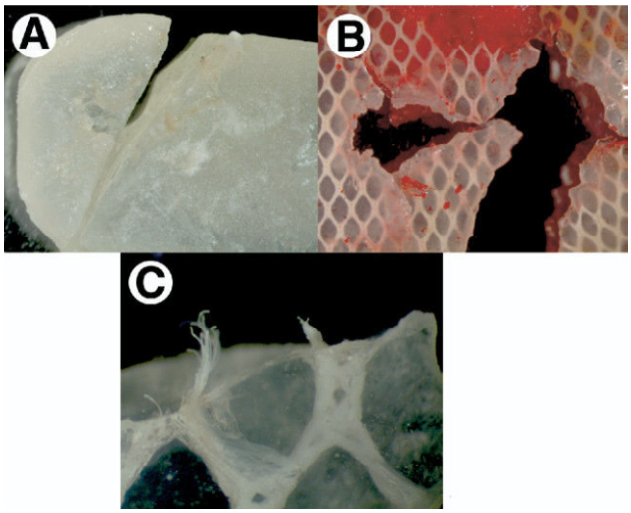

Figure 15: *TMJ Silastic implant fragments with fractures (A, B) and fiber extrusion (C) [185]*

The Proplast-Teflon and Silastic induced synovitis, lymphoadenopathy and foreign body giant reactions associated with osteoarthritis, bone resorption and immunologic dysfunction after the fragmentation of the implant because of mechanical weakness (fig. 15) [459]. *Alonso et al.* observed cadaveric material from failed Proflast-Teflon implants in comparison with discs from patients without surgery history. The presence of Proflast-Teflon wear debris produced a significant quantitative increase of the local multinucleated giant cells and lymphocytes, indicating the activity of a low-grade chronic inflammatory response concurrently with the foreign body immune response [37].
The selection of the biomaterial is essential for the prognosis of these interventions [141, 36]. Autologous grafting, such auricular cartilage, fat, or temporalis muscle have shown better outcomes and are still the subject of research.

Among all these treatments, only intramuscular infiltrations and occlusal therapies have been occasionally indicated for myofacial pain. Surgical interventions have to be considered the last therapeutical option for frequently severe recalcitrant articular cases of TMD.

PART 2

SYSTEMATIC QUALITATIV ANALYSIS AND METAANALYSIS

2.1 Basics of systemic reviews of literature and meta-analyses

In the field of Medical Research the global and prolific production of articles every year give rise to a complicated comprehension of the new knowledge. For instance, the cumulative number of scholarly research articles only for 2009 was estimated at a number over 50 million of references [268]. Medline, one of the most important databases for medicine published by the National Center for Biotechnology Information from USA, added 6,612,387 new indexed citations between 1999 and 2009 [579].

In a bibliometric study of scientific articles on orofacial pain, *Robert et al.* [475] found the major productivity in USA, Japan, UK, Germany, and Canada during 2004-2005. Since the nationality of at least one author was considered, 39.3% of the articles were made with the participation of Europeans, and 30% of American researchers. This data could exemplify the concentration of the world research activity on dentistry, principally in develop countries.

Owing to the necessity of leaking, criticizing, and resuming this multiple information from different sources and qualities, it is being recommended secondary researches, i.e. literature reviews simple or systematic, and meta-analysis.

The general objectives of literature reviews include setting new research in context; to identify core concepts, combining related results; and to guide their application on possible next original research, avoiding redundant works.

The systematic review consists of the scrutiny, comparison, and summary of different available studies that have been previously concluded.

Meta-analysis is a secondary research, which is fundamentally defined by statistic tools that reduces bias and compensates the size-effect of several studies. Since these studies are thematic and methodologically similar, their results are comparable. Actually, the multiplicity of methodologies and failures in reporting makes the meta-analysis difficult to execute. However the contribution of a meta-analysis is irrefutable.

The advantage of the meta-analysis is the possibility to resume the global concurrent evidence related to a specific theme, reducing bias, and ensuring reliability. Regrettably there exists the possibility to overestimate risks and estimations, due to the publication bias, i.e., the tendency to put out only positively statistic significant results, and the effect of the publishing selection [542].

2.2 Risk of bias

The influence of bias in small studies is inversely related with the potency of the treatment, due to the size-effect for statistical significance. This fact makes necessary using mathematic tools for detecting bias and to calculate the effect of the size of the sample.

Jüni described for clinical trial four possible biases, namely selection bias, performance bias, detection bias, and attrition bias [276].

To avoid biases in the selection of articles, *Sterne* pleads for the utilization of graphical methods, such “funnel plots”; or statistical methods, such “selection models”, and “trim and fill” [538]. Nonetheless these mathematical solutions are always limited for the reduced number of studies that are frequently collected for medical meta-analysis.

The selection of the included articles is a central decision in the meta-analysis, but also crucial is the mathematical method for the examination of the available data. Up to now, many different methods have been available to carry out meta-analysis.

The “vote counting” method is the simplest quantitative method, which is based on the relative numbers of studies demonstrating and failing to demonstrate differences or associations. As in the case of methods combining *p*-values from each study, currently the vote counting is chosen only for nonparametric

analysis of individual studies or if the results are reduced only to *p*-values; because these methods in general combine overall results, but their estimation of size-effect is very limited [9].

In medical research the most common methods to analyze dichotomous data are the relative risk (risk ratio) and the odds ratio. The risk ratio is the ratio of the risk of an event in one group in comparison to other, whereas the latter describes the ratio of odds of an event [247].The event in medical research may be the incidence of a disease given exposure status, or improvement.

The continous data in health-related studies are usually analyzed using standardized mean difference (SMD) estimation. The SMD is choosen when the pooled studies have measured the same outcomes with different instruments. The values of the outcomes become comparable through standard units.. However, when the trials assess the outcomes with the same instruments, the mean difference or difference in means can be choosen to calculate the effects in a meta-analysis [247].

The studies are susceptible to be weighted. In cases of high heterogeneity between the pooled studies, a random effect model helps to weight more equally the studies when assuming that a distribution of effects produces this heterogeneity. On the contrary, a fixed effect model assumes that these variations are proper from the study itself. The decision to apply a random or fixed effect model may modify the results of the meta-analysis, and therefore has to be considered at the interpretation of the data.

2.3 Searching consensus for reporting Systematic Reviews

In an attempt to improve the reports of qualitative and quantitative analysis of literature many groups of researchers have dedicated themselves to define guidelines during the last five decades. Only two important contributions are mentioned in this section, namely PRISMA protocol and the Handbook of the Cochrane Collaboration. The later promoted by an international independent organization called Cochrane Collaboration originated in United Kingdom; and the other by CONSORT, an independent group of American experts.

The protocol for reporting PRISMA (Preferred Reporting Items for Systematic reviews and Meta-analysis), initially called QUORUM statement (Quality of

Reporting of Meta-analysis), has been widely accepted to standardize the meta-analysis and systematic reviews [398]. The impact of this publication implied a general significant improvement in reporting meta-analysis [135].

The diagram (fig.16) shows the major steps for a correct selection of literature which is included in a systematic review or meta-analysis. After the screening of the global number of articles related to the defined topic of the research, the information will be selected according to the quality criteria established by the investigators. These criteria must be previously declared.

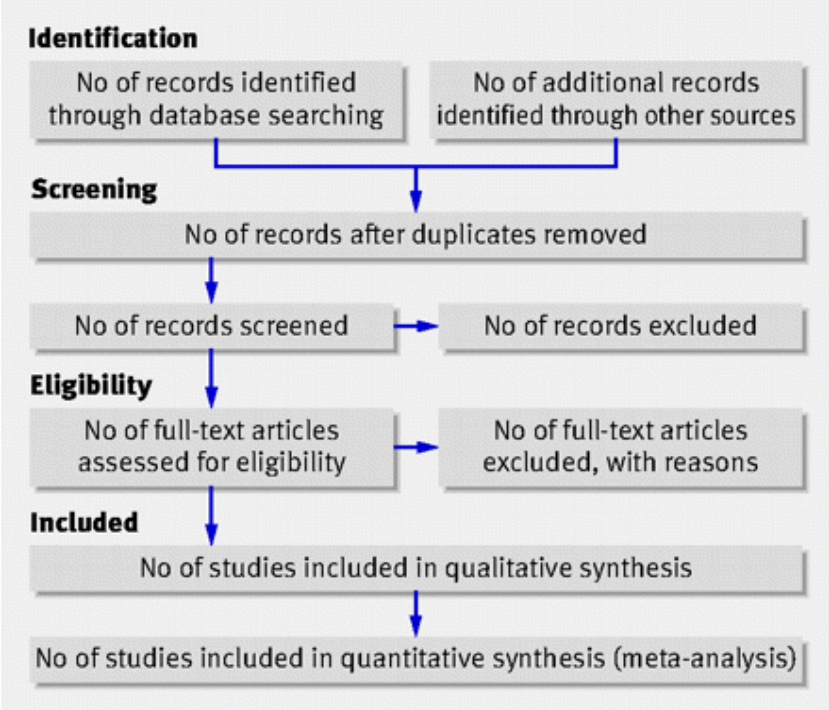

***Figure 16:**. Flow of information through the different phases of a systematic review [398]*

Regarding the structure of the report of a systematic review or meta-analysis, an article should include four principal parts, namely introduction, methods, results and discussion. An effective title defines the methodological character of the study as systematic review or meta-analysis, while the abstract should précis the content of the study. Additionally, information about possible funding must be declared. The SORT statement consists of a checklist of the aforementioned items complete with the recommendations of CONSORT (table 3).

Section/topic	#	Checklist item
TITLE		
Title	1	Identify the report as a systematic review, meta-analysis, or both.
ABSTRACT		
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
INTRODUCTION		
Rationale	3	Describe the rationale for the review in the context of what is already known.
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).
METHODS		
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
RESULTS		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).
DISCUSSION		
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
FUNDING		
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.

***Table 3**. Checklist of items to include when reporting a systematic review or metaanalysis.[399]*

Even though the effectiveness of PRISMA to improve the quality of reporting in systematic reviews is still untested, the rationale of the checklist obeys the evidence that the lack of this information already increased the risk to produce bias [337].

The contribution of the Cochrane Collaboration endorses the Evidence-based Medicine, which can be defined as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients” [484]. Particularly, the publication of the “Cochrane Handbook for Systematic Reviews” has been a decisive element for discussion about the appropriate methods to conduct a qualitative analysis. The Cochrane Collaboration addressed a multinational background and manages the biggest collection of meta-analysis. In 2011 the Cochrane Collaboration was awarded by the World Health Organization with a seat on the World Health Assembly.

In a methodological assessment using the Overview Quality Assessment Questionnaire (OQAQ), the meta-analyses published by the Cochrane Collaboration exhibited higher quality than those published in regular journals, however they were not technically infallible [136].

Guidelines on how to conduct a systematic review and meta-analysis are available with open access under the webpage handbook.cochrane.org (s. for details). The Handbook offers a compilation of information about the rationale to perform the definition of the study, the selection of the data, and their posterior analysis and report.

The next part of this thesis presents a series of systematic reviews and a meta-analysis based on the method proposed by the Cochrane Collaboration.

Initially, a common text for the series of systematic reviews comprises the description of the condition; the general objectives; and from the methods the search methods for identification of studies, and the data collection and analysis. Later, each review is composed of the description of the intervention and the possible mechanisms of action, the PRISMA study flow diagram, and the description of the characteristics of the included and excluded studies. Additionally the author reported the corresponding risk of bias using the Cochrane Collaboration’s ‘risk of bias’ tool [248], and finally of the quality assessment of the studies according to the Delphi list [594].

PART 3

CURRENT THERAPIES FOR TMD.
A SERIES OF SYSTEMATIC REVIEWS

In the following section, the author reports the results of a series of systematic reviews of the different therapeutical options for TMD during the last 13 years. The series comprises systematic reviews of acupuncture/dry needling, low level laser therapy (LLLT), physiotherapeutic treatment (jaw exercises, postural control, among others), splint therapy, and psychosocial interventions for the management of TMD.

3.1 Methods for the series of systematic reviews

A common description of the condition (a brief summary of the chapter 1), and the methods are here firstly defined for the complete series following the structure proposed by the Cochrane Collaboration using the RevMan Program. Afterwards, each therapy is reviewed separately.

Description of the condition

The temporomandibular disorder (TMD) is a complex term that involves different symptomatic definitions which affect the temporomandibular joint and the surrounding structures. Headaches, orofacial pain (chewing musculature, temporomandibular joint or both), ear affections (tinnitus, dizziness), and alterations of jaw biomechanics (limitation or deviation of the mandibular trajectory) are characteristic signs of TMD that can appear in multiple combinations.

The prevalence of TMD reported in different literature reviews fluctuate around 10% over age 18 [566, 334], with a higher percentage of affected women in the

reproductive age. The symptomatic fluctuates along the years from adolescence to adulthood [355, 162], and seems to remit spontaneously in elderly individuals [249].

De Kanter [282] estimated treatment need in Dutch population at 3.1%, while *Rugh* [482] made an estimation of 5% in United States of America, and *Micheelis* [384] estimated at 3.2% in Germany. In a meta-analysis, *Al- Jundi et al.* reported need for treatment in general adults at 15.6% for fixed effect model and at 16.2% for the random-effect model. Interestingly, the estimations were higher for studies based on clinical TMD signs than studies on self-report [33, 34].

In the early 90s *Dworkin et al.* proposed the classification of Research Diagnostic Criteria for TMD (RDC/TMD). Thus far, it had been internationally recognized, is available in 21 languages [260], and recently it had been matched with medical imaging for the osseous diagnosis and disc displacement [19, 364]. The RDC/TMD consists in two complementary axes which compile information about clinical and psychosocial findings. According to the RDC/TMD axis I, there are principally three clinical diagnoses: group I for muscle disorders, group II for disc displacements, and group III for arthralgia, arthrosis and arthritis.

Epidemiological studies showed that the higher percentage of TMD patients is diagnosed with myofacial pain [612], i.e. group I of the RDC/TMD.

Not only different diagnosis in the medical field, but also dissimilar philosophy of treatment evidence the lack of understanding of this pathology. Particularly, the etiology of TMD is still controversial. Currently a multifactorial theory has received a great support among the scientific community. This theory draws attention to the interaction of psychological, neuromuscular and oral pathogenic factors.

Multiple possibilities have been proposed regarding the treatment of TMD. According to the integrity maintenance of the anatomical tissues, they are divided on reversible and irreversible therapies. Currently, recognized standards of treatment for TMD prioritize reversible interventions over invasive ones. A first diagnosed patient should be treated by conservative and reversible therapies, such as patient education, medication, intraoral splints and behavioral treatments with different results. In failure case, it should be elected the modification of the anatomical environmental through surgery or other irreversible option such as occlusal adjustment.

Why it is important to do this review

Due to the high impact on the quality of life of the patients, and the necessity to define a therapeutic model for myofacial pain, which is the most prevalent form of TMD.

Objectives

The purpose of this series of systematic reviews is to evaluate the evidence regarding the alternative treatments for TMD during the last thirteen years (1999-2012)

Methods

a. Criteria for considering studies for this review

Types of studies

Randomized controlled clinical trials (RCTs) conducted in patients with oral myofacial pain published between 1999 until 2012. Quasi-randomized and non-randomized trials, observational studies, narrative reviews, commentaries and letters to editors were excluded.

Types of participants

Adults diagnosed with temporomandibular disorders characterized as myofacial pain, with or without concomitant arthrogenous diagnoses.

b. Search strategies for identification of studies

The study reports were identified through electronic searching of databases and hand-searching. The specific search strategies for each review are available in appendix 1-7

Electronic searches

In order to identify potential relevant studies, we searched the database MEDLINE via Pubmed. Moreover, we conducted a computerized screening of the database and university catalogs via CITAVI software*:* GBV Gemeinsamer Bibliotheksverbund, BVB Bibliotheksverbund Bayern, Hessen HeBIS, Zürich

Universität IDS, The British Library, Web of Science: BIOSIS Citation Index, WorldCat.

Keywords: details of the electronic search strategy of each systematic review are listed in other section (s. Appendix 1-7)

Filters: the Publication dates filter was activated during the electronic search from 1999 to 2012. We applied the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized trials in MEDLINE: sensitivity- maximizing version (2008 revision) PubMed format as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of "The Cochrane Handbook for Systematic Reviews of Interventions", Version 5.0.2 [updated March 2011].

Moreover, only three Languages were included: English, German and Spanish.

Searching other resources

We conducted a handsearch of the Journal of Oral Rehabilitation, Cranio: the Journal of Craniomandibular Practice, and the Journal of Dental Research to identify relevant articles.

Furthermore, the references of all relevant studies and existing reviews were screened for additional relevant publications. The references of relevant books were also screened.

c. Data processing and Analysis

All the potential relevant articles identified with the search strategy were tabulated and selected according to pre-defined selection criteria, first assessing the title and abstracts, and later in a second screening using the full text version. All the full text versions were analyzed by one reviewer, and later verified by other review author. In case of discrepancy the evaluations were discussed, with the possibility to referral to a third review author.

Each report contains one study flow diagram according to the recommendations of QUORUM/PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement. The risk of bias of the randomized clinical trials was assessed using the Cochrane Collaboration's Tool for assessing risk of bias [247]. Moreover a description of the included studies and the reasons for exclusion of the studies are tabulated (s. tables below the corresponding text review). Additionally, we chose the Delphi list, complementary to the

Collaboration's risk of bias tool, to evaluate the quality of the randomized clinical trials.

The Delphi list emanates from a consensus of 33 international experts, in order to evaluate the quality of RCTs [595]. It consists of 9 items:

1. Treatment allocation
a. Was a method of randomization performed?
b. Was the treatment allocation concealed?
2. Were the groups similar at baseline regarding the most important prognostic indicators?
3. Were the eligibility criteria specified?
4. Was the outcome assessor blinded?
5. Was the care provider blinded?
6. Was the patient blinded?
7. Were point estimates and measures of variability presented for the primary outcome measures?
8. Did the analysis include an intention-to-treat analysis?

In this series of systematic reviews, the author analyzed the effects of six different therapies at short- and long term for oral myofacial pain.

3.2 Acupuncture for Myofacial Oral Pain

Description of the intervention: Acupuncture /dry needling

The term acupuncture can be translated from Chinese as to puncture with a needle. In Asiatic countries, during centuries this methodology has been applied therapeutically for multiple affections, including chronic pain in different regions [review: 263]. In some modalities, acupuncture is combined with moxibustion, which is the burning or needling application of moxa, also known as mugwort herb [review: 328]. The traditional Chinese acupuncture point out the existence of vital energetic (Qi energy) channels, named meridians, which in the case of pain would be disrupted. The action of the acupuncture would be unblocking these channels. The fundamental principles and its correspondent diagnosis system woke some skepticism in modern Western medical systems since it was introduced in the 17th century.

Nonetheless, the World Health Organization recently has endorsed acupuncture for some conditions. *Zhang* compiled for the WHO clinical controlled studies on acupuncture in order to provide clinical evidence [636]. He found four reports up to 1998 stating acupuncture as effective as stomatognathic treatments.

Ernst and *White* [176] reported in a systematic review a comparable efficacy of acupuncture with standard treatments for TMD; however the placebo effect in the included studies was not fully rejected.

Some years later, *Goddard* [219] compared the effects of acupuncture applied in traditional acupuncture points, to dry needling inserted in not recognized acupuncture points, named sham acupuncture. There was no significant difference in the reduction of pain measured with VAS scale concerning the application of the same noxious stimulus intensity before and after the acupuncture session. In spite the small size of the sample, it was suggested that dry needling would reduce painful symptoms independently of the applied location.

Even more challenging is to isolate the effect of acupuncture when it adds up to a traditional Chinese treatment. Difficulties to design RCTs of TCM surrounded

the most essential concept of what is medicine for Western and Eastern cultures [318].

A supplementary concept of the traditional acupuncture has been investigated since the 50s. It is believed that some particular areas of the body are somatotopic fields with multiple points of correspondence to different organs; similar to a cartographic projection system. These somatotopic fields are designated Microsystems of acupuncture (fig.17).

The first described microsystem was in the auricle by *Nogier*. Some years later, in 1965, *Voll* discovered enoral acupoints in the mouth, originating the oral acupuncture [240]. The microsystem acupoints would be identifiable only when malfunctioning of the correlated organ [240].

Especially inspired in the oral acupuncture, *Gleditsch* developed a recent technique, named the very-point method, to improve the accuracy in the point detection [217].

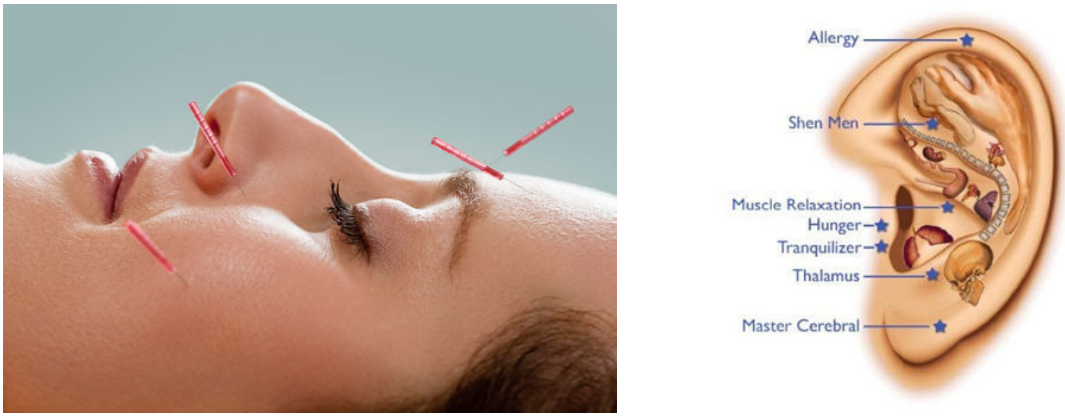

Figure 17: *Acupuncture for Orofacial Pain (left) [642]. Mycrosystem: Auricular acupuncture (right) [640]*

Allegedly, the effects of the Microsystems acupuncture are sharper than those obtained from the application of traditional acupuncture. However this action remains briefly, making necessary the stimulation of other acupoints, usually with traditional acupuncture [218].

Dry needling or intramuscular stimulation is a similar technique to the acupuncture, but they differ in the underlying principle. The needle effect would produce pain relief independent of the substance applied, when a needle is inserted directly on the trigger points. Its effectiveness has been proved for TMD patients, but there is no evidence of any advantage over other therapeutic

options [69, 562]. *Kao* suggested that some acupuncture points are also myofacial trigger points [283].

Two systematic reviews support the election of needling (acupuncture, dry needling) as an alternative method to manage the TMD [562, 124].

How the intervention might work: Acupuncture / dry needling

The effectiveness of the traditional Chinese acupuncture lies on the generation of "Deqi" sensations, which are complex of sensory perceptions described by acupuncturist as a grabbing or pulling sensation once the needle is inserted in the skin and reaches the vital channels or meridians of "Qi" energy in the body.

It has been suggested that the action of the acupuncture or dry needling is based on the gate control theory. The painful sensory input would be inhibited by another sensorial stimuli (needling) at a central nervous system level. Other authors argued that the pain modulatory pathway, called diffuse noxious inhibitory control (DNIC), may be responsible of the painful input inhibition when inducing a new sensory input (needling). In spite of the lack of evidence to explain the exact mechanism to pain relief obtained by the needling, some studies highlighted the inductive effect that acupuncture could have on the production of serotonin, endorphins and acetylcholine within the central nervous system, which would be related to its analgesic effect.

Results of the search

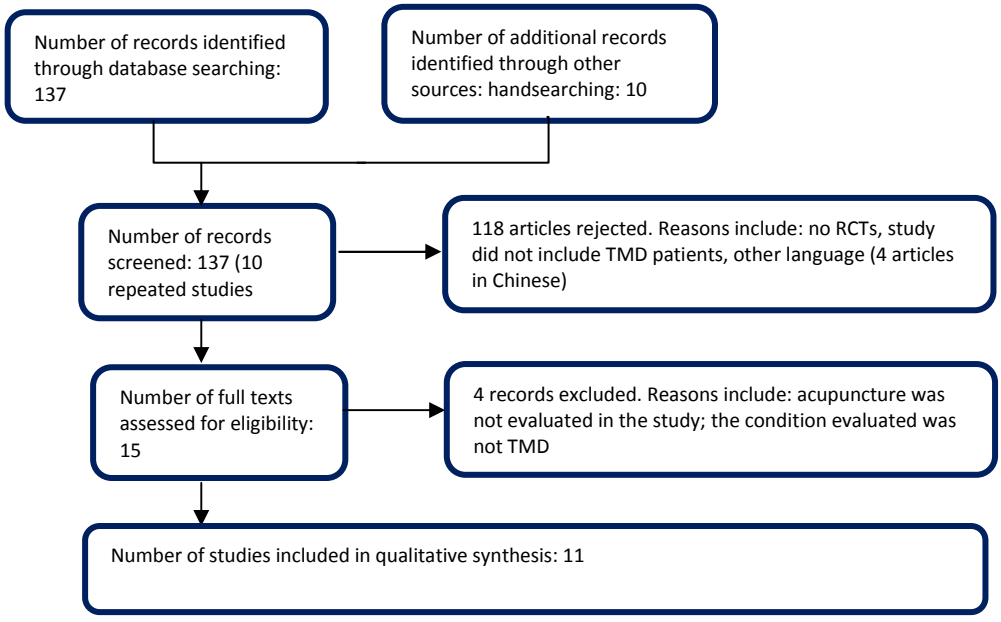

***Diagram 1**. Study flow diagram: Acupuncture for Myofacial Pain (1999-2012)*

Included studies

Eleven (11) RCTs (n=510) fulfilled the criteria for this review (diagram 1). Two reported on trigger-point acupuncture (*Fernández-Carnero 2010*, *Itoh 2012*), two on oral acupuncture with very-point method (*Schmid-Schwap 2006*, *Simma 2009*), five on traditional Chinese acupuncture (*Goddard 2002*, *Shen 2007*, *Shen 2009*, *Smith 2007*, *Vicente-Barrero 2012*) and two on traditional Chinese medicine (*Ritenbaugh 2008*, *Ritenbaugh 2012*).

Eight RCTs compared the acupuncture intervention with sham acupuncture (*Fernández-Carnero 2010*, *Goddard 2002*, *Itoh 2012*, *Schmid-Schwap 2006*, *Shen 2007*, *Shen 2009*, *Simma 2009*, *Smith 2007*); and three studies compared the intervention with other interventions: *Ritenbaugh 2008* (splint therapy and self-care strategies vs. naturopathic medicine), *Ritenbaugh 2012* (self-care strategies and CBT), and *Vicente-Barrero 2012* (decompression splint).

Six studies of acupuncture were conducted only to measure immediate effects (*Goddard 2002*, *Schmid-Schwap 2006*, *Shen 2007*; *Shen 2009*, *Simma 2009*) without follow-up. In a crossover study, *Fernández-Carnero 2010* programmed two experimental sessions at least 7 days apart, assessing outcomes 5 minutes after the intervention. Due to the study design, the total sample of these above 6 mentioned studies was analyzed. The absence of drop outs is first the consequence of the lack of follow-up period.

On the contrary, *Itoh 2012* defined a weekly treatment for five weeks, with a follow-up at 10 weeks; meanwhile *Smith 2007* conducted a treatment for 3 weeks with a follow-up one week later. Finally, *Vicente-Barrero 2012* applied 15 sessions with a follow-up at 1 month. From these studies, *Itoh 2012* reported one exclusion associated to worsening of symptoms in the acupuncture group. One patient did not complete the acupuncture sessions in the study by *Smith 2007*, however all the participants ended the control period; and the study by *Vicente-Barrero 2012* did not addressed this issue.

The studies on traditional Chinese medicine (TCM) were designed in 19 sessions with a linearly defined follow-up of 3 months to be comparable with the other interventions (*Ritenbaugh 2008*), or in 20 sessions with a follow-up at 18 weeks (*Ritenbaugh 2012*).

A stepped-care protocol was chosen for the study by *Ritenbaugh 2012*, reallocating patients in each control point according to the scores of the

outcome "worst facial pain". In this manner, patients scoring under the cut-point received self-care strategies, and patients scoring over the cut-point attended sessions of traditional Chinese medicine or psychosocial interventions. Out of 168 patients, 36 were treated only with TCM, and 37 with self-care strategies plus a second period of TCM.

It is noticeable that the study by *Smith 2007* presented an evident imbalance of the outcomes scores at baseline between groups. Thus, the group attending acupuncture had significant higher values of functional impairment and pain, whereas the control group did not show clinical significant scores for both outcomes (5.28 vs. 1.33; and 6.21 vs. 1.42 respectively for functional impairment and pain intensity).

Excluded studies

Four studies were excluded for which reasons are declared in the corresponding table (s. section Characteristics of excluded studies)

Effects of interventions

At immediate term the acupuncture in trigger points produced significant more clinical improvements compared to sham acupuncture in the study by *Fernández-Carnero 2010*. Only women (n=12) participated in this crossover trial, showing increased levels of PPT in masseter muscle and condyle, and significant greater jaw opening compared to the sham group.

Microsystems of acupuncture compared to laser-sham acupuncture did not show significant differences for the outcome of pain in the study by *Schmid-Schwap 2006*. In spite of this, the difference between VAS pain before-after treatment was significant greater for the acupuncture group. In other study on Microsystems of acupuncture compared to laser-sham acupuncture by *Simma 2009* the reduction of pain was significantly greater for the experimental group after treatment.

Acupuncture into traditional Chinese acupoints positively evaluated by *Shen 2009* for pain reduction, however no comparisons between groups were reported. Neither *Shen 2007* nor *Goddard 2002* found significant differences between real and sham acupuncture. Interestingly, in the study by *Shen 2007*,

improvements in painful symptomatology were observed in patients who believed to receive the intervention, independently if they really did.

Both studies on traditional Chinese Medicine (TCM) reported advantages over other therapeutic options at short-term. In the study by *Ritenbaugh 2008* TCM was faster and more effective at 3-months follow-up after ending treatment in reducing pain compared to splint therapy and self-care strategies. In a stepped-care study by *Ritenbaugh 2012*, TCM was superior to self-care strategies in pain relief (worst pain and characteristic facial pain) and improving pain interference. The first study has been carried out in specialized centers where the participants were previously interested in alternative medicine; in contrast the second article was based in community practice setting with recruitment through newspaper advertisements and email list-serves, showing similar positive results.

Considering the risk of bias evaluated for the studies, three trials are set apart from the others. In one study on trigger points acupuncture, high risk bias in the results of the study by *Itoh 2012* is explicitly expressed after the exclusion of a patient in the acupuncture group who experimented a worsening of the symptoms: "if the data from the patient who withdrew because of deterioration of symptoms were included in the analysis, they would have reduced the overall effect in that group."

The effect of the interventions did not reflect any changes in patients clinically “symptomless”, thus the study by *Smith 2007* did not provide relevant information for this review. Finally, the outcomes in the study by *Vicente-Barrero 2012* were insufficiently reported and no analysis between groups is available. However significant improvements were seen in the group of acupuncture treatment, but not in the splint group.

Quality of the evidence

The risk of bias of the studies according to the Cochrane Collaboration is presented in fig. 18 and fig. 19. As commented in the section above, three studies failed in critical aspects of design of clinical trials (*Itoh 2012*, *Smith 2007*, *Vicente-Barrero 2012*). As a result of the biased management of attritions by *Itoh 2012*, and the baseline imbalance of the groups in the study by *Smith 2007*, the reported outcomes became overestimated. The outcomes in the trial by *Vicente-Barrero 2012* were insufficiently reported; the general evaluation of

this trial is at high risk of bias according to the Cochrane Collaboration's risk of bias tool, and also to the Delphi list.

Some criteria of the Collaboration's risk of bias tool were not always applicable. The attrition bias was only important for those trials with follow-up, i.e. *Itoh 2012*, *Smith 2007*, *Vicente-Barrero 2012*, *Ritenbaugh 2008*, and *Ritenbaugh 2012*.

In case of studies with different therapeutic modalities, neither blinding of care provider nor blinding of patients was considered relevant, because technical difficulty. However, we expected to find blinding of participants, and desirable blinding of personnel, in those trials comparing real and sham acupuncture (*Fernández-Carnero 2010*, *Goddard 2002*, *Itoh 2012*, *Schmid-Schwap 2006*, *Shen 2007*, *Shen 2009*, *Simma 2009*, *Smith 2007*). The blinding of participants was effectively reported in 100% of the mentioned studies, but only *Simma 2009* blinded the personnel. We considered blinding of outcome assessment a key risk of bias. Only the study by *Vicente-Barrero 2012* failed in accomplishing this criterion.

It is noticeable that only two RCTs did not apply ITT analyses, which coincidentally showed other important failures (*Itoh 2012*, *Vicente-Barrero 2012*)

The general positive accomplishment of the Delphi list (table 4) was 75.67%. RCTs with score 6 or higher were 90.91% of the included studies.

Study	Allocation random-ized	Allocation conceale d	Groups similar at baseline	Inclusion criteria specified	Blind outcome assess-ment	Blinded care provider	Blinded patients	Point estimates and variability	Intention-to-treat analysis
Fernández-Carero 2010	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Goddard 2002	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Itoh 2012	Yes	Don't know	Yes	Yes	Yes	No	Yes	Yes	No
Ritenbaugh 2008	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Ritenbaugh 2012	Yes	Yes	Yes (for each allocation)	Yes	Yes	No	No	No	Yes
Schmid-Scwap 2006	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Shen 2007	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Shen 2009	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Simma 2009	Yes	Don't know	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Smith 2007	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes
Vicente-Barrero 2012	Don't know	Don't know	Don't know	Yes	No	No	No	No	No

Table 4. *Delphi list: Acupuncture for Myofacial pain*

Characteristics of studies

Characteristics of included studies

Fernández-Carnero 2010

Methods	RCT, crossover trial. Single center; two groups. Follow-up for 7 days.
Participants	12 patients: mean age=25 (SD±6) (R=20-41); 100% women; mean (months) duration of pain= 49.2 Inclusion criteria: myofacial pain diagnosis according to RDC/TMD; pain involving the masseter muscle; duration of symptoms of at least 6 months; pain on palpation of the jaw muscles; limitation of mandibular movement; weekly mean of intensity of pain ≥ 30mmVAS. Exclusion criteria: cervical trauma (whiplash injury); any systematic joint or muscle disease; needle phobia; bleeding disorders; metabolic, neurological, or vascular disease; previous acupuncture, dry needling, or physical therapy in the 6 months prior to study. Location: Spain
Interventions	Two interventions were applied: dry needling (repetitive needle insertion to a depth that provoked local twitch response (at least five responses), at a point above the taut band over the trigger point in the masseter muscle), and sham intervention (insertion of a shorter needle that did not induce any local twitch response) Group A (n=6): first session dry needling, second session sham acupuncture Group B (n=6): first session sham acupuncture, second session dry needling
Outcomes	Pressure pain threshold (PPT) over masseter muscle and mandibular condyle measured with an electronic algometer (kPa) Pain-free maximal jaw opening (mm)
Notes	“Wash out” period of minimal seven days

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:“… used a computerized randomization program to generate intervention allocation (experimental or sham)of the study population”
Allocation concealment (selection bias)	Low risk	Quote: “The order of interventions was randomized by an external clinical assistant”
Blinding of participants and personnel (performance bias)	Low risk	Participants blinded. Incomplete blinding unlikely to influence the outcomes. Quote: Neither the assessor nor the patient was aware of the real objective of the TrP dry needling”
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The preintervention outcome measures were taken by an external assessor, with randomization in the order. (…). Postintervention testing was taken 5 minutes after either intervention by the same external assessor who was blinded to the treatment allocation of the subject.
Incomplete outcome data (attrition bias)	Low risk	No drop outs.

Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Goddard 2002

Methods	RCT. Single center; two groups. No follow-up.
Participants	18 patients: mean age group A=35.49 (SD=10.63); mean age group B=34.53 (SD=6.78); 83.33% women. Inclusion criteria: age 18 or older; seeking treatment; chief complaint of frequent pain at least 4 times/week in jaw muscles for at least 12 weeks duration; myogenous pain in jaw or surrounding areas (temples, face, preauricular area, or inside the ear) at rest or during function; pain to palpation of 3 or more from 20 points in masticatory muscles for diagnosis of myofacial pain according to RDC/TMD Exclusion criteria: clinical and/or radiographic changes in TMJ (groups II and III Axis I RDC/TMD); metabolic, neurological, or vascular disease; neoplasia; psychiatric disorder; drug abuse; facial or cervical trauma; currrent therapy that cannot be stopped during the study; acupuncture during the previous 3 months. Location: USA
Interventions	Group A (n=10): Standard Acupuncture (4 needles inserted to a depth of 10-30 mm [until “chi”] at both right and left Hoku points [Large intestine 4], and at right and left Stomach 6 points, for 30 min. and twirled once for 5 sec. at the halftime session) Group B (n=8): Sham Acupuncture (control group: needles to depth of 2-4 mm, 1cm distant from Hoku and Stomach 6 points)
Outcomes	Pain intensity (VAS) at maximal tolerance to pain of a sensitive area of the masseter muscle
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “A random table was generated and subjects were assigned to 1 of 2 groups…: From correspondence: “a random table was generated by computer and subjects were assigned a number as they were recruited into the study.”
Allocation concealment (selection bias)	Low risk	Not reported in article Comments: computerized allocation with unlikely possible anticipation (s. Random sequence generation)
Blinding of participants and personnel (performance bias)	Low risk	Participants blinded, but not personnel blinded. Quote: “Subjects were blinded to group assignment.”
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The experimenter who performed the algometer readings and collected the pain ratings on a visual analog scale (…) was also blinded to the subject's group assignment”.
Incomplete outcome data (attrition bias)	Low risk	No drop outs. No follow-up
Selective reporting (reporting bias)	Low risk	Included all expected outcomes

Other bias	Low risk	Free of other bias

Itoh 2012

Methods	RCT. Single center, two parallel groups. Follow-up for 10 weeks
Participants	16 participants: 31.25% women; range age 19-24yrs. Inclusion criteria: orofacial pain lasting for 6 months or longer; Helkimo clinical dysfunction index of I or III; no acupuncture in the previous 6 months; failure to respond to the medications prescribed by a specialist. Exclusion criteria: major trauma or systemic disease; other conflicting or concurrent treatments Location: Japan
Interventions	Group A (n=7): trigger point acupuncture (5 weekly 30 min. session acupuncture at trigger points (stainless 0.2 mm 50 mm steel needles, to a depth of 5-15 mm, using the 'sparrow pecking' technique to elicit a local muscle twitch response; needles were retained for a further 15 minutes). Group B (n=8): sham acupuncture (5 weekly 30 min. session sham acupuncture with similar needles as the experimental group, but with smooth tip)
Outcomes	Pain intensity during daily activities (VAS) Maximal mouth opening (mm)
Notes	Patients were told before randomization that they would be allocated to one of two groups

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote : "by use of a computerized randomization program...used block randomisation"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	Quote: "Patients were blinded to their treatment assignment...Prior to treatment, the patients covered their eyes with an eye mask to ensure that they did not know which treatment they were receiving." Personal not blinded. This lack is unlikely to influence the outcomes
Blinding of outcome assessment (detection bias)	Low risk	Quote: "The measurements were performed by an independent investigator who was not informed about the treatment sequence or the treatment the patient received before each measurement."
Incomplete outcome data (attrition bias)	Low risk	Only one drop out for worsening symptoms in group A. Excluded from analysis
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	High risk	Reason for withdrawal was worsening of the symptoms "if the data from the patient who withdrew because of deterioration of symptoms were included in the analysis, they would have reduced the overall effect in that group."

Ritenbaugh 2008

Methods	RCT. Multicenter; three parallel groups. Follow-up for 3 months post treatment.
Participants	160 patients: mean age group A=40.1 (±8.5), mean age group B=40.6 (±9.2), mean age group C=40.5 (±9.4); 100% women; 1.88% some high school, 18.13% high school graduate, 42.5% some college, 14.38% college graduate, 23.13% postgraduate work; 86.25% White, 1.88% Black, 2.5% Asian; 3.75% Native American, 5.63% Other Inclusion criteria: women, age 25-55 yrs.; RDC/TMD diagnose; systemic co-morbidities were not excluded. Exclusion criteria: factors that would prevent full participation in the study (expecting to move, major psychiatric illness, and life-threatening medical conditions such as cancer). Location: USA
Interventions	Group A (n=50 [42]): Traditional Chinese Medicine (TCM) (19 sessions: insertion of up to 20 acupuncture needles to a depth of 0.25-1.25 inches at acupoints according to TCM diagnoses, and additionally acupoints for TMD treatment [ST7 and/or ST6, GB20 and/or GB21, *yintang*, LI4, LV3] for 20-30 min. + herbal prescription + massage [*tuina*] on the neck and shoulders + relaxation tapes) Group B (n=50 [36]): Naturopathic Medicine (practice guidelines related to naturopathic philosophy giving particular attention to the stress + 6 months of multimineral /multivitamin supplement, antioxidants, and a liver support formula + individualized nutritional, stress reduction and exercise recommendations) Group C (n=60 [50]): Specialty Care (splint + individual counseling about self-care and pain management strategies , with possible referrals for physical therapy, psychological and counseling support)
Outcomes	Based on RDC/TMD graded chronic pain scale: worst facial pain, average facial pain, effect of pain on daily activities, effect of pain on social activities.
Notes	The therapies had different durations. The outcomes at the end of treatment and 3 months post-treatment were linearly interpolated (not more than 1 month). The conditional change model was used for statistical tests

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:"Participants were assigned to their treatment groups based on the values of their balancing factors at baseline, using a design-adaptive allocation program with randomization, which was managed solely by the project biostatistician."
Allocation concealment (selection bias)	Low risk	Quote: “Project managers notified participants of their assignments”
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are unlikely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote:“all assessors were blinded to treatment assignment“.
Incomplete outcome data (attrition bias)	Low risk	Missing outcome balanced in numbers across intervention, with similar reasons for missing data

Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Ritenbaugh 2012

Methods	RCT. Multicenter; three parallel groups in sequential allocation. Follow-up for 18 weeks.
Participants	168 patients: in period 1 mean age group A=42.3 (±13.5), mean age group B=42.9 (±13.0); 86.1% women; 10.1% ≤ high school graduate, 38.0% some college, 26.6% college graduate, 25.3% postgraduate work; 83.55% White, 6.35% Nonwhite, 10.1% Unknown or not reported; 31.65% income <$25,000; 29.2% income $25,000-$50,000, 26.55% income $50,000-$100,000, 8.75% income>$100,000, 3.8% do not response income question; 10.15%duration of pain less than 1yr, 49.3%mean duration of pain 1-10 yrs, 40.55%more than 10 yrs of pain duration. In period 2 mean age group A=43.7 (±12.4), mean age group B=43.6 (±12.0); 87.05% women; 17.65% ≤ high school graduate, 27.4% some college, 23.85% college graduate, 30.95% postgraduate work; 84.65% White, 5.9% Nonwhite, 9.45% Unknown or not reported; 28.3% income <$25,000; 29.45% income $25,000-$50,000, 23.5% income $50,000-$100,000, 10.55% income>$100,000, 8.2% do not response income question; 5.9% duration of pain less than 1yr, 50.65%mean duration of pain 1-10 yrs, 43.45%more than 10 yrs of pain duration. Inclusion criteria: worst facial pain ≥ 5; age 18-70 yrs.; RDC/TMD diagnose; presence of 1 of 10 Traditional Chinese Medicine diagnoses (Liver "qi" stagnation; Liver blood "xu"; Liver "yin xu"; Liver Wind; "Qi" and blood stagnation due to injury; Heart blood "xu"; Spleen "qi xu" and Damp retention; Kidney "qi xu"; Kidney "jing xu"; Kidney "yin xu"; Kidney "yang xu"; Wind-Cold invasion); completion of the run-in (TMD class) process. Exclusion criteria: serious pathology of the temporomandibular joint (eg. infection, rheumatoid arthritis, fracture); presence of cancer or acute infection of the teeth, ears, eyes, nose, or throat; individuals undergoing active orthodontic treatment; serious psychiatric conditions; surgical implants for treatment of TMD; bleeding disorders; other life threatening conditions (e.g. cancer, uncontrolled severe hypertension); severe joint/disk displacement; use of full dentures; use of medications for which study herbs are contraindicated; current pregnancy or plans to become pregnant during active treatment Location: USA
Interventions	Group A (n=39 [36 period2]): Traditional Chinese Medicine (TCM) (20 sessions: insertion of up to 20 acupuncture needles to a depth of 0.25-1.25 inches at acupoints according to TCM diagnoses, and additionally acupoints for TMD treatment [ST7 and/or ST6, GB20 and/or GB21, "yintang", LI4, LV3] for 20-30 min. + herbal prescription + massage ["tuina"] + lifestyle and nutrition counseling) Group B (n=40 [15 period2; 20 reallocated]): Self-Care (2 in-person education/training session and 3 phone call follow-ups, which include a first period and a second period: - In Period 1: education about biopsychosocial model, TMD etiology, and self-management + guided reading with structured feedback to explore participant's understanding of and identification with major themes + relaxation and stress management training + self-monitoring of signs and symptoms + "personal TMD self-care plan" + supervised practice and reinforcement of prescribed self-care treatments + maintenance and relapse prevention of the "personal TMD self-care". - In Period 2: resiliency intervention [CBT])

	Group C (n=88 [27 period2; 56 reallocated]): Self-care. Not randomized group (report of worst pain below the cut-point [predefined as WFP = 7in the Period1, and WFP=5 in the Period2]) Cointervention: all groups received education about TMD + jaw relaxation techniques (run-in phase)
Outcomes	Based on RDC/TMD characteristic pain index (average of worst, usual and actual pain) Pain interference on daily activities, social activities, and ability to work Sleep quality (1-item summary sleep measure) Brief depression measure (PHQ2) Patient Enablement Instrument (PEI) Well being (Arizona Integrative Outcomes Scale [AIOS]) Medication (dosage and frequency) Graded Chronic Pain Score
Notes	Two groups were randomized, and other assigned according to the outcome worst facial pain (WFP): "Those with pain below the cut-point automatically went to SC and are denoted as group s" In a second period, patients of this group which remain with low levels of pain were excluded from the main analysis. Elder et al. (169) reported medication use in a subsample of this RCT.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Dynamic allocations to treatment groups at weeks 2 and 10 were accomplished by an automated design adaptive allocation procedure that sequentially balanced the SC and TCM groups with regard to WFP, gender, depression, and age as each person became eligible for allocation...Allocations were computer-generated..." Comments:This study used a sequential allocation
Allocation concealment (selection bias)	Low risk	Quote: “Dr. Aickin using a computer program to which he alone had access, thereby concealing the allocation process from all other project staff. Moreover, participants were allocated in blocks, and an undisclosed feature of the allocation program rendered accurate prediction of allocation extremely unlikely. Allocations were provided to the project managers after data collection and at the time when participants needed to be informed. Staff played no role in generating allocations nor had any potential to manage or affect the process.”"Practitioners were not aware of the specifics of the study design, nor were they aware of any details of participant assessments prior to beginning treatments."Per the design, participants could be assigned to SC because they were below the pain cut-point or could be allocated by minimization if they were above the cut-point. However, practitioners were not informed of these aspects of the design, nor of the source of individual assignments to SC.""Specific study staff had their access restricted to only the information that was needed for their roles, and they could not view other participant-related information. This permitted overall study management while maintaining blinding."

Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are unlikely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “A single trained interviewer at the Tucson call center used a computer-assisted telephone interview (CATI) system to collect all of the short-term follow-up data at weeks 2, 10, and 18, the data used for the outcome analyses presented here. Calls were recorded for random quality assurance checks. The interviewer was kept unaware of study design details and blinded to individual participant treatment assignment. Participants were encouraged not to divulge any treatment-related information to the interviewer, and the interviewer was trained to avoid any such discussions.“
Incomplete outcome data (attrition bias)	Low risk	Quote: "The analysis of the first 2 dynamic allocations presented here was undertaken on an intent-to-treat basis. Missing data were rare and were not replaced by imputation."
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Schmid-Schwap 2006

Methods	RCT. Single center; two groups. No follow-up.
Participants	23 patients: mean age group A=35±14 (R=17-59), mean age group B=40±14 (R=23-68); 100% women. Inclusion criteria: women; TMJ pain and tenderness on pressure of the craniomandibular musculature. Exclusion criteria: patients with crepitation noises suggesting arthritic changes; pretreated patients. Location: Austria
Interventions	Group A (n=11): acupuncture therapy (very-point method after palpation: intraoral infiltrated with insulin syringes 0.33mm with 0.5 ml. procaine [Maxilla retromolar, mandible retromolar, maxilla-vestibulum and mandible-vestibulum]; and extraoral points punctured with acupuncture needles for 20 minutes [Large intestine 4, small intestine 2 and 3 [hand], ear and sternum]) Group B (n=12): sham laser treatment (minilaser not activated)
Outcomes	TMJ pain (VAS) Mouth opening (mm) Muscle status Axiographic curves by a jaw track device: quality, symmetry and curve characteristics.
Notes	Patients were told about the possibility to receive a placebo. No adverse reactions

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:“ A randomization list applying blocks of 10 was prepared”

Allocation concealment (selection bias)	Low risk	Quote: “For each list entry the respective treatment (acupuncture or placebo) was written on a card and put into an opaque envelope numbered consecutively and sealed. After enrollment of a patient the envelope was opened and the respective therapy assigned.
Blinding of participants and personnel (performance bias)	Low risk	Patients blinded Quote: “Patients were blinded for treatment. Before randomization they were told that therapy might be a sham treatment”
Blinding of outcome assessment (detection bias)	Low risk	Quote: “Personnel doing the assessment was blinded for treatment.”
Incomplete outcome data (attrition bias)	Low risk	No drop-outs. No follow-up
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias.

Shen 2007

Methods	RCT. Single center; two groups. No follow-up.
Participants	15 patients: mean age total=43.1 (SD±13.6); mean age group A=45.2 (±12.3); mean age group B=41.8 (±14.9); 100% women (data from correspondence) Inclusion criteria: age 18 or older; myofacial pain syndrome of the masticatory muscles diagnosis; chronic jaw muscle pain for at least 12 weeks (at least 4 times per week); pain intensity of at least 4 on a 0- to-10 numerical scale, lasting at least 1 hour per day; pain in the jaw, temples, face, preauricular area or in the ear at rest or during function. Exclusion criteria: current use of opioids; metabolic, neurological, or vascular diseases; coagulopathies; neoplasia. Location: USA
Interventions	Group A (n=9): acupuncture (needle inserted to a depth of 10-20 mm at LI4 acupoint [left hand] for 15 min. twirled once for 5 seconds after 5 minutes into treatment) Group B (n=6): sham acupuncture (blunted needle insertion 1cm distal to LI4 acupoint without penetration)
Outcomes	Facial pain, jaw and face tightness, headache, and neck pain measured on an 11-point numeric scale (NRS). Pain at maximal tolerable mechanical pressure (VAS)
Notes	Patients were aware of the possibility to receive placebo: analysis of the perceived treatment as a predictor of the outcomes

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Treatment (ie, acupuncture or sham acupuncture) was randomly assigned to study subjects based on order of involvement.“ From correspondence: the authors use systematically a protocol of randomization based on a random table generated by computer which thereafter is assigned in order of involvement. (s. included studies Goddard 2002,

		and Shen 2009)
Allocation concealment (selection bias)	Low risk	Not reported Comments: computerized allocation (s. included study Goddard 2002)
Blinding of participants and personnel (performance bias)	Low risk	Blinding of patient, but not personnel. Quote:"… it was not possible to blind the acupuncturist to the treatment…the study subjects, who were (also) blinded to the treatment."
Blinding of outcome assessment (detection bias)	Low risk	Quote: "…an independent observer, who was blinded to the treatment, collected the data from the study subjects"
Incomplete outcome data (attrition bias)	Low risk	No drop outs. No follow-up
Selective reporting (reporting bias)	Low risk	Include the expected outcomes. Two outcomes (toothache and face tightness) were dropped because a lack of sensitivity.
Other bias	Low risk	Free of other bias

Shen 2009

Methods	RCT. Single center; two groups. No follow-up.
Participants	28 patients: mean age group A=36.94 (±13.82); mean age group B=44.83 (±11.61); 100% women. Inclusion criteria: age 18 or older; chronic myofacial pain of the jaw muscles diagnosis; pain at least 4 times a week for at least 12 weeks; average pain intensity of at least 4 on a 10-point scale, lasting at least 1 hour per day; pain in the jaw, temples, face, pre-auricular area, or in the ear at rest or during function. Exclusion criteria: pregnancy; currently use of opioids; metabolic, neurological or vascular diseases; coagulopathy; neoplasia Location: USA
Interventions	Group A (n=16): real acupuncture (needle insertion to depth of 10-20 mm into the left hand LI4 acupoint for 15 min, performing quick quarter turns of the needle for 15 sec. after 5 min. into the treatment) Group B (n=12): sham acupuncture (blunted needle without penetration at 1cm distal to LI4)
Outcomes	Jaw and facial pain; jaw and facial tightness; headache; and neck pain measured on 11-point numerical rate scales Masseter muscle pain (VAS)
Notes	The patients were aware of the possibility to receive placebo.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A list of 50 random numbers was generated by computer and subjects were assigned a number subsequently by enrollment"
Allocation concealment (selection bias)	Low risk	Quote: "Subjects with an odd number received sham acupuncture, while those with an even number received real acupuncture". Comments: systematic method for allocation used by this research team (s. included study Goddard 2002)

Blinding of participants and personnel (performance bias)	Unclear risk	Blinding of patients, but not personnel. Incomplete blinding unlikely to influence the outcomes. Quote: “To ensure blinding of both subject and experimenter, needles were inserted through … The acupuncturist was aware of the study condition, but was instructed not to speak to the patient or experimenter during the session.”
Blinding of outcome assessment (detection bias)	Low risk	Quote: “Using an analog algometer...the blinded experimenter applied pressure to the right masseter muscle….”
Incomplete outcome data (attrition bias)	Low risk	No drop outs. No follow-up
Selective reporting (reporting bias)	Low risk	Include all expected outcomes.
Other bias	Low risk	Free of other bias

Simma 2009

Methods	RCT. Single center; two groups. No follow-up.
Participants	23 patients: range age=18-64; 100% women. Inclusion criteria: women, age 18 and 65 yrs.; with dysfunction and pain in the stomatognathic system (myofacial pain and craniomandibular disorders), not receiving treatment. Location: Austria
Interventions	Group A (n=11): Acupuncture (very-point technique after palpation with superficial injection canulas at the region of maximum sensitivity [upper and low jaw retromolar, upper and lower jaw vestibulum, LI4, SI3,2, auricle, sternum, Adler Langer points, others]) Group B (n=12): Sham laser treatment (laser pen)
Outcomes	Pain (VAS), muscle pain upon palpation (4-point scale)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Patients were randomised using a computer generated random permutation list into two groups “
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	Patients and personnel blinded. Quote:“The patients were unaware of whether they were receiving verum or placebo treatment…” “Treatment was performed double blind as neither the patient nor the evaluating person were informed about the nonfunctioning laser pen”
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The physician who palpated the different muscles and registered patients’ pain scores was blinded to their verum or placebo status.“
Incomplete outcome data (attrition bias)	Low risk	No drop outs. No follow-up

Selective reporting (reporting bias)	Unclear risk	No sufficient information
Other bias	Low risk	Free of other bias

Smith 2007

Methods	RCT. Single center; two parallel groups. Treatment for 3 weeks, follow-up for 1 month.
Participants	27 patients: mean age total= 40.5 (±13.63), mean age group A=38.3 (±13.39); mean age group B=43.2 (±4.04); 88.89% women. Inclusion criteria: myofacial pain according to RDC/TMD for at least 6 months; pain on TMJ; two or more of the following diagnostic criteria: pain on palpation of the associated muscles, limitation or deviation of mandibular movement, intermitent joint sounds such clicking or cracking (but not crepitus), headache may also be present. Exclusion criteria: cervical trauma (whiplash/chronic cervical problems); systematic joint and muscle disease; metal allergy, needle phobia; bleeding disorders. Location: UK
Interventions	Group A (n=15): real Acupuncture (six treatments of needles inserted to a depth of 6-12mm bilaterally at ST7 for 20 min. tapped for 10 sec. every 5 min.) Group B (n=12): sham acupuncture (blunted needles)
Outcomes	Patient functional impairment (VAS) Pain intensity (VAS). Pain distribution Muscle and TMJ tenderness, headaches Maximal and pain-free opening (mm). Lateral movement measurement (mm). Muscle tenderness, TMJ tenderness, headaches, deviation TMJ sounds using a stereo stethoscope.
Notes	Patients were aware of the possibility to receive placebo. At the end of the study none of them believed to be treated with sham needle.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “A computerized randomization programme was used to generate group allocation of patients…”
Allocation concealment (selection bias)	Low risk	“(allocation of patients)…which were concealed in opaque envelopes by a person not involved with the study”
Blinding of participants and personnel (performance bias)	Low risk	Participants blinded, but not personnel. Quote: “Both the assessor and the patient were blinded regarding the group allocation. However, the clinician performing either intervention was aware of the group affiliation.”
Blinding of outcome assessment (detection bias)	Low risk	Quote: “All patients were reassessed…by the same blinded TMD clinician who had preformed the initial assessment”.
Incomplete outcome data (attrition bias)	Unclear risk	One patient did not attend all the treatment sessions, but the total number of the patients attended the endpoint assessment. There is no information about possible

		missing data.
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	High risk	Baseline imbalance. Sham group showed “normal” values for functional impairment, pain intensity, and mouth opening. At the second visit only 1 patient (8.33%) in the control group reported pain, instead 100% of the intervention group presented pain.

Vicente-Barrero 2012

Methods	RCT. Single center, two parallel groups. Follow-up for 30 days.
Participants	20 participants: mean age=39 (R=18-58); 85% women Inclusion criteria: Three-month or longer history of at least two of the following signs or symptoms: pain upon palpation of the temporomandibular joint (TMJ) or associated muscles of mastication, restriction or deviation of jaw movement, headache plus joint noise. Headache and joint noise were not considered when they occurred separately; legal age ;normal vertical dimension with complete or almost complete dentition. Exclusion criteria: Legal involvement such as traffic accidents, sick leave, etc.; dental malocclusion with variations from normal vertical dimension; malignancies or other diseases, especially those involving other joints; bone and/or degenerative diseases; headache associated with general organic conditions; fibromyalgia; mental disorders; previous treatment with acupuncture and/or decompression splint; previous surgery of the TMJ; orthodontic treatment at the time of the study; wearing a complete removable prosthesis; allergy to metal.
Interventions	Group A (n=10): acupuncture (15 30 min. sessions with local EX-HN5, SJ 21, GB2, SJ17, ST6 acupoints and distal LI-4, ST-36, SJ5 and GB34 acupoints) with steel 0.25 mm x 25 mm needles to a depth of 3-5mm epicutaneous. Group B (n=10): decompression splint (nocturnal wearing)
Outcomes	Mouth opening and lateral jaw-deviation (mm) Sensitivity to pressure on preauricular area, masseter muscle, temporal muscle and trapezius (pounds) Pain (VAS)
Notes	No comparison between groups.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding
Blinding of outcome assessment (detection bias)	High risk	The same operator was responsible for the examination before and after treatment.
Incomplete outcome data (attrition bias)	Unclear risk	Not sufficient information

Selective reporting (reporting bias)	High risk	Insufficient report of outcomes
Other bias	Unclear risk	Insufficient information

Footnotes

Characteristics of excluded studies

Katsoulis 2010

Reason for exclusion	Other intervention was evaluated: LLLT

Mazzetto 2007

Reason for exclusion	Other intervention was evaluated: LLLT

Venancio 2008

Reason for exclusion	Diagnosis: headache, including orofacial trigger points

Venancio 2009

Reason for exclusion	Other intervention was evaluated: Infiltration trigger points

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

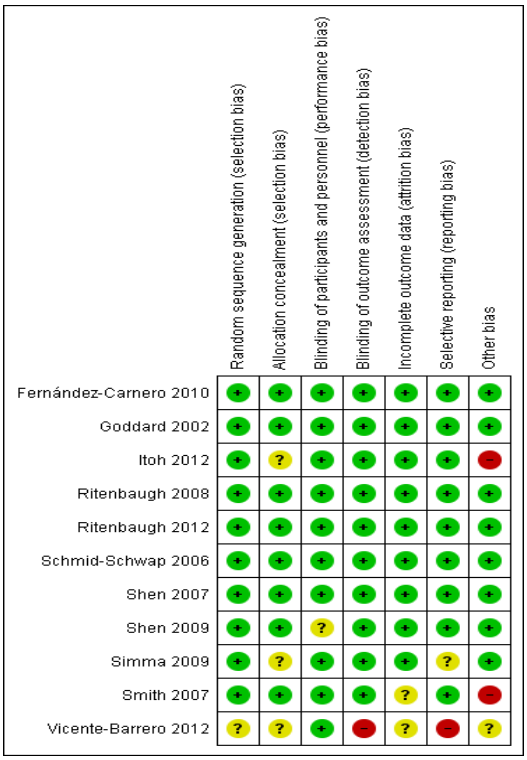

Figure 18. *Risk of bias summary: review authors' judgements about each risk of bias item for each included study*

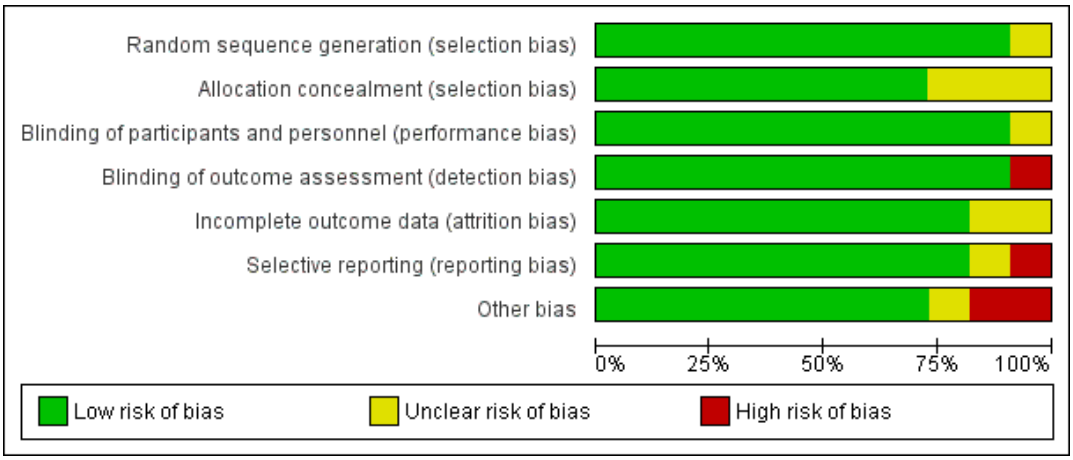

Figure 19*. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.*

References to studies: Acupuncture for Myofacial Pain

Included studies

Fernández-Carnero 2010
Fernandez-Carnero J, La Touche R, Ortega-Santiago R, Galan-del-Rio F, Pesquera J, Ge H-Y; Fernandez-de-Las-Penas C: Short-term effects of dry needling of active myofascial trigger points in the masseter muscle in patients with temporomandibular disorders. J Orofac Pain 2010;24:106-112 [PubMed: 20213036]

Goddard 2002
Goddard G, Karibe H, McNeill C, Villafuerte E: Acupuncture and sham acupuncture reduce muscle pain in myofascial pain patients. J Orofac Pain 2002;16:71-76 [PubMed: 11889662]

Itoh 2012
Itoh K, Asai S, Ohyabu H, Imai K, Kitakoji H: Effects of trigger point acupuncture treatment on temporomandibular disorders: a preliminary randomized clinical trial. J Acupunct Meridian Stud 2012;5:57-62 [PubMed: 22483183]

Ritenbaugh 2008
Ritenbaugh C, Hammerschlag R, Calabrese C, Mist S, Aickin M, Sutherland E, Leben J, Debar L, Elder C, Dworkin SF: A pilot whole systems clinical trial of traditional Chinese medicine and naturopathic medicine for the treatment of temporomandibular disorders. J Altern Complement Med 2008;14:475-487 [PubMed: 18564953]

Ritenbaugh 2012
Ritenbaugh C, Hammerschlag R, Dworkin SF, Aickin MG, Mist SD, Elder CR, Harris RE: Comparative effectiveness of traditional chinese medicine and psychosocial care in the treatment of temporomandibular disorders-associated chronic facial pain. J Pain 2012;13:1075-1089 [PubMed: 23059454]

Schmid-Schwap 2006
Schmid-Schwap M, Simma-Kletschka I, Stockner A, Sengstbratl M, Gleditsch J, Kundi M, Piehslinger E: Oral acupuncture in the therapy of craniomandibular dysfunction syndrome -- a randomized controlled trial. Wien Klin Wochenschr 2006;118:36-42 [PubMed: 16489524]

Shen 2007
Shen YF, Goddard G: The short-term effects of acupuncture on myofascial pain patients after clenching. Pain Pract 2007;7:256-264 [PubMed: 17714105]

Shen 2009
Shen YF, Younger J, Goddard G, Mackey S: Randomized clinical trial of acupuncture for myofascial pain of the jaw muscles. J Orofac Pain 2009;23:353-359 [PubMed: 19888488]

Simma 2009
Simma I, Gleditsch JM, Simma L, Piehslinger E: Immediate effects of microsystem acupuncture in patients with oromyofacial pain and craniomandibular disorders (CMD): a double-blind, placebo-controlled trial. Br Dent J 2009;207:E26 [PubMed: 19876045]

Smith 2007
Smith P, Mosscrop D, Davies S, Sloan P, Al-Ani Z: The efficacy of acupuncture in the treatment of temporomandibular joint myofascial pain: a randomised controlled trial. J Dent 2007;35:259-267 [PubMed: 17095133]

Vicente-Barrero 2012
Vicente-Barrero M, Yu-Lu S-L, Zhang B, Bocanegra-Perez S, Duran-Moreno D, Lopez-Marquez A, Knezevic M, Castellano-Navarro J-M, Liminana-Canal J-M: The efficacy of acupuncture and decompression splints in the treatment of temporomandibular joint pain-dysfunction syndrome. Med Oral Patol Oral Cir Bucal 2012 doi:10.4317/medoral.17567 [PubMed: 22549668]

Excluded studies

Katsoulis 2010
Katsoulis J, Ausfeld-Hafter B, Windecker-Getaz I, Katsoulis K, Blagojevic N, Mericske-Stern R: Laser acupuncture for myofascial pain of the masticatory muscles. A controlled pilot study. Schweiz Monatschr Zahmed 2010;120:213-225 [PubMed: 20238281]

Mazzetto 2007
Mazzetto MO, Carrasco TG, Bidinelo EF, Andrade Pizzo RCde, Mazzetto RG: Low intensity laser application in temporomandibular disorders: a phase I double-blind study. Cranio 2007;27:243-247 [PubMed: 17696035]

Venancio 2008
Venancio RdeA, Alencar FGPJ, Zamperini C: Different substances and dry-needling injections in patients with myofascial pain and headaches. Cranio 2008;26:96-103 [PubMed: 18468269]

Venancio 2009
Venancio RdeA, Alencar FGPJ, Zamperini C: Botulinum toxin, lidocaine, and dry-needling injections in patients with myofascial pain and headaches. Cranio 2009;27:46-53 [PubMed: 19241799]

3.3 Low Level Laser Therapy for Myofacial Pain

Description of the intervention: Low-level laser therapy

Laser therapy can be regarded as an experimental therapy. Applications of the laser technology in Medicine started at the early 70s. Some authors proposed that acupunctural stimulation may be provoked by low level ranges of electromagnetic radiation. That is the origin of the Low Level Laser Therapy (LLLT), also known as laser acupuncture. Nonetheless, laser therapy is not always related to acupunctural references and is often used on trigger points (fig. 20).

Despite it has been positively evaluated for some muscular [523, 232] and articular [74] conditions, contradictory reports did not discard the merely placebo effect of LLLT [125]. Even articles appealed that LLLT has no effect at all in medical treatments [203]. Discussions further about the lack of standardization of doses and techniques attempt to explain these differences on clinical outcomes.

In a systematic review, many methodological deficiencies were found in studies of LLLT for lateral epicondylitis, however some evidence of the effectivity of LLLT on trigger points was supported [104]. It has been suggested that the necessary irradiation dosage for clinical success depends on the individual characteristics of the patients [523].

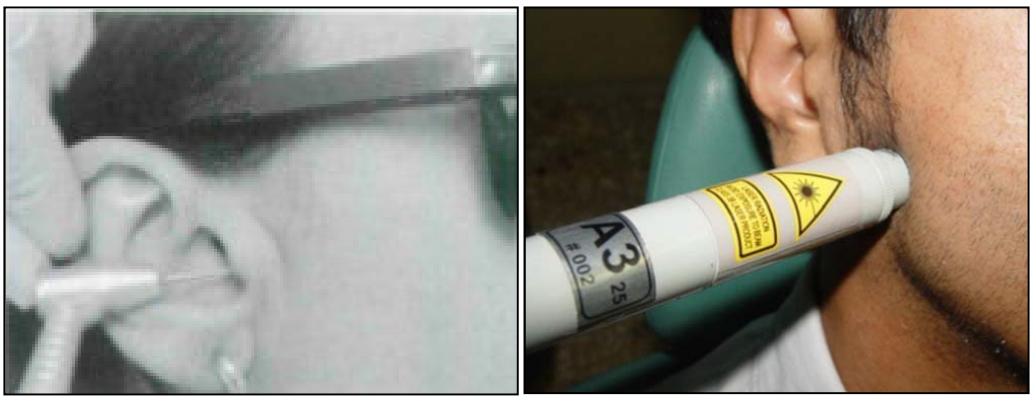

Figure 20: *laser application with the acupuncture point in the external auditive dukt toward retrodiskal region (left) [Mazzetto 2007, excluded study]. Application of Low Level Laser to the tender point in masseter muscle (right) [Shirani 2009, excluded study]*

In other study, patients with myofascial pain syndrome showed clinical improvement after LLLT treatment compared to placebo laser [233]. A

combinated therapy of stretching exercises and LLLT was reported more effective than only stretching exercises for the treatment of myofascial pain syndrome in a RCT including 62 patients [236]. In other RCT however, this combination did not result in any significant difference between groups [152]. As an adjuvant in whiplash treatment, *Bjordal* reported no effect of LLLT [23]. In the oral area, *Medeiros* reported an increase of bite strength in volunteers with masseter pain upon palpation after the application of laser therapy compared to placebo [376].

Many of the systematic reviews in LLLT reported difficulties to conclude judgments due to the poor quality of the reports [180, 510].

How the intervention might work: LLLT

Currently, the mechanism of action of the low level laser on acupunctural points is unkown. Some authors support the theory that LLLT acts over inflammatory agents reducing prostaglandins or inhibiting the cyclooxygenasa-2 [488, 519]. Alternatively some theories suggest that the action of LLLT is linked to the release of endogenous endorphins, or modifications in the conduction of nerve impulse at local level [75]. Other local effects has been suspected, for instance variations of microcirculation. In one study, however no significant changes were observed in the microcirculation of irradiated zones [572]. No conclusive evidence exists until now.

Results of the search

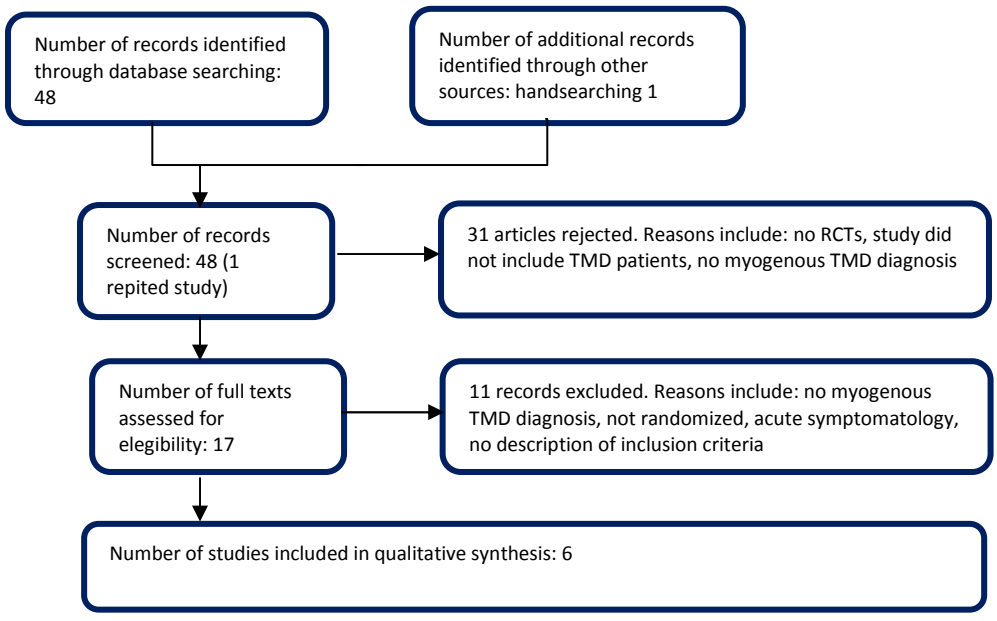

***Diagram 2**. Study flow diagram: LLLT for Myofacial Pain (1999-2012)*

Included studies

In spite of that inclusion criteria called myofascial pain syndrome, the fact of a unique localization of trigger points in masseter and temporal is closer to myofacial pain in the study by *Carrasco 2009*, and the reason to be included in this review. In the same way, the diagnostic of tendomyopathy of the masticatory muscles in the study by *Katsoulis 2010* was assimilated to myofacial pain. *Kulekcioglu 2003* distinguishes in the sample a 50% of myogenous TMD, and all the other studies included myofacial pain according to the RDC/TMD.

Six studies were included (diagram 2). All studies compared laser acupuncture with a placebo, saving the study by *Öz 2010* that compared laser therapy with splint. *Katsoulis 2010* and *Öz 2010* implemented 3 month-follow up, while all the other studies comprised a period of 1 month follow-up.

The application of laser varied in dosage and characteristics of the irradiation. Every research team indicated a regimen of twice sessions weekly, apart from the study by *Kulekcioglu 2003* where the frequency was not specified. *Carrasco 2009* tried 8 sessions of three different GaAlAs doses (25, 60, and 105 J/cm^2 at 780nm, 50, 60 and 70 mW); *Katsoulis 2010* treated with 6 sessions 40-60J at 690nm 40mW; *Kulekcioglu 2003* used 15 sessions GaAs 3J/cm^2 at 904nm 17mW; *Moraes 2012* applied 8 sessions GaAlAs 70J/cm^2 at 808nm 100mW; *Öz 2010* used 10 sessions 3J/cm^2 820nm 300mW; and *Venezian 2010* programmed 8 sessions GaAlAs780nm in two different doses (25J/cm^2 50mW, and 60J/cm^2 60mW)

LLLT was applied on trigger points or tender points (*Carrasco 2009*, *Kulekcioglu 2003*, *Moraes 2012*, *Öz 2010*, *Venezian 2010*); except for one study following the concepts of traditional Chinese Medicine (*Katsoulis 2010*)

Excluded studies

From the excluded studies (s. Characteristics of excluded studies), three studies were not randomized, seven did not match the condition criteria and one did not specify the inclusion criteria.

Effects of intervention

Apparently, an important placebo effect influenced the results of the studies on LLLT vs. Placebo. No differences between laser acupuncture and placebo were found in the study by *Carrasco 2009*. *Kulekcioglu 2003* did not observe significant differences between LLLT and placebo groups for neither pain intensity nor joint sounds; however they reported a positive improvement of jaw motion. These results were not different between the subgroups of patients of myogenous and arthrogenous TMD.

Although the EMG activity was not significantly different between laser and placebo interventions in the study by *Venezian 2010*, the betterment in the experimental group had longer effects.

Two studies did not report comparisons within groups. Improvement of the clinical parameters was reported for the laser group, and not for the placebo, however no analysis between groups was included in the study by *Moraes 2012*. Likewise, statistical comparison between groups was not reported by *Katsoulis 2010*.

The only study evaluating clinical efficiency of LLLT vs. splint (Öz 2010) showed pain relief, and jaw motion measurements enhancement in both groups similarly after treatment. However, these results represented only immediate changes in clinical outcomes.

Quality of the evidence

We registered a high heterogeneity in the laser application between studies. Most of these trials poorly described demographics of the participants and the randomization methods.

The included RCTs were mainly at unclear risk of bias (fig. 21, fig. 22). Although the relative simple design of study, blinding was not reported in all trials comparing LLLT with placebo LLLT (not active laser).

Only the trial by *Katsoulis 2010* described ITT analysis. Moreover, *Carrasco 2009* and *Venezian 2010* defined more than one placebo group, virtually identical (they supposedly differ in doses, but the laser was inactive).

The general positive accomplishment of the Delphi list (table 5) was 64.78%. RCTs with score 6 or higher were 66.67% of the included studies.

Study	Allocation random-ized	Allocation concealed	Groups similar at baseline	Inclusion criteria specified	Blind outcome assess-ment	Blinded care provider	Blinded patients	Point estimates and variability	Intention-to-treat analysis
Carrasco 2009	Yes	Don't know	Yes	Yes	Yes	Yes	Yes	Yes	Don't know
Katsoulis 2010	Yes	Don't know	Yes	Yes	Don't know	Yes	Yes	No	Yes
Kulekcioglu 2003	Yes	Don't know	Yes	Yes	Yes	No	Yes	Yes	Don't know
Moraes 2012	Yes	Don't know	Yes	Yes	Don't know	Don't know	Don't know	Yes	No
Venezian 2010	Yes	Don't know	Yes	Yes	Yes	Yes	Yes	Yes	Don't know
Öz 2010	Yes	No	Yes	Yes	Yes	No	No	Yes	No

Table 5. *Delphi list: LLLT*

Characteristics of studies

Characteristics of included studies

Carrasco 2009

Methods	RCT. Single center, 6 parallel groups. Follow-up for 30 days
Participants	60 participants (no demographic information of the sample) Inclusion criteria: complaint of MPS, presenting only one active trigger point in the anterior masseter and anterior temporal muscles combination of regional pain, reference pain pattern, palpable taut band, presence of trigger point, motion restriction and induction of pain with pressure on a trigger point Exclusion criteria: systemic, infectious, inflammatory, tumoral, cardiopulmonary, and psychiatric diseases that posed a conflict to the clinical picture; TMD disk derangement patients; multiple active or latent trigger points; patients regularly taking medicines such as analgesics, anti-inflammatory and/or psychotropic medication, use of an occlusal splint, or other treatment for pain control Location: Brazil
Interventions	Group A (n=10):LLLT at 25J/cm^2 Group B (n=10):LLLT at 60J/cm^2 Group C (n=10):LLLT at 105J/cm^2 Group D (n=10):placebo LLLT at 25J/cm^2 Group E (n=10):placebo LLLT at 60J/cm^2 Group F (n=10):placebo LLLT at 105J/cm^2 Continous application of laser twice a week for four weeks (GaAlAs, 780nm wavelength, continuous mode 50, 60 and 70 mW)
Outcomes	Pain intensity (VAS)
Notes	Diagnosis of myofascial pain according to Travell, that is, for the presence of trigger points.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...were randomly allocated..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	Quote:"...conducted in a double-blind fashion. Two identical probes (one active and one that emitted no radiation) were used. Neither the clinician nor the subject knew whether or not the diode used was active or not until the data analysis was complete"
Blinding of outcome assessment (detection bias)	Low risk	Assessor blinded. Quote: " One examiner, blinded to the test and control groups, evaluated all patients."
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes

Other bias	High risk	Three groups are equal (three inactive placebo of different energy parameters). No demographic information

Katsoulis 2010

Methods	RCT. Single center; three parallel groups. Follow-up for 3 months.
Participants	11 patients: mean age=33 (range=22-61); mean age group A=38 (range=30-61), mean age group B=34 (range=30-38), mean age group C=28 (22-41); 90.91% women. Inclusion criteria: age between 18 and 70 years, tendomyopathy of the masticatory musculature diagnosis according to RDC/TMD, pain intensity ≥ 30 en VAS during the last 14 days. Exclusion criteria: arthropathy of TMJ, arthralgia oderTMJ arthritis; facial fractures, acute dental problems; history of ear, nose or throat illnesses, general medical complications requiring treatment, psychological illness, clinical diagnosis of rheumatoid arthritis, current pregnancy, abuse ofantipsychotic medication, drugs or alcohol or ongoing other treatment for TMD (myoarthropathy) Location: Switzerland
Interventions	Group A (n=4): neither randomized, nor blinded group for verum Group B (n=3): randomized and blinded verum Group C (n=4): randomized and blinded placebo
Outcomes	Maximum pain intensity
Notes	Group A excluded from analysis in the present review

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "(patients) were split by means of block randomization to (2 groups)"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	Participants and personnel blinded for group B and C. Quote: "The examining dentists were blinded as to the group assignment of the group 2 and 3 patients. The patients wore special protective glasses during the therapy so they could not see whether the laser appliance was switched on or not."
Blinding of outcome assessment (detection bias)	Unclear risk	Blinding of outcome assessment not reported
Incomplete outcome data (attrition bias)	Low risk	No drop outs
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Other bias	Low risk	Free of other bias

Kulekcioglu 2003

Methods	RCT. Single center, two parallel groups. Follow-up for 1 month
Participants	35 participants: mean age= 37.0 ±12.3 years (R=20-59); 80%women Inclusion criteria: orofacial pain, TMJ sounds, limited mouth opening, or TMJ locking Exclusion criteria: congenital abnormality, concomitant inflammatory or neoplastic conditions, and those with a recent history of acute trauma or any form of treatment within the last month Location: Turkey
Interventions	Group A (n=20): LLLT (15 sessions of LLLT + program consisting of range of motion exercises, stretching exercises and postural training) Group B (n=15): placebo (laser not turned on + program of range of motion exercises, stretching exercises and postural training)
Outcomes	Pain intensity (VAS) Number of tender points and joint sounds Maximal active and passive mouth opening, right and left lateral jaw motion (mm)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were then randomly assigned..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Unclear risk	Participants but not personnel were blinded. Incomplete blinding
Blinding of outcome assessment (detection bias)	Low risk	Quote: "All patients were evaluated by the first investigator who was blinded to treatment groups."
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Moraes 2012

Methods	RCT. Single center, two parallel groups. Treatment 4 weeks, 30 days follow-up
Participants	21 participants: mean age=27.76 (10.44); 90.48%women; 85.71% had high school degree Inclusion criteria: reporting pain in the facial region at a minimum intensity of 5 on the visual analog scale (VAS) with a duration of at least 3 months; diagnosis of myofascial pain according to the RDC/TMD (axis I, groups Ia and Ib) Exclusion criteria: patients missing more than two posterior teeth (excluding third molars); presence of full denture or removable partial denture; presence of gross malocclusion (overbite and overjet greater than 6 mm, unilateral or anterior crossbite, or a discrepancy of centric relation to maximum intercuspation greater than 5 mm); patients undergoing orthodontic treatment, medical treatment, or on medication for pain.

	Location: Brazil
Interventions	Group A (n=14 [12]): LLLT (GaAlAs, 808nm, 100mW, 70J/cm^2, continuous mode, applied at the trigger points of the anterior temporal and masseter muscles [previously noted in the clinical assessment]: five points were applied on each muscle, four forming a cross and one a central point) Group B (n=12 [9]): laser placebo
Outcomes	Pain intensity (VAS) PPT in anterior temporal and masseter muscles (kg/cm^2) Chewing test
Notes	All patients were instructed not to take nonsteroidal antiinflammatory drugs or other analgesics during treatment and follow-up.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote:"...randomly divided into two groups"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Unclear risk	Quote:" A blind study was conducted..."
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed
Incomplete outcome data (attrition bias)	Unclear risk	Missing data balanced across groups
Selective reporting (reporting bias)	Unclear risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Venezian 2010

Methods	RCT. Single center, four parallel groups. 1 month treatment, follow-up for 30 days.
Participants	48 participants: mean age=41.58 yrs; 89.58%women Inclusion criteria: diagnose of myofascial pain (group I.a and I.b) according to RDC/TMD; ages ranged 18-60yrs. Exclusion criteria: chronic analgesic, anti-inflammatory, or psychotropic medication users, and also if they used an occlusal splint or had previously had any other kind of TMD treatment. Location: Brazil
Interventions	8 sessions of GaAlAs Low Level Laser 780 nm. infrared was applied continuous and punctually within the upper, medium, and lower thirds of the masseter muscle (three points) and the anterior region of the temporal muscle (one point). Group A (n=12): dose of 25 J/cm2 (50mW for 20 seconds) Group B (n=12): dose of 25 J/cm2 (50mW for 20 seconds, placebo treatment: not active) Group C (n=12): dose of 60 J/cm2 (60mW for 40 seconds) Group D (n=12): dose of 60 J/cm2 (60mW for 40 seconds placebo treatment, not active)
Outcomes	EMG Pain to palpation (VAS)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:"...using a computer program"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	Quote: "The researcher who performed the applications and evaluations was not aware of which point applied was the effective or the placebo dose. The patients did not know which group they had been assigned to."
Blinding of outcome assessment (detection bias)	Low risk	Quote: "The points were identified only after finishing the data collection."
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	High risk	Two groups are equal (two inactive placebo of different energy parameters).

Öz 2010

Methods	RCT. Single center; two parallel groups. Follow-up for 3 months.
Participants	40 (out of 44) patients: mean age group A=31.25 (±8.23), mean age group B=34.52 (±12.82); 85.0% women; mean years of education group A=9.65 (±5.40); mean years of education group B=10.50 (±3.84); mean months of pain duration group A=8.2 (±2.40), mean months of pain duration group B=7.9 (±2.58) Inclusion criteria: age 18-60 yrs.; diagnosis of MP according to RDC/TMD; natural posterior occlusion; no TMD treatment in the last 2 years; orofacial pain for at least 6 months. Exclusion criteria: TMD of articular origin diagnosed according to RDC/TMD; psychiatric disorders, heart disease, or pacemakers; removable prosthesis or the absence of more than 1 tooth per quadrant and major malocclusion (anterior open bite, unilaterally maxillary lingual crossbite, overjet >6 mm, slide from the retruded contact position to intercuspal position >2 mm); pregnancy; symptoms that could be caused by other orofacial region diseases (eg, toothache, neuralgia, migraine); treatment or any medication for headache or bruxism during the previous year; local skin infections over the masseter muscle. Location: Turkey
Interventions	Group A (n=20): low-level laser therapy onto trigger points to 3J/cm^2 by applying 300-mW output power for 10 sec. from a 2-mm distance; 2 times per week for 10 sessions Group B (n=20): stabilization splint according to Okeson (401), full time wearing for 3 months
Outcomes	Pain location. Pressure pain threshold (PPT) Functional examination according to RDC/TMD: Active and passive mouth opening, muscle tenderness to palpation
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "…were randomly divided into 2 groups. Patients in both groups were age and sex matched" "Randomization was done before the arrangements for the date of therapy were made." From correspondence: "they (the patients) were divided in two groups; men and women. Then men were grouped into 2 age groups; 18-40, 40-60. The men in 18-40 group were divided into two groups; one group for study, one group for control. By every procedure, the groups were equal in number and the selection was done on the name list randomly: first name for one group, second for the other. Each division was performed by different prosthodontists in the department. The names of them were not included in the study. The same procedure was done for the women group, too".
Allocation concealment (selection bias)	High risk	Quote: "Selection bias was considered through a defined and concealed randomization process" From correspondence: alternation (s. random sequence generation)
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. This lack is not likely to influence the outcomes
Blinding of outcome assessment (detection bias)	Low risk	Quote: "Assessment of the participants was conducted by an independent investigator who was unaware of the study."
Incomplete outcome data (attrition bias)	Low risk	"As treated" analysis. Balanced groups
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Other bias	Unclear risk	The evaluation of the interventions differed in time due to different treatment duration

Footnotes

Characteristics of excluded studies

Carrasco 2008

Reason for exclusion	No myogenous TMD patients

Cetiner 2006

Reason for exclusion	Not randomized

da Cunha 2008

Reason for exclusion	No description of inclusion criteria

Emshoff 2008

Reason for exclusion	No myogenous TMD patients

Fikácková 2007

Reason for exclusion	Not randomized

Kato 2006

Reason for exclusion	Not randomized

Lassemi 2008

Reason for exclusion	No description of inclusion criteria

Marini 2010

Reason for exclusion	No myogenous TMD patients

Mazzetto 2007

Reason for exclusion	No myogenous TMD patients

Mazzetto 2010

Reason for exclusion	No myogenous TMD patients

Shirani 2009

Reason for exclusion	No TMD (acute pain)

Venancio 2005

Reason for exclusion	No myogenous TMD patients

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

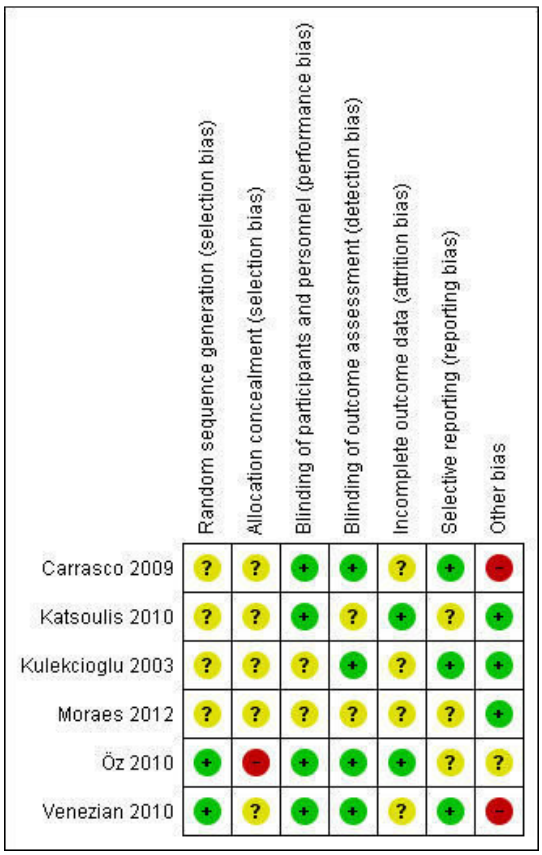

***Figure 21**. Risk of bias summary: review authors' judgements about each risk of bias item for each included study*

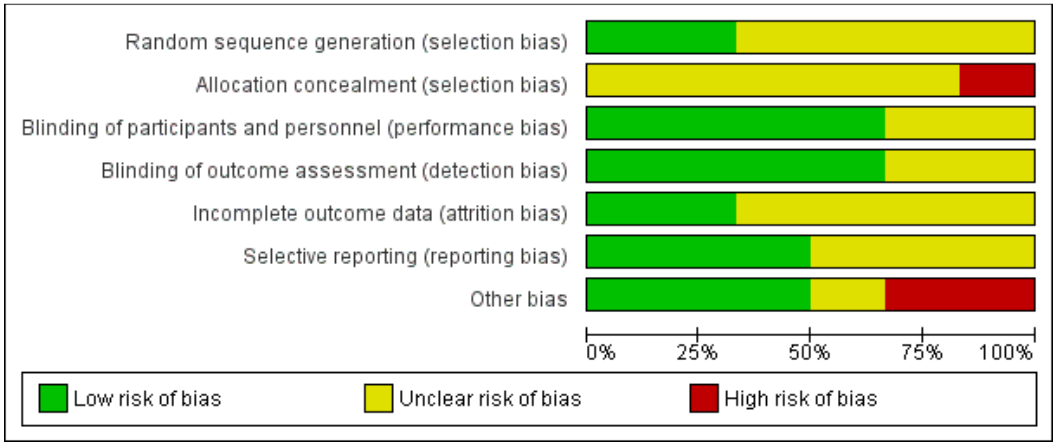

***Figure 22.** Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.*

References to studies: Low-Level Laser Therapy for Myofacial Pain

Included studies

Carrasco 2009
Carrasco TG, Guerisoli LDC, Guerisoli DMZ, Mazzetto MO: Evaluation of low intensity laser therapy in myofascial pain syndrome. Cranio 2009;27:243-247 [PubMed: 19891258]

Katsoulis 2010
Katsoulis J, Ausfeld-Hafter B, Windecker-Getaz I, Katsoulis K, Blagojevic N, Mericske-Stern R: Laser acupuncture for myofascial pain of the masticatory muscles. A controlled pilot study. Schweiz Monatschr Zahmed 2010;120:213-225 [PubMed: 20238281]

Kulekcioglu 2003
Kulekcioglu S, Sivrioglu K, Ozcan O, Parlak M: Effectiveness of low-level laser therapy in temporomandibular disorder. Scand J Rheumatol 2003;32:114-118 [PubMed: 12737331]

Moraes 2012
Moraes Maia MLde, Ribeiro MAG, Maia LGM, Stuginski-Barbosa J, Costa YM, Porporatti AL, Conti PCR, Bonjardim LR: Evaluation of low-level laser therapy effectiveness on the pain and masticatory performance of patients with myofascial pain. Lasers Med Sci published online Nov 2012 doi: 10.1007/s10103-012-1228-7 [PubMed: 23143142]

Öz 2010
Oz S, Gokcen-Rohlig B, Saruhanoglu A, Tuncer EB: Management of myofascial pain: low-level laser therapy versus occlusal splints. J Craniofac Surg 2010;21:1722-1728 [Pubmed: 21119408]

Venezian 2010
Venezian GC, da Silva MAMR, Mazzetto RG, Mazzetto MO: Low level laser effects on pain to palpation and electromyographic activity in TMD patients: a double-blind, randomized, placebo-controlled study. Cranio 2010;28:84-91 [PubMed: 20491229]

Excluded studies

Carrasco 2008
Carrasco TG, Mazzetto MO, Mazzetto RG, Mestriner W: Low intensity laser therapy in temporomandibular disorder: a phase II double-blind study. Cranio 2008;26:274-281 [PubMed: 19004308]

Cetiner 2006
Cetiner,S, Kahraman SA, Yucetas S: Evaluation of low-level laser therapy in the treatment of temporomandibular disorders. Photomed Laser Surg 2006;24:637-641 [PubMed: 17069496]

da Cunha 2008
da Cunha LA, Firoozmand LM, da Silva AP, Camargo SEA, Oliveira W: Efficacy of low-level laser therapy in the treatment of temporomandibular disorder. Int Dent J 2008;58:213-217 [PubMed: 18783114]

Emshoff 2008
Emshoff R, Bosch R, Pumpel E, Schoning H, Strobl H: Low-level laser therapy for treatment of temporomandibular joint pain: a double-blind and placebo-controlled trial. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:452-456 [PubMed: 18329580]

Fikácková 2007
Fikackova H, Dostalova T, Navratil L, Klaschka J: Effectiveness of low-level laser therapy in temporomandibular joint disorders: a placebo-controlled study. Photomed Laser Surg 2007;25:297-303 [PubMed: 17803388]

Kato 2006
Kato MT, Kogawa EM, Santos CN, Conti PCR: TENS and low-level laser therapy in the management of temporomandibular disorders. J Appl Oral Sci 2006;14:130-135 [PubMed: 19089044]

Marini 2010
Marini I, Gatto MR, Bonetti GA: Effects of superpulsed low-level laser therapy on temporomandibular joint pain. Clin J Pain 2010;26:611-616 [PubMed: 20664343]

Mazzetto 2007
Mazzetto MO, Carrasco TG, Bidinelo EF, Andrade Pizzo RCde, Mazzetto RG: Low intensity laser application in temporomandibular disorders: a phase I double-blind study. Cranio 2007;25: 186-192 [PubMed: 17696035]

Mazzetto 2010
Mazzetto MO, Hotta TH, Pizzo RCdeA: Measurements of jaw movements and TMJ pain intensity in patients treated with GaAlAs laser. Braz Dent J 2010;21:356-360 [PubMed: 20976388]

Shirani 2009
Shirani AM, Gutknecht N, Taghizadeh M, Mir M: Low-level laser therapy and myofacial pain dysfunction syndrome: a randomized controlled clinical trial. Lasers Med Sci 2009;24:715-720 [PubMed: 19002646]

Venancio 2005
Venancio RdeA, Camparis CM, Lizarelli RdeFZ: Low intensity laser therapy in the treatment of temporomandibular disorders: a double-blind study. J Oral Rehabil 2005;32:800-807 [PubMed: 16202043]

3.4 Drugs for Myofacial Pain

Description of the intervention: Pharmacological therapy

Pharmaceutics for TMD are usually considered as a coadjuvant therapy aim to relieve the pain and additionally to improve the general condition of the patient to continue a combined treatment according to their diagnosis. Although some of the drugs for TMD are being used to tackle parafunctional habits.

Depending on the intensity and chronicity of the pain, multiple drugs are available for TMD treatment. The mode of administration varies also according to their principal expected effect. According to the routes of administration, the author categorized the pharmacotherapy into three groups: oral administration, topic administration, and intramuscular injections.

The pharmaceutical drugs most usually prescribed are those with oral administration, including analgesics (non-steroidal anti-inflammatory agents and COX-2 inhibitors), muscle relaxants, and also stronger drugs as antidepressants (tricyclic antidepressants) and anticonvulsants (benzodiazepines and antiepileptic agents).

How the intervention might work: Pharmacological therapies

In cases of TMD, the analgesia is the mostly expected result as first or secondary drug action. In this section the author present a brief description of the mechanism of action of the before mentioned drugs.

- The **Non-steroidal anti-inflammatory agents (NSAIDs)** are widely indicated for acute pain, and considered for the first approaching in chronic pain. The NSAIDs interrupt the plasma cascade systems stopping the inflammatory reaction. In animal models for inflammation in the temporomandibular joint, the selective inhibition of the cyclooxygenase enzyme by the action of cyclooxygenase 2 (COX-2) inhibitors produced an attenuated expression of immunoreactive calcitonin gene-related peptide, which is a neuropeptide that participates in inflammatory reactions [257]. In other study, COX-2 inhibitors apparently regulated the central COX pathways [21]. It is remarkable that genetic factors determine the analgesic response to these

drugs [329]. Clinical results showed successful preliminary data of pain relief in a group of TMD patients using an association of indomethacin, betamethasone and methocarbamol [468]. As coadjuvant the NSAIDs are extensively indicated in TMD treatments. The combined therapy with oral appliances and NSAIDs has shown a significant advantage over splint therapy alone [378].
In topic administration, NSAIDs have shown to be effective for the treatment of MPS [48], however for TMD are reported only as a coadjuvant agent.

- **Neuromuscular agents** target directly the acetylcholine receptors at the neuromuscular junction. This action reduces the tenderness and symptomatology of musculoskeletal spasm associated to myogenous TMDs. In spite their frequent indication for myofacial pain, scarce evidence support its use. A systematic review of literature conducted in 2009 [333] on cyclobenzaprine concluded that there is no sufficient evidence to conclude clinical effectiveness even for the treatment of MPS. Promising results related to the use of tizanidine hydrochloride for myofacial pain [365] have not been yet validated through clinical trials.

Some of other drugs with a secondary effect of analgesia can be included in the therapy of myofacial pain: Tricyclic anti-depressant, benzodiazepines, and antiepileptic drugs, as well as propanolol (off label use for tension headache).

- **Tricyclic anti-depressants** are usually added in the pharmacotherapy of MPS. Amitriptyline is also extensively used for chronic tension-type headache. *Bendtsen* and *Jensen* [65] suggested that the principal action of amitriptyline is to reduce the myofacial tenderness. Besides this effect, amitriptyline diminishes the peripheral nociceptive transmission, and may produce a segmental reduction of the central sensitization. A pilot study on TMD patients reported a significant improvement of symptomatic TMD at 6 weeks and one year after the treatment with an adjusted low dosage of amitriptyline [451]; as a collateral effect a part of the depressed patients reduced their depression scores. However there was a decrease on the effectiveness of this tricyclic anti-depressant over the time, especially in patients diagnosed with myofacial pain without concomitant arthrogenous TMD.

- Some **benzodiazepines and antiepileptic** drugs have been studied for TMD. Among the benzodiazepines clonazepam is normally recommended in the specialized literature for some associated psychological conditions [412, 361]. Patients with sleep bruxism treated with clonazepam have shown improvements not only in bruxism indexes but also in psychological parameters [490, 491].
Likewise, the antiepileptic agent Gabapentin has shown efficiency to resolve the painful condition of chronic masticatory myalgia, as suggested the randomized clinical trial which compared the action of this drug with a placebo [297]. Anticonvulsants for orofacial pain were recently reviewed in 2011. The authors found limited evidence to indicate anticonvulsants, reporting only the already mentioned study related to myofacial pain [369].

- Other drugs are under observation in order to verify its efficacy for TMD, e.g. propanolol [175] currently indicated off-label for headache.

Different topical agents can be indicated to relieve pain. Alternative to NSAIDs, the clinician can include anesthetic agents, vanilloids, and other less conventional agents in patch or cream form.

- **Anesthetic agents** such lidocaine and prilocaine blocked temporarily the nerve transmission. The anesthetic agents are preferably used as injections applied in the TMJ or sometimes intramuscular for severe cases of pain, and can be also occasionally indicated in cream form. Infiltration of trigger points is more frequently indicated for myofascial pain syndrome [12, 54, 264]

- **Capsaicin** is the active agent extracted from hot chili peppers of the genus Capsicum. It produces a gradual chemical desensitization after repeated applications. One study showed a relative effectiveness of capsaicin cream in the treatment for chronic musculoskeletal diseases, but not compared to NSAIDs [370]. *Winocur et al.* [610] reported no statistically significant differences between capsaicin and placebo for the therapy in patients with unilateral localized pain of the temporomandibular joint. However, the high response to the placebo has been characteristic for almost all the studies of therapy modalities for TMD [531].

New investigations are in course about the action of an analog of capsaicin, named Resiniferatoxin, which is obtained from the cactus-like plant Euphorbium resinifera. These both chemical agents are vanilloids [13], which implies they should act similarly blocking the TRPV1, a cellular receptor of periferical neurons [489]. It is believed that the effect of the resiniferatoxin is much more potent than the effect of capsaicin [621].

Finally, among the drugs for intramuscular injections some corticosteroids, anesthetic agents (e.g. procaine, lidocaine, mepivacaine) and botulinum toxin are indicated for myofacial pain; however there is no enough evidence of its effectiveness against trigger points [511].

- **Corticosteroids** are synthetic drugs with a similar effect to the steroidal hormones. These drugs are principally indicated in Dentistry for inflammatory conditions, however not as first option due to its immunosuppressive effects. In TMD patients, the association of lidocaine and corticosteroid improved the post-injection sensitivity, but the therapeutic effects did not differ among the other groups treated only with lidocaine or with dry-needling [592].

Undesired side effects injections of corticosteroids are mostly related with immunosupression, but also isolated reports of other complications are for example psychosis secondary [68]

- The **botulinum toxin (BTX)** is a neurotoxin produced by the Clostridium botulinum, an anaerobic Gram (-) bacteria. The BTX protein complex is a 50,000 Dalton neurotoxin associated with stabilizing proteins, which finally compose a 300,000 to 900,000 Daltons molecule, depending on the serotype and species of C.botulinum. The active complex is dissociated under the alkalinization of the initial acid pH, i.e., in physiological medium the neurotoxin is always active. This toxin comprises two protein chains united by a disulfide bridge. One of those is a heavy chain (100,000 Daltons) that allows the internalization via endocytosis of the molecule into the nerve cell, where the neurotoxin is dissociated to the two basic chains. The release of the other chain, the light chain *(*50,000 Daltons), makes it active when migrates to the cytosol. In the cytosol, the light chain cleaves the SNARE proteins (Soluble NSF Attachment protein Receptor) with high specificity.

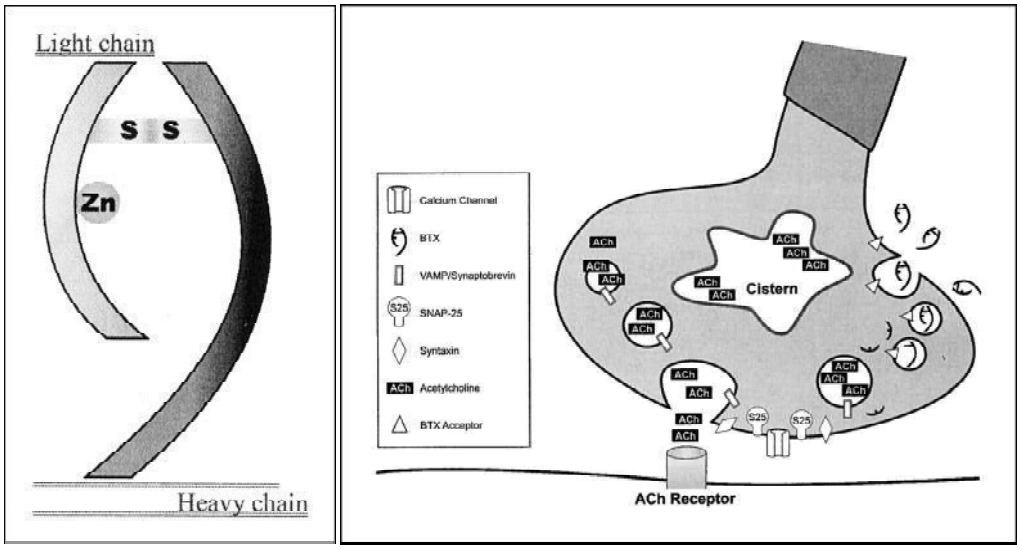

Figure 23. *Botulinum Toxin A active (left). Pharmacology of the Botulinum Toxin at the neuromuscular junction: endocytosis of the BTx-light chain is translocated into the cytoplasm and acts as an endopeptidase-light chain cleaves specific cellular proteins (SNAP-25, syntaxin, VAMP or synaptobrevin) that participate in the fusion of synaptic vesicles to the plasma membrane (right)* [43]

The light chain in every serotype (A, B, C_1, D, E, F, G) acts in enzymatic way over a different location of the SNARE proteins. The serotypes A and C cleave the SNAP-25 (Synaptosomal-Associated Protein of 25Daltons) blocking the presynaptic membrane; and the serotypes B, D, F, and G cleave the synaptobrevin II (also called VAMP) blocking the synaptic vesicles [112]. Nonetheless the result action is actually the same, i.e. to prevent the vesicular fusion with the cellular membrane, and therefore the inhibition of the release of acetylcholine at the junction. Two out of the seven serotypes are commercially available. The BTX A came out into the market with the name of BOTOX® and BOTOX® Cosmetic (Allergan), Dysport® (Ipsen), and Prosigne® (Cristália). A few years later of the first appearance of the serotype A, BTX B is sold under commercial names of Neurobloc and Myobloc (Élan Pharmaceuticals).

The difference between the serotypes A and B are the percentage of cleaving, which is higher for serotype A than B (90-95% against 70%), which implies greater doses needed for a therapeutic effect with BTX B. However, both A and B generate a reversible neuromuscular blocking, through the impediment of acetylcholine transmission at the motor end plate. Besides, BTX may have a dose-dependent inhibitory effect on some mediators of the inflammatory process [517, 43, 123], may modulate vascular activity, and may reduce the

glandular secretion. Because of these properties, the botulinum toxin is indicated for muscular disease.

In Germany, the Bundesamt für Arzneimittel und Medizinprodukte (BfArM) allows the use of BTX for some illness, that include the idiopathic blepharospasm, hemifacial spasmus, rotating torticollis spasmodicus, spastic pes equinus in cerebral palsy, spastic arm after a stroke primary axillary hyperhidrosis, and treatment for Glabella wrinkles. Every other utilization is considered off-label use. Therefore, the dental use must be supported by the informed consent of the patient.

Venancio et al. [593] compared the outcome of three different groups of patients with myofacial pain and headaches, who received BTX, lidocaine, or dry-needling injections as a treatment. After a 12 weeks follow-up the three options improved the baseline condition, but up to the 4-week the patients treated with BTX and lidocaine reported less use of concomitant medication, suggesting a longer action for this drugs. In another study [280], these three therapeutic options were contrasted for MPS (cervical or periscapular pain). Again, the three alternatives relieved pain at trigger points, but lidocaine and BTX were more efficient to improve work disability, fatigue and even pain than dry-needling. Moreover, the BTX had the additional effect to improve the psychological indexes related to depression and anxiety.

In Dentistry, BTX has been successfully used for the treatment of oromandibular dystonia [629], Frey's syndrome and sialorrhea [359]. In addition, a group of muscular problems are been tackled by BTX such as trismus [186], myalgia and hypertrophy of chewing musculature [447] among others.

Von Lindern et al. reported that patients with chronic facial pain refractory to conservative treatments, associated to muscular hyperactivity, could improve these painful symptoms in up to 90% with local injections of BTX A [338, 339]. In other clinical study, *Freund* and *Schwartz* treated 46 TMD patients with BTX injections; as a result it had been produced significant improvements in pain, function, mouth opening, and tenderness to palpation [197]. Other studies had obtained positive results in cases of TMD [60, 83]. Furthermore, BTX has been employed successfully in contouring lower face [463].

Despite these encouraging results, the use of BT must to be validated with more clinical trials that consolidate its application. Currently it is reserved for the recurrent cases and/or refractory to conventional treatments.

The risks associated to the Botox application had been observed more frequently in women, aging mean 50 years. The serious and non-serious adverse effect (AE) for the BTX use reported to the US Food and Drug Administration (FDA) were reviewed by *Coté et al* [117]. They summarized the following serious adverse effect for the BTX therapy (217 cases in 13.5 years): death (28 patients, 26 of those had elevated risk of mortality); potential risks described in the FDA-approved labeling (e.g., dysphagia [n=26], muscle weakness [n=13], allergic reactions [n=11], flu-like syndromes [n=10], injection site trauma [n=9], arrhythmia [n=9], myocardial infarction [n=6]); seizure (17 patients). For cosmetic use, 36 patients showed serious adverse effects included on labeled ones by FDA. Furthermore, 995 non-serious adverse effects were reported: lack of intended cosmetic effect (63%); injection site reaction (19%); ptosis (11%); muscle weakness (5%), headache (5%).

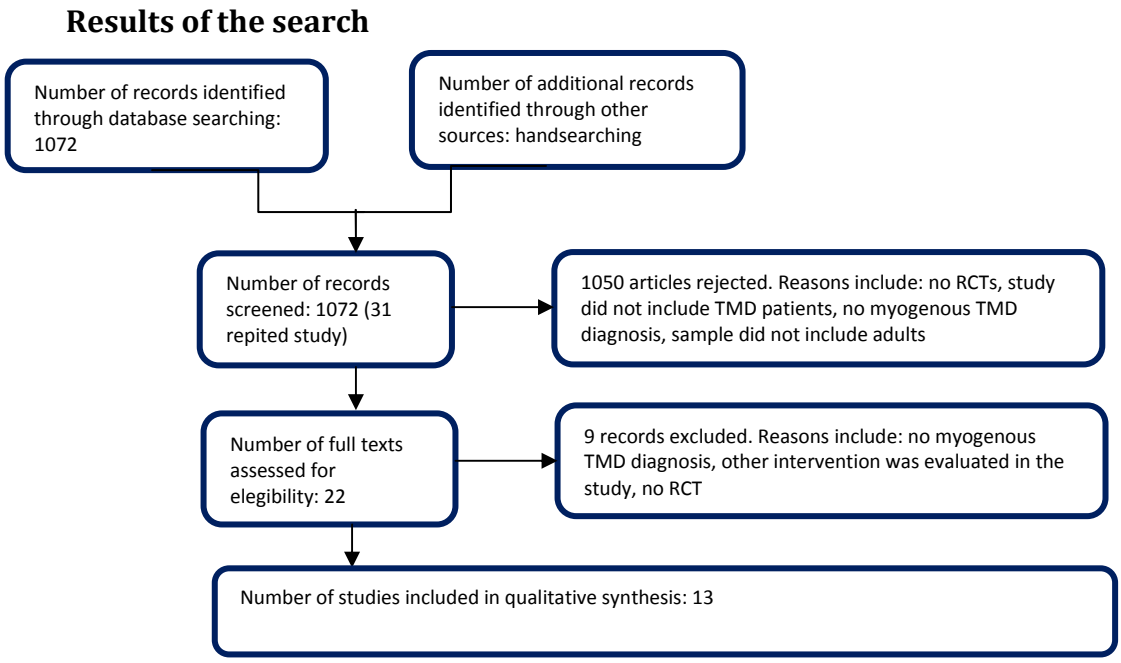

Diagram 3. *Study flow diagram: Drugs for Myofacial Pain (1999-2012)*

Included studies

The included RCTs (diagram 3) in drugs for TMD are very diversified, not only in the drug studied, but also in the administration routes and follow-up periods. Drugs with topical application were studied by *Li 2009*, *Lobo 2004*; drugs with oral administration by *Herman 2002*, *Kimos 2007*, *Pramod 2011*; and injectable

drugs were studied by *Guarda-Nardini 2008*, *Guarda-Nardini 2012*, *Kurtoglu 2008*, *Lindern 2003*, *Ozkan 2011*.

The follow-up period varied from 14 days to 6 months, however except for the study by *Guarda-Nardini 2008*, all the studies presented short-term results.

Kimos 2007 indicated anticonvulsants (gabapentin) to the experimental group. *Pramod 2011* studied benzodiazepines (diazepam), while *Herman 2002* compared benzodiazepines (clonazepam) to muscle relaxants (cyclobenzaprine) and placebo. Four studies worked with botulinum toxin (*Guarda-Nardini 2008*, *Guarda-Nardini 2012*, *Kurtoglu 2008*, *Lindern 2003*). *Ozkan 2011* intervened with anesthetic agents (lidocaine) and corticosteroids (triamcinolone acetonide). Finally, two studies applied specific cream formulas, namely a Chinese composite of herbs known as Poing On, and other mixture of topical methyl salicylate, zinc, copper and herbs (*Li 2009*, *Lobo 2004* respectively).

All the studies with botulinum toxin used the serotype A. The administration points were the muscles masseter and temporalis, and one study included also intraoral intramuscular infiltrations of the pterygoideus medialis (*Lindern 2003*), on the most actives or tender zones.

Excluded studies

Rizzatti-Barbosa 2003 combined benzodiazepines (not specified) with anticholinergic drugs (orphenadrine citrate, in the study regarded as muscle relaxant) and splint therapy in different regimens. Besides of this imprecision, we considered the randomization process invalid. It was based on preformed groups at which one intervention was assigned afterwards.

Other trials were excluded because they evaluated other conditions, other interventions, or the pharmacotherapy was considered a cointervention (s. Characteristics of excluded studies).

Effect of the intervention

Three injectable medications were indicated in trials for myofacial pain: botulinum toxin, and a combination of lidocaine and corticosteroids.

Results of the effectiveness of Botulinum toxin for myofacial pain were not propitious. *Guarda-Nardini 2008* did not find significant differences between the

effects of the toxin and a placebo, except for pain at chewing and the perception of treatment efficacy reported by the patients. In other study (*Guarda-Nardini 2012*), the botulinum toxin was as effective as fascial manipulation, being superior only in the improvement of lateral jaw movement ranges. In the study by *Kurtoglu 2008*, EMG changes at maximal clenching were significantly different over time for the group treated with botulinum toxin compared to placebo in all the measured masticatory muscles; however these differences started from the baseline. Neither pain nor psychological outcomes were dissimilar between groups. On the contrary, *Lindern 2003* reported significant differences between the experimental group and the placebo, the reduction of pain was of 32mm in VAS for the first group vs. 4mm for placebo.

In the study by *Ozkan 2011*, splint therapy was complemented by the action of two sessions of trigger point injections with lidocaine and one session with triamcinolone acetonide. Although the comparison group consisting in only splint therapy was efficient in time to reduce pain, the experimental group showed significant better improvements at 12 weeks follow-up in pain during jaw movements, number of trigger points and intensity of pain. Pain intensity dropped in this group about 60 mm in VAS scale from baseline.

Among the drugs of oral administration, cyclobenzaprine, gabapentin and diazepam showed some effectiveness in the therapy of myofacial pain. *Herman 2002* observed greater improvements of symptomatology with a combination of cyclobenzaprine and self-care strategies in comparison to the other groups of treatment bringing self-care together with clonazepam or placebo, which not differed from each other. Pain intensity scores, measured by VAS, dropped 45mm in the first group, and 20mm in the other groups. The adjusted scores of pain intensity to baseline, sex and gender exhibited a significant difference in favour of the cyclobenzaprine group.

Gabapentin was more effective than placebo to relieve general and muscular pain at 1 month follow-up (*Kimos 2007*), reducing pain in 51.04% (approx. 40mm in VAS scale compared to 24% in the placebo intervention. In contrast, the outcomes of pain intensity and muscle tenderness were not favourable for the intervention with diazepam compared to placebo (*Pramod 2011*), however the authors observed increased mouth opening at 8-weeks follow-up for the study group.

The results of trials on topical drugs were positive respect pain relief for both

creams compared to placebo (*Li 2009*, *Lobo 2004*). Using "Ping On" ointment decreased VAS-pain in 55% from baseline (approx. 28mm reduction in VAS). The results in the study by *Lobo 2004* reported about 20mm decrease in the NRS scale for general pain and pain in masseter muscle using topical methyl salicylate, which represented 39% of pain reduction from baseline and 50% muscular pain relief, however no comparisons between groups were mentioned. Regarding the side effects, all studies but *Ozkan 2011* addressed this issue or informed about the tolerance of the patients to the therapy. Almost all the included drugs caused temporary perturbances. Studies with botulinum toxin reported no side effects (*Kurtoglu 2008*); one report of temporary discomfort by chewing (*Guarda-Nardini 2012*); one case of swallowing difficulty or temporary paralysis of a facial muscle; and good tolerance without addressing lateral effects (*Guarda-Nardini 2008*).

Patients receiving oral drugs suffered well known secondary effects of the drugs. In the study by *Herman 2002* percentages of patients per group were: 62% in the cyclobenzaprine group (morning drowsiness, dry mouth, and nightmares), 40% in the clonazepam group (morning drowsiness, and headache), and 20% in the placebo group (drowsiness, dry mouth, and increase in premenstrual symptoms). Side effects did not differ in frequency between groups.

The most frequently reported side effects in the study of gabapentin (*Kimos 2007*) were dizziness (28%), drowsiness (28%), and memory and cognitive impairment (16%). In spite the frequency of reports between groups was not significant for any symptom, 4 patients dropped out the study due to the side effects.

Finally, the adverse effects of the included topical drugs were eye irritation (26%), burning sensation (13%) and itchiness (4%) for the "Ping On" ointment; and skin irritation and/or burning on the site of application (8%) for the methyl salicylate cream.

Quality of the evidence

The figures 24 and 25 summarize the quality of the evidence according to the Cochrane Collaboration for the studies of drugs in the treatment of myofacial pain.

One study (*Kimos 2007*) accomplished all criteria of low risk bias for both Cochrane Collaboration's tool and the Delphi list. On the other hand, four RCTs (*Guarda-Nardini 2012*, *Guarda-Nardini 2008*, *Lindern 2003*, *Ozkan 2011*) were evaluated as having unclear risk of bias on key criteria (blinding of outcome assessment). These 4 trials were from moderate to poor quality according to the Delphi list.

No one of the included studies was evaluated at high risk of bias for any criteria at the Collaboration's tool.

The general positive accomplishment of the Delphi list (table 6) was 71.1%. RCTs with score 6 or higher were 60.0% of the included studies.

Study	Allocation randomized	Allocation concealed	Groups similar at baseline	Inclusion criteria specified	Blind outcome assessment	Blinded care provider	Blinded patients	Point estimates and variability	Intention-to-treat analysis
Guarda-Nardini 2008	Yes	Don't know	Yes	Yes	Don't know	Don't know	Don't know	Yes	Don't know
Guarda-Nardini 2012	Yes	Don't know	Yes	Yes	Don't know	No	No	Yes	Yes
Herman 2002	Yes	Don't know	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kimos 2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kurtoglu 2008	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Li 2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Lindern, von 2003	Yes	Don't know	Don't know	No	No	No	Yes	No	Don't know
Lobo 2004	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Ozkan 2011	Yes	Don't know	Yes	Yes	Don't know	No	No	Yes	Don't know
Pramod 2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No

Table 6: *Delphi list: Drugs for myofacial pain*

Characteristics of studies

Characteristics of included studies

Guarda-Nardini 2008

Methods	RCT. Single center, two parallel groups. Follow up for 6 months
Participants	20 participants: age range=25-45; 50% women Inclusion criteria: presence of bruxism diagnosed using a validated set of screening-oriented clinical diagnostic criteria (patient exhibited, at least five nights a week, grinding/bruxing sounds during sleep for the past six months, as reported by his/her bed partner, and at least one of the following adjunctive criteria: observation of tooth wear or shiny spots on restorations, report of morning masticatory muscle fatigue or pain, masseteric hypertrophy upon digital palpation); and myofascial pain according to RDC/TMD groups Ia or Ib (report of pain or ache in the jaw, temples, face, preauricular area, or inside the ear at rest or during function; pain reported by the subject in response to palpation of three or more of 20 muscle sites, at least one of the sites must be on the same side as the pain complaint) Exclusion criteria: history of any treatment for bruxism and/or TMD during six months prior to the study; the presence of neuromuscular pathologies preventing the use of botulinum toxin (i.e., myasthenia gravis); a reported hypersensibility to clostridium botulinum type A neurotoxin. Location: Italy
Interventions	Group A (n=10): injections of Botulinum toxin (four Type A botulinum toxin (Botox, Allergan, inc., Irivine, CA) intramuscular injections for each side (30 U) within the masseter muscles and three injections (20 U) within the anterior temporalis muscles, for a treatment total of 100 U. The injections were made during a single appointment under anatomo-topographic and/or u lt rasonographic control) Group B (n=10): saline placebo injections
Outcomes	Pain at rest and at chewing (VAS) Mastication efficiency (VAS) Maximum non-assisted and assisted mouth opening, protrusive and laterotrusive movements (mm); Functional limitation during usual jaw movements (0-4) Subjective efficacy of the treatment (0-4)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The design of the study provided a double-blind, controlled placebo, randomized clinical trial..."
Allocation concealment (selection bias)	Unclear risk	(s. sequence generation)
Blinding of participants and personnel (performance bias)	Unclear risk	(s. selection bias)
Blinding of outcome assessment (detection bias)	Unclear risk	(s. selection bias)
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed

Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Guarda-Nardini 2012

Methods	RCT. Single center, two prallel groups. Follow-up for 3 months
Participants	30 participants: mean age=45.45 (R=23-69); 73.33%women Inclusion criteria: diagnosis of myofascial pain, with or without limited opening (RDC/TMD) and bilateral pain lasting for at least six months Exclusion criteria: systemic neurological and/or rheumatological disorders; RDC/ TMD diagnoses of arthralgia and/or osteoarthritis Location: Italy
Interventions	Group A (n=15) Botulinum toxin injections (single session of multiple botulin toxin injections in the temporalis and masseter muscles using a 0.7 mm 30G needle, with a total of about 150U of botulinum toxin (Dysport, Ipsen, Ltd., UK) was injected per each treated side. A five-injection minimum with a reverse pyramid pattern was performed in the masseter muscles, and a chess-board pattern was used for the temporalis muscles.) Group B (n=15) Fascial manipulation (three (±1) 50 min sessions of Fascial Manipulation on a weekly basis, for a total of 150 (±50) min over a two- to four-week span)
Outcomes	Maximum pain level (VAS) Maximum mouth opening, protrusion, right and left laterotrusion (mm)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "simple one-to-one randomization procedure"
Allocation concealment (selection	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed
Incomplete outcome data (attrition bias)	Low risk	Quote:"(patients)...none of them dropped out"
Selective reporting (reporting bias)	Unclear risk	Not sufficient information
Other bias	Unclear risk	The interventions have different duration, which was not considered in analysis.

Herman 2002

Methods	RCT. Single center; three parallel groups. Follow-up (treatment) for 3 weeks.
Participants	41 patients: mean age group A=26.9 (SD=10.1), mean age group B=24.0(SD=4.8), mean age group C=30.3 (SD=8.6); 80.49% women. Inclusion criteria: age 18-65 yrs.; jaw pain upon awakening, occurring a minimum of 2 days per week; diagnosis of myofacial pain (axis 1 group I) according to RDC/TMD, concurrent diagnoses of TMJ arthralgia and disc

	displacement with reduction were allowed; self-report of an average jaw pain intensity in the past week of at least 4 on VAS; self-report of psychological stability (subjects taking antidepressants were considered stable if they reported no current depression, and had been on a stable regimen of psychotropic medications for 3 months. Exclusion criteria: any dental, orofacial problem or TMD not meeting the definition of myofacial pain as defined by the RDC/TMD; self-report of persistent depression or an unstable regimen of psychotropic medication of less than 3 months as indicated by their history; jaw pain of potential systemic (e.g. fibromyalgia, widespread pain); clinical or radiographic evidence of osseous, odontogenic, or TMJ pathology; report of liver dysfunction, alcoholism, glaucoma, history of seizures, impaired renal function, use of monoamine oxidase inhibitors, acute recovery phase of myocardial infarction, arrhythmia, heart block or conduction disturbances, congestive heart failure, hyperthyroidism, pregnancy, or any other contraindications to clonazepam or cyclobenzaprine (including drug allergies). Location: USA
Interventions	Group A (n=13): self-care program + Clonazepam 0.5mg daily Group B (n=15): self-care program + placebo (lactose filler) Group B (n=13): self-care program + Cyclobenzaprine 10mg daily
Outcomes	Symptom Severity Index (SSI) for jaw pain TMJ pain and temple pain Pittsburgh Sleep Quality Index (PSQI)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Subjects were allocated to their treatment group by means of a randomized block design with the blocking variable being the current use of psychotropic medications“
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	Participants and personnel blinded Quote: “The capsules were formulated to have the same appearance (…) Neither the treating doctor nor the subject was aware of the treatment assignment until completion of the intervention.”
Blinding of outcome assessment (detection bias)	Low risk	Data based on self-report Comments: probably done (s. performance bias)
Incomplete outcome data (attrition bias)	Low risk	Quote: “The final sample consisted of 33 women and 8 men with no subject dropouts or withdrawals”
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Kimos 2007

Methods	RCT. Single center; two parallel groups. Follow-up for 12 weeks
Participants	*50 patients:* mean age= 33.58; 100% women. *Inclusion criteria:* age 18-45 yrs.; diagnosis of masticatory muscle pain based on the diagnostic RDC/TMD (constant pain or ache in their masticatory muscles, face, and preauricular area or inside the ear at rest or during function); masticatory muscle pain for at least 6 months; chronic masticatory muscle pain not attributable to recent acute trauma, previous infection, or an active inflammatory cause; moderate to severe baseline score of 50 mm or greater VAS; pain upon palpation in at least three of the following points: Temporalis (anterior, medial and posterior bellies), Masseter (deep belly, and the inferior and anterior portion of the superficial belly). *Exclusion criteria:* clinical evidence of inflammatory TMD; pregnant or nursing females; epilepsy, cardiac, renal or hepatic disorders; history of intolerance to gabapentin or to any of the components of the formulation; dental or periodontal disease, oral pathology lesions, oral infection, or neuropathic facial pain; patients wearing an occlusal splint appliance for less than 6 months. *Location*: Canada
Interventions	*Group A (n=24 [25])*: gabapentin minimum effective dose for each patient (Patients were started on 300 mg per day and the dose was increased by 300 mg every 3 days until pain was controlled with no adverse effects. The maximum dose was 4200 mg. If the study medication had to be discontinued for any reason, dosage was gradually decreased 300 mg every 3 days) *Group B (n=20 [25]):* placebo
Outcomes	Pain intensity (VAS), Palpation Index (number of tender sites) Daily function (VAS) Side effects
Notes	Acetaminophen 500 mg. was used for break-through pain Gabapentin was donated by a pharmaceutical company

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:“A computer-generated randomization code list was utilized to randomly allocate patients in two study groups”
Allocation concealment (selection bias)	Low risk	Quote: “For double-blinding purposes, concealed randomization and the according allocation were implemented by a research assistant.“ From correspondence: “we used a clinical pharmacist (research assistant) to randomize the patients and to provide the patients with their medication.”
Blinding of participants and personnel (performance bias)	Low risk	Quote: “Neither the patients nor the main investigator was aware of the random group allocation.” “…the active and placebo medications were packed in identical looking capsules by the pharmaceutical company (…) Both, active medication and placebo capsules were packed in identical clear bottles labelled according to Investigational Pre-Packing Control Records, established by Section C.05.011 of the Food and Dr*ug Regulations”*

Blinding of outcome assessment (detection bias)	Low risk	From correspondence: “PK did all of the outcome measurements and data analysis, but neither he or the patient knew if they were the treatment or control group.”
Incomplete outcome data (attrition bias)	Low risk	Quote: “The data derived from this study were analyzed by intent-to-treat analysis .”
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Kurtoglu 2008

Methods	RCT. Single center, two parallel groups. 28 days follow-up
Participants	24 patients: mean age=26.5 (R=16-53); 83.3%women Inclusion criteria: Patients with myofascial pain, with or without functional disc displacement, who had undergone conservative TMD treatment without complete relief of symptoms. Exclusion criteria: age below 14 years; history of allergic reactions to BTX-A (Allergan Pharmaceuticals Ltd, Mayo, Ireland); pregnancy, and lactation Location: Turkey
Interventions	Group A (n=12): botulinum toxin (bilateral injections of botulinum toxin A+ 2 cc of saline in the most active area of the masseter [3 points] an temporalis muscles [2 points]) Group B (n=12): placebo (only 2 cc of saline, same procedure than experimental group)
Outcomes	EMG RDC/TMD axis II
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Shuffling envelopes
Allocation concealment (selection bias)	Low risk	Quote: "...envelopes containing papers marked “placebo (control),” were closed tightly, mixed thoroughly, and given numbers from 1 to 24"
Blinding of participants and personnel (performance bias)	Low risk	Quote: "The first examiner, who dealt with randomization and blinding, also prepared the material for injection." "...both syringes were similar in appearance. Thus, the second and third examiners were unaware of the contents of syringes"
Blinding of outcome assessment (detection bias)	Low risk	Quote: "The second examiner collected the EMG and questionnaire data, and recorded the date and each subject’s name. Subjects filling out the questionnaire were alone in a quiet room" (he was unaware of the allocation, s. performance bias)
Incomplete outcome data (attrition bias)	Low risk	Quote "...none of the subjects was recorded as lost to follow-up".

Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Li 2009

Methods	RCT. Single center; two parallel groups. Follow-up for 4 weeks.
Participants	45 (out of 55) patients: mean age group A(analyzed) =43.96 (±13.13), mean age group B(analyzed)=47.14 (±9.30); 71.11% women (analyzed); mean months of pain duration group A=29.61 (±31.44); mean months of pain duration group B=35.82 (±31.53) Inclusion criteria: diagnosis of Group I (muscle disorders) according to RDC/TMD, including both painful and nonpainful disorders; at least 1 month of daily or nearly daily joint and muscle pain; subjects with myogenic pain were included if they met inclusion and exclusion criteria since patients with TMDs are known to exhibit muscle pain secondary to their joint dysfunction Exclusion criteria*: infectious arthritis, crystal-induced arthropathies, musculoskeletal disorders, pain attributable to confirmed migraine or head pain condition other than tension headache; acute infection or disease of teeth, ears, eyes, nose, or throats; untreated depressive disorder or not on stable antidepressant medication for more than 6 months; dental diseases that required ongoing treatment; subjects who are not competent in giving consents; pregnant or lactating women; sensitivity to the ingredients of Ping On ointment. Location: China
Interventions	Group A (n=23): Ping On ointment over the painful area and then massaged in a circular motion for 5 min. twice a day Group B (n=22): placebo cream over the painful area and then massaged in a circular motion for 5 min. twice a day
Outcomes	Pain diary (VAS) Mandibular function, vertical mouth opening without pain
Notes	Confusing inclusion/exclusion criteria in the article From correspondence: typo mistake in the publication. The phrase "subjects with a primary diagnosis of myofacial pain based on the RDC" should not be in the exclusion criteria. Excluded from this summary.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The eligible subjects were randomized using blocked randomization into one of the two groups…”
Allocation concealment (selection bias)	Low risk	Quote: “The people involved in the randomization and in preparation and distribution of study articles were independent from the investigators”
Blinding of participants and personnel (performance bias)	Low risk	Patients and personnel blinded Quote: “…both the investigators and subjects were blinded as to the treatment allocation. While there were differences in the texture, color, and odor of the placebo and active ointment, the investigators did not see either ointment at any time and were instructed not to ask any questions regarding the ointment used by a subject. The ointment to be given to participants was sealed in an

		opaque, tightly sealed container and then a bag in which no smell could be detected."
Blinding of outcome assessment (detection bias)	Low risk	Quote:"…subjects were asked to complete the daily diary at home including the VAS, use of oral analgesics, and occurrence of adverse effects if there were any".
Incomplete outcome data (attrition bias)	Low risk	Missing data balanced in numbers across intervention groups, with similar reasons for missing data.
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Lindern 2003

Methods	RCT. Single center, two groups. 4 week treatment, 1-3 months follow-up
Participants	90 participants (demographic data not reported) Inclusion criteria: chronic facial pain caused by hyperactivity of the masticatory muscles, parafunctional movement and hypermobility disorders. Previous experience of non-successful conservative treatment. Exclusion criteria: other causes of pain, particularly arthropathy, were reliably ruled out clinically and by imaging diagnostics. Undefined pain syndromes with unclear patterns of radiation and no reference muscle Location: Germany
Interventions	Group A (n=60): botulinum toxin injections (an average of 35 MU Botox liquidated in 0.7 mL NaCl saline. The majority of the injections were administered intraorally. Only 23% required extraoral injection due to location) Group B (n=30): placebo (0.7 mL NaCl pure saline)
Outcomes	Subjective pain (VAS)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...in a prospective, single blinded, randomized placebo controlled study"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Unclear risk	Participants blinded. Quote: "The patients were not informed whether they were treated with Botox or the placebo." (s. selection bias)
Blinding of outcome assessment (detection bias)	Unclear risk	(s. selection bias)
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Other bias	Unclear risk	Inclusion diagnostic criteria was not explicited. Demographic data not reported

Lobo 2004

Methods	RCT. Single center; two parallel groups. Follow-up for 20 days (15 days treatment).
Participants	52 patients: 90.38% women. Inclusion criteria: age 18-60; report of pain in the masseter muscle either at rest or during function; pain on palpation of the masseter muscle; pain in the TMJ either at rest or during function; good general health. Exclusion criteria: face, head and/or neck trauma within the past year; lesions in the oral cavity or deeper structures; systemic disease; pain or psychotropic medication use within a one month period; diagnosis of migraine; pregnancy. Location:USA
Interventions	Group A (n=26):Theraflex cream ¼ to ½ teaspoon of cream on the afflicted masseter or over the jaw joint during seven min. twice daily for 2 weeks Group B (n=26): placebo cream ¼ to ½ teaspoon of cream on the afflicted masseter or over the jaw joint during seven min. twice daily for 2 weeks
Outcomes	Pain level (NGRS)
Notes	Subgroups according to pain localization: group A= 14 TMJ + 12 masseter; group B= 14 TMJ + 12 masseter Supported by NaBob/Rx, manufacturer of Theraflex From correspondence: “we studied a 20 day treatment period. No cream was applied for 5 days leading up to the treatment period.”

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Urn randomization in a box. From correspondence: “we used a sealed non-transparent box with a small opening just large enough for taking the numbers out. Double blinding was assured by having a non-researcher employee select and record treatment selections (experimental or placebo) from the box.”
Allocation concealment (selection bias)	Low risk	Quote: “…blind selection from a pool of 52 numbers… Once the number was chosen, it was not returned to the box. A Gelb Center employee not on the research team performed selection. Numbers assigned to each subject were monitored by the employee and were not disclosed until the study was completed”
Blinding of participants and personnel (performance bias)	Low risk	Quote: “The study was conducted in a randomized double-blind fashion.“ From correspondence: patients, personnel and outcome assessment blinded
Blinding of outcome assessment (detection bias)	Low risk	(s. performance bias)
Incomplete outcome data (attrition bias)	Low risk	From correspondence: no drop outs
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Unclear risk	Study supported by medicament manufacturer

Ozkan 2011

Methods	RCT. Single center two groups. Treatment for 1 week/3months, follow-up for 12 weeks after completing treatment.
Participants	50 participants: mean age=30.38; 88%women Inclusion criteria: pain of muscular origin with or without limited opening, duration of pain at least 3 months including a complaint of pain associated with localized areas of tenderness to palpation in masticatory muscles, combined with self-assessed myofascial pain of at least 40 mm on VAS. Exclusion criteria: odontogenic reasons for the orofacial pain; evidence of bone pathology (rheumatoid arthritis, osteoarthrosis, condylar resorption) and TMJ pain; previous treatment for TMD; use of complete dentures; other causes of pain (e.g. trigeminal neuralgia, atypical facial pain) Location: Turkey
Interventions	Group A (n=25): stabilization splint (splint at night for a period of three months) Group B (n=25): stabilization splint + injections into trigger points (2 sessions with solution of 0.5 ml lidocaine + 0.5 ml saline; and a third session with 0.1 ml triamcinolone acetanide. 22 injections in masseter muscle, 13 injections in temporalis, and 20 injections in lateral pterygoid muscles).
Outcomes	Maximal incisal opening (MIO), Pain during mandibular movements, and at rest Number of trigger points in masticatory muscles Intensity of myofascial pain (VAS) Frequency of myofascial pain
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "...and randomly assigned to two equal Group"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Unclear risk	No possible blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Pramod 2011

Methods	RCT. Single center, two parallel groups. 3 weeks treatment follow-up for 5 weeks.
Participants	35 participants: up to 50yrs. old ; 60%women Inclusion criteria: Daily pain in the pre-auricular region at least of three months duration; muscle tenderness to palpation in one or more muscle of mastication; those who were diagnosed as TMD earlier, but not treated with diazepam (patients being treated with some other medication were included provided a washout period of 15 days). Exclusion criteria: evident changes in TMJ detected on radiographic

	examination; pain attributable to recent facial trauma, dental surgery, or placement of a dental appliance; other local causes of pain (dental abscess, trigeminal neuralgia or migraine); presence of other disorder that required ongoing treatment with analgesics, muscle relaxants, or mood altering drugs, which would confound the evaluation of TMD pain; allergy or other contraindications to the study drugs; patients taking medication for other medical conditions during the last 15 days. Location: India
Interventions	Group A (n=10): placebo Group B (n=25): diazepam 5mg. tablet daily in the evening after a small meal
Outcomes	Pain intensity (VAS) Masticatory muscle tenderness viz. in masseter, medial pterygoid, lateral pterygoid and temporalis Mouth opening (mm)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned..."
Allocation concealment (selection bias)	Low risk	"The allocation sequence was known only to another staff in the department, who dispensed the tablets along with the detailed instructions."
Blinding of participants and personnel (performance bias)	Low risk	Quote: "allocation was concealed from... patients during all stages." "The placebo tablets were formulated to have the same appearance as active drug. Neither the doctor nor the patients were aware of the treatment given until completion of the interventions.
Blinding of outcome assessment (detection bias)	Low risk	Quote:"...allocation was concealed from the doctor (who assessed the patients)"
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Footnotes

Characteristics of excluded studies

Abrahamsen 2009

Reason for exclusion	Pharmacotherapy is a cointervention in the study

Aktas 2010

Reason for exclusion	No myogenous TMD patients

Alpaslan 2001

Reason for exclusion	No myogenous TMD patients

Ayesh 2008

Reason for exclusion	No myogenous TMD patients

Berguer 2008

Reason for exclusion	This study did not include a pharmacological intervention (neurorefloxology vs. placebo)

Cahlin 2011

Reason for exclusion	No myogenous TMD patients

Carrasco 2008

Reason for exclusion	No pharmacological intervention (LLLT vs. sham laser acupuncture)

Di Rienzo 2004

Reason for exclusion	No myogenous TMD patients

Furst 2001

Reason for exclusion	No myogenous TMD patients

Haketa 2010

Reason for exclusion	No myogenous TMD patients

Ibanez-García 2009

Reason for exclusion	No diagnosis of TMD. Inclusion criteria: muscle trigger points in masseter.

Inchingolo 2011

Reason for exclusion	Not randomized

Marini 2010

Reason for exclusion	No myogenous TMD patients

Marini 2012

Reason for exclusion	No myogenous TMD patients

Mejersjo 2008

Reason for exclusion	No myogenous TMD patients

Minagi 2001

Reason for exclusion	No myogenous TMD patients

Minakuchi 2004

Reason for exclusion	No myogenous TMD patients

Morey 2010

Reason for exclusion	No myogenous TMD patients

Naikmasur 2008

Reason for exclusion	Duration of different interventions is not comparable

Nguyen 2001

Reason for exclusion	No myogenous TMD patients

Nilsson 2007

Reason for exclusion	Sample did not include adults

Nilsson 2009

Reason for exclusion	Sample did not include adults

Rizzatti-Barbosa 2003

Reason for exclusion	Not randomized

Santos 2010

Reason for exclusion	No pharmacological intervention (LLLT vs placebo)

Schiffman 2007

Reason for exclusion	No myogenous TMD patients

Stiesch-Scholz 2002

Reason for exclusion	No myogenous TMD patients

Ta 2004

Reason for exclusion	No myogenous TMD patients

Thie 2001

Reason for exclusion	No myogenous TMD patients

Truelove 2006

Reason for exclusion	Pharmacotherapy is a cointervention in the study

Wahlund 2003

Reason for exclusion	Sample did not include adults

Wahlund 2003b

Reason for exclusion	Sample did not include adults

Watanabe 1999

Reason for exclusion	This article presents studies on animals and humans. The clinical trial was not randomized.

Wieselmann-Penkner 2001

Reason for exclusion	Other interventions evaluated.

Winocur 2000

Reason for exclusion	No myogenous TMD patients; quote:"patients who suffered from localized unilateral pain in the TMJ area".

Yoda 2002

Reason for exclusion	No myogenous TMD patients

Yuasa 2001

Reason for exclusion	No myogenous TMD patients

Ziegler 2003

Reason for exclusion	No myogenous TMD patients

Ziegler 2010

Reason for exclusion	No myogenous TMD patients

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

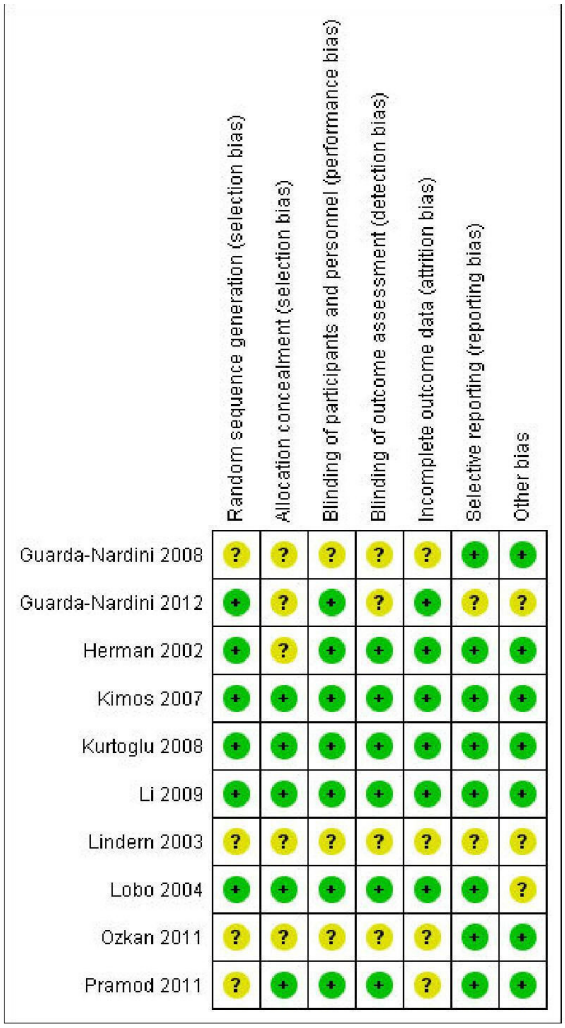

Figure 24. *Risk of bias summary: review authors' judgements about each risk of bias item for each included study*

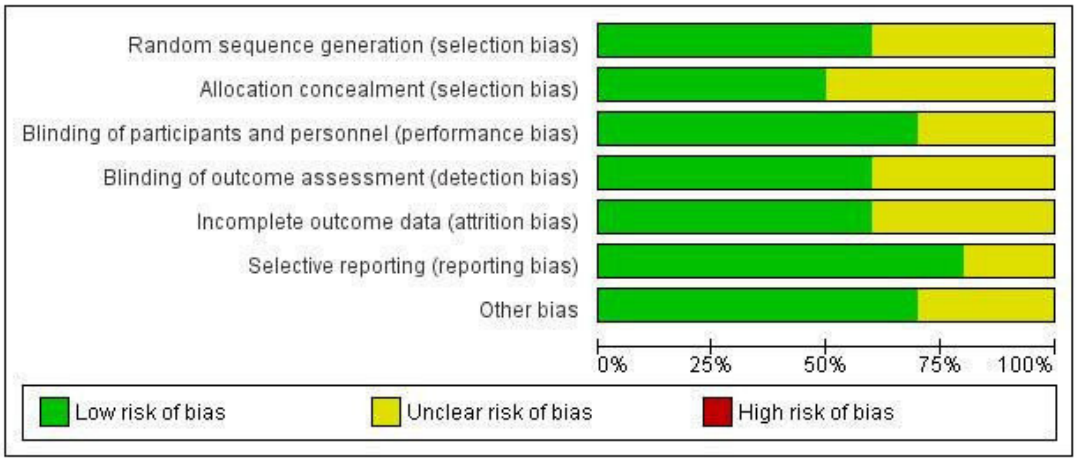

Figure 25. *Risk of bias graph.*

References to studies: Drugs for Myofacial Pain

Included studies

Guarda-Nardini 2008
Guarda-Nardini L, Manfredini D, Salamone M, Salmaso L, Tonello S, Ferronato G: Efficacy of botulinum toxin in treating myofascial pain in bruxers: a controlled placebo pilot study. Cranio 2008;26:126-135 [PubMed: 18468272]

Guarda-Nardini 2012
Guarda-Nardini L, Stecco A, Stecco C, Masiero S, Manfredini D: Myofascial pain of the jaw muscles: comparison of short-term effectiveness of botulinum toxin injections and fascial manipulation technique. Cranio 2012;30:95-102 [PubMed: 22606852]

Herman 2002
Herman CR, Schiffman EL, Look JO, Rindal DB: The effectiveness of adding pharmacologic treatment with clonazepam or cyclobenzaprine to patient education and self-care for the treatment of jaw pain upon awakening: a randomized clinical trial. J Orofac Pain 2002;16:64-70 [PubMed: 11889661]

Kimos 2007
Kimos P, Biggs C, Mah J, Heo G, Rashiq S, Thie NMR, Major PW: Analgesic action of gabapentin on chronic pain in the masticatory muscles: a randomized controlled trial. Pain 2007;127:151-160 [PubMed: 17030096]

Kurtoglu 2008
Kurtoglu C, Gur OH, Kurkcu M, Sertdemir Y, Guler-Uysal F, Uysal H: Effect of botulinum toxin-A in myofascial pain patients with or without functional disc displacement. J Oral Maxillofac Surg 2008;66:1644-1651 (2008) [PubMed: 18634953]

Li 2009
Li LCF, Wong RWK, Rabie ABM: Clinical effect of a topical herbal ointment on pain in temporomandibular disorders: a randomized placebo-controlled trial. J Altern Complement Med 2009;15:1311-1317 [PubMed: 20001836]

Lindern 2003
Lindern JJvon, Niederhagen B, Berge S, Appel T: Type A botulinum toxin in the treatment of chronic facial pain associated with masticatory hyperactivity. J Oral Maxillofac Surg 2003;61:774-778 [PubMed: 12856249]

Lobo 2004
Lobo SL, Mehta N, Forgione AG, Melis M, Al-Badawi E, Ceneviz C, Zawawi KH: Use of Theraflex-TMJ topical cream for the treatment of temporomandibular joint and muscle pain. Cranio 2004;22:137-144 [PubMed: 15134414]

Ozkan 2011
Ozkan F, Cakir Ozkan N, Erkorkmaz U: Trigger point injection therapy in the management of myofascial temporomandibular pain. Agri 2011;23:119-125 [PubMed: 21935818]

Pramod 2011
Pramod GV, Shambulingappa P, Shashikanth MC, Lele S: Analgesic efficacy of diazepam and placebo in patients with temporomandibular disorders: a double blind randomized clinical trial. Indian J Dent Res 2011;22:404-409 [PubMed: 22048580]

Excluded studies

Abrahamsen 2009
Abrahamsen R, Zachariae R, Svensson P: Effect of hypnosis on oral function and psychological factors in temporomandibular disorders patients. J Oral Rehabil 2009;36:556-570 [PubMed: 19604319]

Aktas 2010
Aktas I, Yalcin S, Sencer S: Intra-articular injection of tenoxicam following temporomandibular joint arthrocentesis: a pilot study. Int J Oral Maxillofac Surg 2010;39:440-445 [PubMed: 20211542]

Alpaslan 2001
Alpaslan GH, Alpaslan C: Efficacy of temporomandibular joint arthrocentesis with and without injection of sodium hyaluronate in treatment of internal derangements. J Oral Maxillofac Surg 2001;59:613-618 [PubMed: 11381380]

Ayesh 2008
Ayesh EE: Jensen TS, Svensson P: Effects of intra-articular ketamine on pain and somatosensory function in temporomandibular joint arthralgia patients. Pain 2008;137:286-294 [PubMed: 17923328]

Berguer 2008
Berguer A, Kovacs F, Abraira V, Mufraggi N, Royuela A, Muriel A, Gestoso M, Falahat F, Martin-Granizo R, Zamora J: Neuro-reflexotherapy for the management of myofascial temporomandibular joint pain: a double-blind, placebo-controlled, randomized clinical trial. J Oral Maxillofac Surg 2008;66:1664-1677 [PubMed: 18634956]

Cahlin 2011
Cahlin BJ, Dahlstrom L: No effect of glucosamine sulfate on osteoarthritis in the temporomandibular joints--a randomized, controlled, short-term study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:760-766 [PubMed: 22001199]

Carrasco 2008
Carrasco TG, Mazzetto MO, Mazzetto RG, Mestriner W: Low intensity laser therapy in temporomandibular disorder: a phase II double-blind study. Cranio 2008;26:274-281 [PubMed: 19004308]

Di Rienzo 2004
Di Rienzo Businco L, Di Rienzo Businco A, D'Emilia M, Lauriello M, Coen Tirelli G: Topical versus systemic diclofenac in the treatment of temporo-mandibular joint dysfunction symptoms. Acta Otorhinolaringol Ital 2004;24:279-283 [PubMed: 15871609]

Furst 2001
Furst IM, Kryshtalskyj B, Weinberg S: The use of intra-articular opioids and bupivacaine for analgesia following temporomandibular joint arthroscopy: a prospective, randomized trial. J Oral Maxillofac Surg 2001;59:979-983 [PubMed: 11526558]

Haketa 2010
Haketa T, Kino K, Sugisaki M, Takaoka M, Ohta T: Randomized clinical trial of treatment for TMJ disc displacement. J Dent Res 2010;89:1259-1263 [PubMed: 20739691]

Ibanez-García 2009
Ibanez-Garcia J, Alburquerque-Sendin F, Rodriguez-Blanco C, Girao D, Atienza-Meseguer A, Planella-Abella S, Fernandez-de-Las Penas C: Changes in masseter muscle trigger points following strain-counterstrain or neuro-muscular technique. J Bodyw Mov Ther 2009;13:2-10 [PubMed: 19118788]

Inchingolo 2011
Inchingolo F, Tatullo M, Marrelli M, Inchingolo AM, Tarullo A, Inchingolo AD, Dipalma G, Podo Brunetti S, Cagiano R: Combined occlusal and pharmacological therapy in the treatment of temporo-mandibular disorders. Eur Rev Med Pharmacol Sci 2011;15:1296-1300 [PubMed: 22195362]

Marini 2010
Marini I, Gatto MR, Bonetti GA: Effects of superpulsed low-level laser therapy on temporomandibular joint pain. Clin J Pain 2010;26:611-616 [PubMed: 20664343]

Marini 2012
Marini I, Bartolucci ML, Bortolotti F, Gatto MR, Bonetti GA: Palmitoylethanolamide versus a nonsteroidal anti-inflammatory drug in the treatment of temporomandibular joint inflammatory pain. J Orofac Pain 2012;26:99-104 [PubMed: 22558609]

Mejersjo 2008
Mejersjo C, Wenneberg B: Diclofenac sodium and occlusal splint therapy in TMJ osteoarthritis: a randomized controlled trial. J Oral Rehabil 2008;35:729-738 [PubMed: 18482350]

Minagi 2001
Minagi S, Shimamura M, Sato T, Natsuaki N, Ohta M: Effect of a thick palatal appliance on muscular symptoms in craniomandibular disorders: a preliminary study. J Oral Rehabil 2001;28:1129-1132 [PubMed: 11842840]

Minakuchi 2004
Minakuchi H, Kuboki T, Maekawa K, Matsuka Y, Yatani H: Self-reported remission, difficulty, and satisfaction with nonsurgical therapy used to treat anterior disc displacement without reduction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;98:435-440 [PubMed: 15472659]

Morey-Mas 2010
Morey-Mas M-A, Caubet-Biayna J, Varela-Sende L, Iriarte-Ortabe J-I: Sodium hyaluronate improves outcomes after arthroscopic lysis and lavage in patients with Wilkes stage III and IV disease. J Oral Maxillofac Surg 2010;68:1069-1074 [PubMed: 20144496]

Naikmasur 2008
Naikmasur V, Bhargava P, Guttal K, Burde K: Soft occlusal splint therapy in the management of myofascial pain dysfunction syndrome: a follow-up study. Indian J Dent Res 2008;19:196-203 [PubMed: 18797094]

Nguyen 2001
Nguyen P, Mohamed SE, Gardiner D, Salinas T: A randomized double-blind clinical trial of the effect of chondroitin sulfate and glucosamine hydrochloride on temporomandibular joint disorders: a pilot study. Cranio 2001;19:130-139 [PubMed: 11842864]

Nilsson 2007
Nilsson I-M: Reliability, validity, incidence and impact of temporormandibular pain disorders in adolescents. Swed Dent J Suppl 2007;183:7-86 [PubMed: 17506471]

Nilsson 2009
Nilsson I-M, Drangsholt M, List T: Impact of temporomandibular disorder pain in adolescents: differences by age and gender. J Orofac Pain 2009;23:115-122 [PubMed: 19492536]

Rizzatti-Barbosa 2003
Rizzatti-Barbosa CM, Martinelli DA, Ambrosano GMB, Albergaria-Barbosa JRde: Therapeutic response of benzodiazepine, orphenadrine citrate and occlusal splint association in TMD pain. Cranio 2003;21:116-120 [PubMed: 12723857]

Santos 2010
Santos TdeS, Piva MR, Ribeiro MH, Antunes AA, Melo AR, Silva EDdeOE: Lasertherapy efficacy in temporomandibular disorders: control study. Braz J Otorhinolaringol 2010;76:294-299 [PubMed: 20658006]

Schiffman 2007
Schiffman EL, Look JO, Hodges JS, Swift JQ, Decker KL, Hathaway KM, Templeton RB, Fricton JR: Randomized effectiveness study of four therapeutic strategies for TMJ closed lock. J Dent Res 2007;86:58-63 [PubMed: 17189464]

Stiesch-Scholz 2002
Stiesch-Scholz M, Fink M, Tschernitschek H, Rossbach A: Medical and physical therapy of temporomandibular joint disk displacement without reduction. Cranio 2002;20:85-90 [PubMed: 12002834]

Ta 2004
Ta LE, Dionne RA: Treatment of painful temporomandibular joints with a cyclooxygenase-2 inhibitor: a randomized placebo-controlled comparison of celecoxib to naproxen. Pain 2004;111:13-21 [PubMed: 15327804]

Thie 2001
Thie NM, Prasad NG, Major PW: Evaluation of glucosamine sulfate compared to ibuprofen for the treatment of temporomandibular joint osteoarthritis: a randomized double blind controlled 3 month clinical trial. J Rheumatol 2001;28:1347-1355 [PubMed: 11409130]

Truelove 2006
Truelove E, Huggins KH, Mancl L, Dworkin SF: The efficacy of traditional, low-cost and nonsplint therapies for temporomandibular disorder: a randomized controlled trial. J Am Dent Assoc 2006;137:1097-1107 [PubMed: 16873325]

Wahlund 2003
Wahlund K, List T, Larsson Bo: Treatment of temporomandibular disorders among adolescents: a comparison between occlusal appliance, relaxation training, and brief information. Acta Odontol Scand 2003;61:203-211 [PubMed: 14582587]

Wahlund 2003b
Wahlund K: Temporomandibular disorders in adolescents. Epidemiological and methodological studies and a randomized controlled trial. Swed Dent J Suppl 2003;164:2-64 [PubMed: 14717039]

Watanabe 1999
Watanabe M, Tabata T, Huh JI, Inai T, Tsuboi A, Sasaki K, Endo Y: Possible involvement of histamine in muscular fatigue in temporomandibular disorders: animal and human studies. J Dent Res 1999;78:769-775 [PubMed: 10096452]

Wieselmann-Penkner 2001
Wieselmann-Penkner K, Janda M, Lorenzoni M, Polansky R: A comparison of the muscular relaxation effect of TENS and EMG-biofeedback in patients with bruxism. J Oral Rehabil 2001;28:849-853 [PubMed: 11580823]

Winocur 2000
Winocur E, Gavish A, Halachmi M, Eli I, Gazit E: Topical application of capsaicin for the treatment of localized pain in the temporomandibular joint area. J Orofac Pain 2000;14:31-16 [PubMed: 11203735]

Yoda 2002
Yoda T, Imai H, Shinjyo Y, Sakamoto I, Abe M, Enomoto S: Effect of arthrocentesis on TMJ disturbance of mouth closure with loud clicking: a preliminary study. Cranio 2002;20:18-22 [PubMed: 11831339]

Yuasa 2001
Yuasa H, Kurita K: Randomized clinical trial of primary treatment for temporomandibular joint disk displacement without reduction and without osseous changes: a combination of NSAIDs and mouth-opening exercise versus no treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001;91:671-675 [PubMed: 11402280]

Ziegler 2003
Ziegler CM, Haag C, Muhling J: Treatment of recurrent temporomandibular joint dislocation with intramuscular botulinum toxin injection. Clin Oral Invest 2003;7:52-55 [Pubmed: 12673439]

Ziegler 2010
Ziegler CM, Wiechnik J, Muhling J: Analgesic effects of intra-articular morphine in patients with temporomandibular joint disorders: a prospective, double-blind, placebo-controlled clinical trial. J Oral Maxillofac Surg 2010;68:622-627 [Pubmed: 20171481]

3.5 Physiotherapy for Myofacial Pain

Description of the intervention: Physiotherapeutical treatments

Although the curriculum for the specialist therapeutic attention for TMD has not been yet defined, the physiotherapy is a common prescription by dentists for a multidisciplinary treatment. Physiotherapy for TMD may include jaw exercises, massage, muscle relaxation, and other more complex alternatives combining EMG-biofeedback, posture training among others [51].

Different series of jaw exercises have been proposed for the TMD therapy. The three principal modalities are passive, active, and isometric exercises.

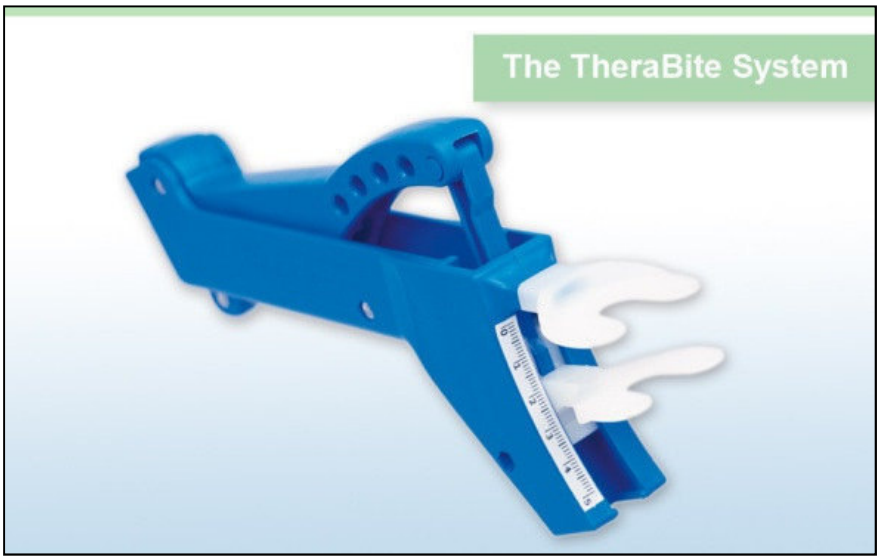

Figure 26. *Device for passive exercises Therabite® (left)*

The passive exercises focus on the improvement of the mouth opening through mechanical gradual jaw opening, whether manual or through devices such as Therabite® Jaw Motion Rehabilitation System (fig.26), OraStretch® Press, and Jaw Dynasplint® System. These patient-controlled devices are indicated for postsurgical interventions in the TMJ, trismus and myofacial pain, but not for patients with severe disc displacement [285, 379]. Likewise the positive results of manual exercises, e.g. mandibular manipulation, are apparently limited to patients with no advanced stages of disc displacement [310].

Concerning the active exercises, the patients repeat several times per day a sequence of maximal mandibular movements in excursive directions and mouth opening. The home-exercises have to be controlled with a mirror. The objective is to enhance the stretching capacity of the masticatory muscles [285].

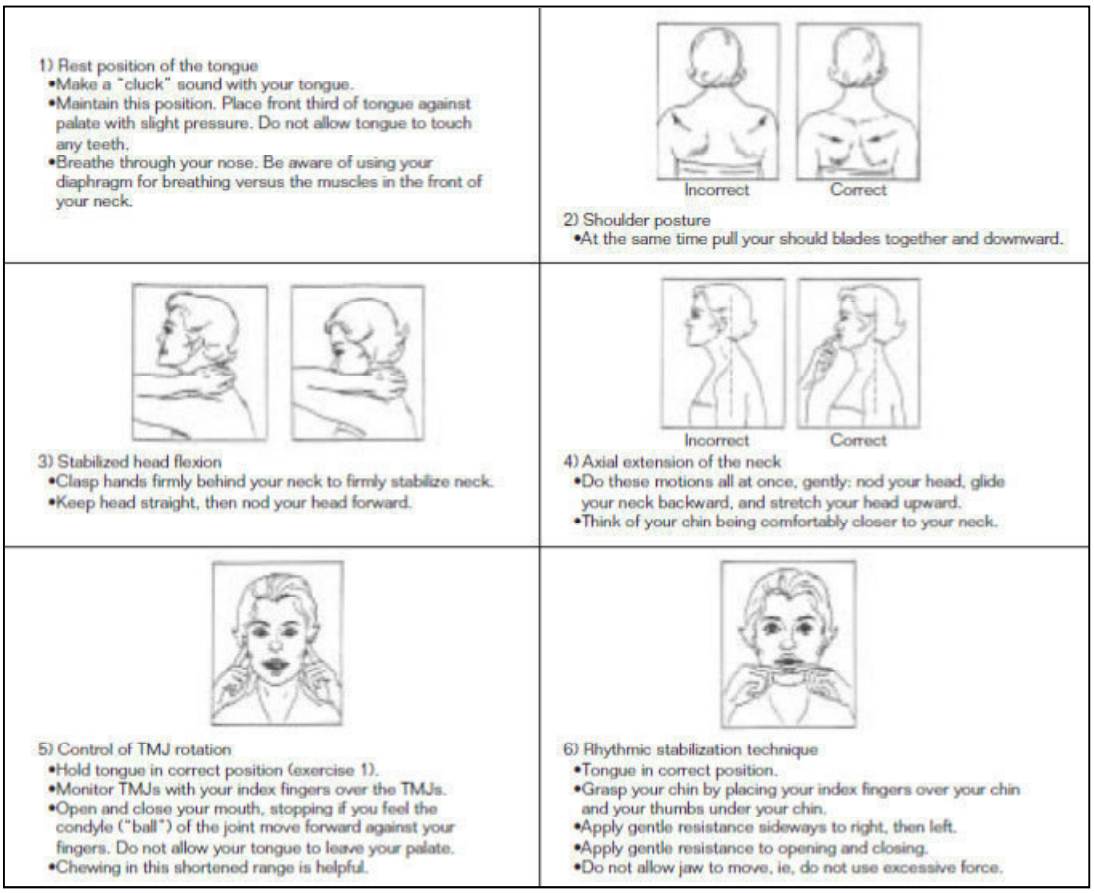

Figure 27. *Rocabados's 6x6 Exercise Program [404]*

Finally, the isometric exercises consist of jaw movements which are offset by opposing forces. As a result, the generation of this isometric contraction allows the normalization of the muscle activity through the relaxation of the contralateral muscle, reducing the symptomatology. *Rocabado* [477] proposed a series of exercises, called the 6x6 program (fig.27), which are based on different jaw movements with opposing resistance. A case-series of the application of 6x6 exercises as a therapy reported positive results in the treatment of TMD [138]. However, a clinical trial did not find any significant difference between patients under *Rocabado*'s 6x6 exercises program and self-care compared to a group receiving only self-care [404].

Some of the physiotherapeutical regimes have a cognitive-behavioral component in the sense of it aims to modify a parafunctional activity through the

awareness of it. In this approach, EMG-biofeedback was included due to the primarily effect on the muscular activity enhancing relaxation.

The EMG-biofeedback is based on the self-regulation of the muscular activity through the graphical methods. These allow the patient to be more conscious about his own boy motion. In the case of EMG, the electrical signal is represented as a graphic visual which describes the muscular contraction-relaxation phases.

In a meta-analysis, *Crider* and *Glaros* identified the EMG-Biofeedback to be efficient enough to manage TMD. 69% of the patients reported to be treated with EMG in the included clinical trials were successfully evaluated, against a 35% of improvement in the control cases [120].

How the intervention might work

Physiotherapy for TMD tackles the muscular activity of the masticatory muscles, and sometimes additionally the cervical and back muscle groups aiming to reduce pain and muscle contracture and the presence of trigger points. Two fundamental actions are expected: relaxation and /or improvement of the jaw motion range. Some of these articles allude directly to breaking off the neuromuscular "vicious cycle" theory.

Results of the search

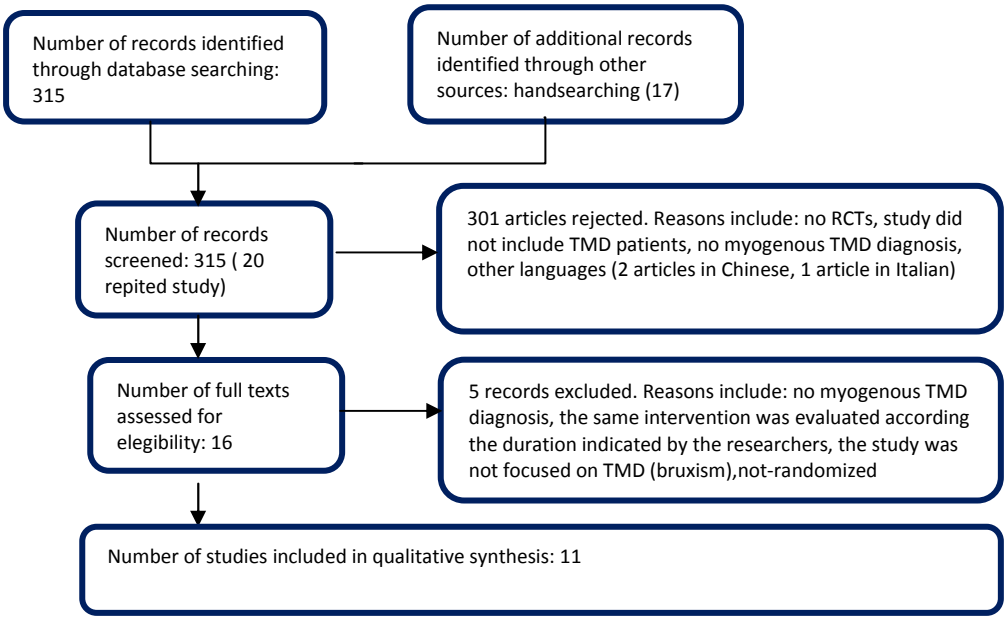

Diagram 4. *Study flow diagram: Physiotherapeutical modalities for the treatment of Myofacial Pain (1999-2012)*

Included studies

Jaw exercises were reported in all but one the physiotherapeutic RCTs including passive, active and isometric exercises. These exercises were indicated alone or in combination with other treatments.

A unique physiotherapeutic intervention consisting of jaw exercises was reported in four studies, and two studies applied specific formats for physiotherapeutic muscular exercises. The effectiveness of a protocol of jaw exercises consisting in isometric and stretching exercises were evaluated by *Magnusson1999*. In other study, *Tavera 2012* compared jaw stretching exercises and heat application with two groups, one receiving splint therapy, and other an experimental ear system device. Stretching exercises for the masticatory muscles, cervical spine, head and upper limbs were contrasted to global postural education by *Maluf 2010*. Other active jaw exercises using a controlled chewing protocol were tested by *Gavish 2006* in contrast with a control group.

Moreover, being a part of assisted therapies *Félicio 2010* applied Orofacial Myofunctional Therapy to treat TMD and compared the results with splint therapy, a non-treatment control group, and additionally a non-randomized non-symptomatic control group. On the other hand, *Wieselmann-Penkner 2001* contrasted a group under EMG-biofeedback therapy and other under a myomonitor training based on incremental dosages of Transcutaneous Electrical Nerve Stimulation (TENS).

Four other studies combined jaw exercises with other therapeutic techniques. A sequence of active exercises (stretching and range motion exercises) was compared in combination with low level laser therapy or placebo laser in the study by *Kulekcioglu 2003*. A similar protocol of physiotherapy was implemented in the study by *Truelove 2006*, but also adding self-care strategies and compared to other multi-approach therapy based on splint (later better analyzed in the section of „usual treatment“)

Other study reported on passive exercises using a patient-controlled device as a continuative therapy after splint therapy and jaw manual manipulation, compared to a wooden tongue depressor and a control group (*Maloney 2002*).

One study (*Kalamir 2012*), compared specific digital massages in the consultation room for 5 weeks (so called, intraoral myofacial therapy) with and

without self-care strategies and counseling (including stretching and isometric jaw exercises), using a non-treatment group as reference for a period of 12 months.
The RCT by *Wright 2000* was the only one not including jaw exercises, but posture training at short-term.

Excluded studies

All but two of the excluded studies did not match the criteria for the condition (s. Characteristics of excluded studies). Although the study by *Laat 2003* recruited myofacial pain patients, the intervention groups differed only in the duration of the same treatment. The intervention consisted in counseling and physiotherapy (stretching exercises, thermal packs, massage and ultrasound) in unlike protocols. One group of patients started the physiotherapy concomitantly with the counseling, while the other group first initiated 2 weeks after counseling. No statistical differences were found between the groups.
In the study by *Grace 2002*, two groups of patients received "usual treatment" (splint therapy+ self-care strategies, including home exercises and education+ analgesics); one of them adding an oral exercise device, while a third group of patients used the same device accompanied only by self-care strategies. The clinical improvements at the end of the treatment were not different between groups. The reason for exclusion was the generation of the random sequence. The randomization method can be regarded as a systematic non-random approach with a sequence generated by the order of admission of the patients (clearly inadequate according to Cochrane Handbook).

Effect of the intervention

The exclusive indication of jaw exercises was only reported by *Magnusson1999*. Although the outcomes were not statistically analyzed, the original scores are available showing a similar efficacy of jaw exercises and splint therapy for pain relief. The study by *Tavera 2012* added hot packs after a sequence of jaw stretching exercises which induced improvement in patients with myofacial pain. However these positive results, expressed only in percentage of changes from baseline, did not differ from the group using splint nor the group wearing a new device called TMD*es*.

Stretching exercises for jaw, neck and shoulders muscles indicated in the study by *Maluf 2010* enhanced pain scores and EMG-performance as like as the global postural training. Other active jaw exercises oriented to strengthening masticatory muscles did not prevail over a control group receiving counseling only. Nonetheless, in this study by *Gavish 2006*, the pain and functional electromyographic outcomes improved significantly within the experimental group only.

In the study by *Félicio 2010* the orofacial myofunctional therapy (OMT) and the splint therapy exhibited clinical improvements for the condition. As expected, both control groups, one symptomatic and other healthy matched group, did not change during the study. The OMT was superior to splint therapy for the next parameters: severity of signs and symptoms of muscular pain and TMJ pain; the frequency of headache; mandibular posture and tongue appearance/position, tongue, lip and mandible mobility; deglutition and mastication. In comparison to the non-treatment control group, the OMT was significantly more effective for the next outcomes: severity of muscular pain, TMJ pain, cervical pain, fullness and TMJ noise; frequency of muscle pain and tinnitus; mandibular posture and tongue appearance/position, tongue mobility, mastication, mandible mobility and deglutition. Interestingly, the OMT group approximated to the asymptomatic group at the end of the treatment in severity of otalgia, tinnitus, tooth sensitivity, fullness, difficulty to swallow and the performance of the orofacial myofunctional evaluation.

A therapy of muscle relaxation directed by visual representation of the electromyographic activity impacted akin to myomonitor training in the study by *Wieselmann-Penkner 2001*. In spite of the decrease in EMG-activity for both treatments, there were no significant changes within groups from baseline to the 1-month follow-up. The authors found only a relative higher EMG register for myomonitor training in one muscle compared to EMG-biofeedback.

In the next three RCTs, the impact of the physiotherapy is not completely distinguishable from the action of the other components of the combined therapy. Placebo, low level laser therapy or splint may have influenced the outcomes decisively.

Kulekcioglu 2003 reported analogous pain relief for jaw stretching exercises in combination with LLLT or placebo; however the mean changes of mouth ranges

increased significantly more for the group with LLLT. Myogenous and arthrogenous TMD diagnoses did not influence the results of the therapy.

The study of passive opening stretches and thermal packs into a strategy of self-care and counseling resulted as much effective as the other multi-approach alternatives including a hard or a soft splint. Pain scores dropped in all the groups equally, and range mandibular motion and tender zones upon palpation improved in like fashion between groups (*Truelove 2006*).

The participants in the study by *Maloney 2002* presented less than 35mm of mouth opening when diagnosed, and did not upgrade these values after 1 month of splint therapy and jaw facial manipulation. The subsequent replacement of this physiotherapeutic strategy for passive exercises was tested, but maintaining the splint action. The study showed better improvements for the group using a manual self-controlled device to increment the mandibular opening than the groups using wooden tongue depressors or a control group. The differences were significant for both arthrogenic and myogenic TMD patients.

In the study by *Kalamir 2012*, the self-care strategies and counseling caused a positive impact increasing the efficacy of the intraoral myofacial therapy (IMT) at long-term. Until 6-months follow-up, the improvements between groups were equivalent, while the control group did not experience any change during all the observation time. Nonetheless, the combination of IMT plus self-care strategies was significantly more effective for pain relief at 1-year follow-up than the only routine of massages, principally because it continued acting over the outcomes.

Posture training in the study by *Wright 2000* showed significantly more improvements than a control group with self-care-strategies. These improvements in TMD symptoms were correlated with neck pain relief, and with a greater postural difference between head and shoulders at baseline.

Quality of the evidence

The risk of bias according to the Cochrane Collaboration of the included studies is presented in figures 28 and 29. Three studies failed in the key criteria of risk of bias blinding of outcome assessment (*Félicio 2010*, *Magnusson1999*, *Tavera 2012*), and two other RCTs reported this item insufficiently (*Maloney 2002*, *Wieselmann-Penkner 2001*). These two latter studies published poorly the

details of the study design in almost every item, for instance they failed describing the inclusion criteria and demographics of the sample.

We consider not relevant the blinding of participants and personnel when therapies were different. Therefore, three RCTs were coincidentally good evaluated (*Kalamir 2012*, *Maluf 2010*, *Truelove 2006*).

The general positive accomplishment of the Delphi list (table 7) was 54.56%. RCTs with score 6 or higher were 36.36% of the included studies.

Study	Allocation random-ized	Allocation concealed	Groups similar at baseline	Inclusion criteria specified	Blind outcome assess-ment	Blinded care provider	Blinded patients	Point estimates and variability	Intention-to-treat analysis
Félicio 2010	Yes	Yes	Yes (randomized groups)	Yes	No	No	No	Yes	No
Gavish 2006	Yes	Don't know	Yes	Yes	Yes	No	No	Yes	Yes
Kalamir 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes (control group)	Yes	Yes
Kulekcioglu 2003	Yes	Don't know	Yes	No	Yes	No	Yes	Yes	No
Magnusson 1999	Yes	Yes	Don't know	Yes	No	No	No	No	No
Maloney 2002	Yes	Don't know	Don't know	No	Don't know	No	No	Yes	No
Maluf 2010	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
Tavera 2012	Yes	Don't know	Yes	Yes	No	No	No	No	No
Truelove 2006	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Wieselmann-Penkner 2001	Yes	Don't know	Yes	No	Don't know	Don't know	Don't know	Yes	No
Wright 2000	Yes	Don't know	Yes	Yes	Yes	No	No	Yes	No

Table 7: *Delphi list: Physiotherapeutical treatments for myofacial pain*

Characteristics of studies

Characteristics of included studies

Félicio 2010

Methods	RCT. Single center; four parallel groups. Follow-up for 120 days.
Participants	30 patients (randomized) + 10 healthy subjects (not randomized): mean age group A=31 (R=13-43), mean age group B=29 (R=17-64), mean age group C=34 (R=14-63), mean age group D=27 (R=18-68); 100% women. Inclusion criteria: long-lasting associated articular and muscular TMD based on the RDC/TMD, For control group: absence of TMD. Exclusion criteria: associated neurological or cognitive deficit, previous or current tumors or traumas in the head and neck region, and orthodontic treatment. Location: Brazil
Interventions	Group A (n=10): Oral myofunctional therapy (OMT) Group B (n=10): Occlusal splint Group C (n=10): Symptomatic control (no treatment) Group D (n=10): Asymptomatic control
Outcomes	Mandibular range motion TMJ function Muscle and TMJ tenderness to palpation Pain during movements. Perception regarding the disorder (Helkimo's Anamnestic Dysfunction Index and ProTMDMulti Protocol) Orofacial Myofunctional evaluation with scores (OMES Protocol)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "…using the GraphPad software"
Allocation concealment (selection bias)	Low risk	Not reported in article. From correspondence: central allocation managed by the leader author
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Unclear risk	Quote: "All subjects with TMD and AC subjects selected were considered for analysis"
Selective reporting (reporting bias)	Low risk	Include all the principal expected outcomes
Other bias	Low risk	Free of other bias

Gavish 2006

Methods	RCT. Single center; two parallel groups. Follow-up for 8 weeks.
Participants	20 patients: mean age group A=27.1 (±10.1); mean age group B=27.3 (±5.9); 100% women. Inclusion criteria: women; age 20-45; dolicocephalism face configuration; diagnosis myofacial pain (group Ia RDC/TMD), pain at least 6 months; sensitivity to palpation of muscle masseter (grade 2 or 3); masseter muscles that did not significantly increase in volume in maximal clench; natural dentition with no more than one missing tooth per quadrant, without dental diseases; and increased pain during a chewing test ≥ 15/100 VAS. Exclusion criteria: TMJ disease or disorder; systemic chronic disease or continuous use of medication; history of trauma to the facial or cervical regions; previous treatment for MFP during the last 6 months. Location: Israel
Interventions	Group A (n=10): Exercise chewing group Group B (n=10): Control (only support and encouragement)
Outcomes	Present Pain (VAS) Pain intensity (CPI) Pain relief scale (PRS)(VAS) Mean muscle sensitivity to palpation (MMS)(0-4 scale at four sites of masticatory muscles) Disability score. EMG during maximal voluntary clench Pain level at end of chewing phase of the chewing test (VAS)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: “Patients were randomly divided into two age-matched groups“
Allocation concealment (selection	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote:”Examiners were blinded to the patient group affiliation”
Incomplete outcome data (attrition bias)	Low risk	No drop outs. Quote: “All participating patients appeared for follow-up appointments.”
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Kalamir 2012

Methods	RCT. Single center; three parallel groups. Follow-up for 6 months.
Participants	93 patients: mean age group A=35 (6.7), mean age group B=34 (6.1), mean age group C=35 (5); 53.76% women. Inclusion criteria: age range 18-50 yrs; daily history of periauricular pain with or without joint sounds for at least 3 months; voluntary participation, and a willingness to contribute long-term follow-up data; myogenous TMD (RDC/TMD); minimum baseline graded chronic pain scale (GCPS) scores of 3/10 on each of the three symptom outcome measures. Exclusion criteria: previous attendance at the practitioners clinic, edentulous; history of malignancy in the last 5 yrs; other physical contraindications such as active inflammatory arthritide, fractures,

	dislocations, or known instability of the jaws or neck; metabolic diseases; connective tissue and rheumatologic disorders; hematological disorders; severe depression or somatization according to axis II RDC/TMD. Location: Australia
Interventions	Group A (n=10): waiting-list control group Group B (n=10): 2 weakly 15-min of intra-oral myofacial therapies for 5 weeks Group C (n=10): Intra-oral myofacial therapy (IMT) + self-care
Outcomes	Resting pain (11-point GPCS)* Pain at maximum opening Pain during clenching Inter-incisal opening range (mm.-calliper)
Notes	From correspondence: GCPS was defined as a 11-point Likert-scale, not including any calculation with disability or pain interference scores

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a web-based random number generator and consecutively allocated each numbered participant file to1 of the 3 groups... consecutive participants were block randomized using a pregenerated schedule into 3 groups"
Allocation concealment (selection bias)	Low risk	Quote: " (receptionist) prepared files, and consecutively numbered them for allocation. These numbers were used to allocate the patients by an assistant blinded to assessments."
Blinding of participants and personnel (performance bias)	Low risk	Quote: "The practitioner (primary author) was blinded to the randomization schedule and assessment outcomes until the conclusion of the study". The control group was also blinded
Blinding of outcome assessment (detection bias)	Low risk	Quote*:* "assessor, who was blinded to group allocation..."
Incomplete outcome data (attrition bias)	Low risk	Quote: "with one dropout in the control group after 6 months, citing impatience with "being in the wait-list" Other participants generally complied well with their scheduled appointments... The data were analyzed on an intention to treat basis replacing missing values with baseline figures."
Selective reporting (reporting bias)	Low risk	Low risk Australian Clinical Trials Register, registration no.ACTRN12610000329066 http://www.anzctr.org.au/trial_view.aspx?id=320772 High consistency with previous report (279)
Other bias	Low risk	Free of other bias

Kulekcioglu 2003

Methods	RCT. Single center, two parallel groups. Follow-up for 1 month
Participants	35 participants: mean age= 37.0 ±12.3 years (R=20-59); 80%women Inclusion criteria: orofacial pain, TMJ sounds, limited mouth opening, or TMJ locking Exclusion criteria: congenital abnormality, concomitant inflammatory or neoplastic conditions, and those with a recent history of acute trauma or

	any form of treatment within the last month Location: Turkey
Interventions	Group A (n=20): LLLT (15 sessions of LLLT + program consisting of range of motion exercises, stretching exercises and postural training) Group B (n=15): placebo (laser not turned on + program of range of motion exercises, stretching exercises and postural training)
Outcomes	Pain intensity (VAS) Number of tender points and joint sounds Maximal active and passive mouth opening, right and left lateral jaw motion (mm)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were then randomly assigned..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Unclear risk	Participants but not personnel were blinded. Incomplete blinding
Blinding of outcome assessment (detection bias)	Low risk	Quote: "All patients were evaluated by the first investigator who was blinded to treatment groups."
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Magnusson1999

Methods	RCT. Single center; two parallel groups. Follow-up for 6 months
Participants	26 patients: mean age group A=37 (R=16-67); mean age group B=32 (R=20-50) Inclusion criteria: myogenous TMD patients; patients referred to specialist clinic where the main subjective symptom was tension-type headache and/or orofacial pain of non-neurogenic or non-dental origin; history of pain of at least one year. Exclusion criteria: previous TMD treatment; general disease affecting the masticatory system; obvious morphological or functional malocclusion. Location: Sweden
Interventions	Group A (n=14 [9]): Michigan stabilization appliance, wore during night Group B (n=12 [9]): therapeutic jaw exercises (stretching and proprioceptive neuromuscular facilitation)
Outcomes	Helkimo Clinical dysfunction index: Impaired mandibular mobility; impaired TMJ function; TMJ pain; muscle pain; pain on movement Helkimo Anamnestic Index: Joint sound; tiredness in jaws; difficulty in opening the mouth; pain when opening the mouth; pain in the face or jaws.
Notes	After 3 months, some of the patients (n=8) were assigned to a combined treatment.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The patients were randomly assigned to receive either jaw exercises or interocclusal appliance therapy” From correspondence: shuffled envelopes
Allocation concealment (selection bias)	Unclear risk	Not reported in article From correspondence: “When a patient fulfilled the inclusion criteria, we opened an envelope and checked what treatment the patient was to receive.”
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Low risk	Reasons for missing data are unlikely related to true outcome, and are balanced in groups
Selective reporting (reporting bias)	Low risk	Include all expected outcomes. The authors follow a standardized functional examination in their research.
Other bias	Low risk	Free of other bias

Maloney 2002

Methods	RCT. Single center; three parallel groups. Follow-up for 4 weeks.
Participants	35 participants Location: USA
Interventions	Group A: Therabite device Group B: Wooden tongue depressors (1.25 mm in thickness and 14 mm width; two tongue depressors were placed bilaterally between the upper and lower teeth, and tongue depressors were added to gently force mouth opening and achieve a moderate stretch.) Group C: Control Cointervention: stabilization splint for all groups, 1 month previous and continuing during the the allocated intervention
Outcomes	Pain (NRS) Jaw opening, lateral and protrusive movements
Notes	Therabite Corporation supported by a grant this study

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were allocated randomly..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed

Incomplete outcome data (attrition bias)	High risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	No sufficient information
Other bias	High risk	Authors did not state conflict of interest with the Therabite Corporation

Maluf 2010

Methods	RCT. Single center; two parallel groups. Follow-up for 8 weeks.
Participants	28 patients: mean age group A=30.0 (±4.3), mean age group B= 30.08 (±7.07); 100% women; 8.33%higher education Inclusion criteria: chronic pain (duration N3 months), Helkimo index III, myogenic TMD, and presence of parafunctional habits, such as bruxism, teeth clenching, mouth breathing, and lip biting. Exclusion criteria: surgery or trauma in the orofacial region; systemic or degenerative diseases in spine and upper limbs; and undergoing odontologic, psychologic, or physical therapy treatments. Location: Brazil
Interventions	Group A (n=14 [12]): Global posture reeducation (8sessions 30min. global stretching with 2 postures for 15 min. each) Group B (n=14 [12]): Static stretching (8 sessions 30min. static stretching treatment with stretching positions for 30sec. and slow breathing) Cointervention: 10 min. manual therapy maneuvers associated to breathing exercises, to stretch the fasciae that recover the shoulders, as well as the cervical spine muscles
Outcomes	Severity symptoms for TMJ pain, headache, cervicalgia, teeth clenching, ear symptoms, restricted sleep, and restricted mastication (VAS) Pain thresholds (PPT) measured in the masseter, anterior temporalis, sternocleidomastoid, and upper trapezius muscles EMG activity in the masseter, anterior temporalis, sternocleidomastoid, and upper trapezius muscles
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Shuffling envelopes Quote: “(subjects)… were randomized, by means of opaque envelopes, into 2 treatment groups….”
Allocation concealment (selection bias)	Low risk	Quote: “…randomized, by means of opaque envelopes…”
Blinding of participants and personnel (performance bias)	Low risk	Participants and personnel not blind, but the outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: *“All evaluations and interventions were made …by an experienced investigator previously trained and blinded.”*
Incomplete outcome data (attrition bias)	Low risk	Quote: “…4 subjects abandoned treatment for work-related reasons” Balanced attrition between groups, for similar reasons.
Selective reporting (reporting bias)	Low risk	Include all expected outcomes

Other bias	Low risk	Free of other bias

Tavera 2012

Methods	RCT. Single center, three parallel groups. Follow-up for 3 months
Participants	152 enrolled [out of 175 randomized] participants: mean age=37.2; 84.03% women Inclusion criteria: jaw pain or dysfunction; completed informed consent process; RDC/TMD diagnosis (at least one of the following: myofascial pain, arthralgia, disc displacement with reduction); presence of one or more of the following findings associated with pain as demonstrated with a VAS score of >4: increased (>60 mm) or decreased (<40 mm) range of interincisal jaw opening, pain upon any jaw movement, pain on digital palpation (~1 lb. pressure) of the periauricular area or external auditory meatal areas, pain on digital palpation (~1 lb. pressure) in two or more muscles of mastication, or joint sound with pain. Excluded criteria: diagnosis of rheumatoid arthritis, osteoarthritis, osteoarthrosis or another connective tissue disorder; history of direct trauma to the jaw; use of an occlusal appliance to treat a TMD within the previous six months; prior TMJ or ear surgery; physical or behavioral disorder, which, in the opinion of the principal investigator, would interfere with the use of the device or compliance with the study protocol; unsuitable ear canal anatomy (e.g., congenital deformity) not allowing for fit of the study device; use of a narcotic pain medication in the last seven days, or aspirin or a nonsteroidal anti-inflammatory agent in the last 24 hours; a history of ear pain unrelated to TMJ; a history of ear drainage in the past two years; active ear drainage, swelling, or redness as observed on targeted physical exam; not an appropriate candidate for an intraoral splint due to missing or poor quality dentition or untreated pain of dental origin.
Interventions	Group A (n=60): TMDes (ear system) device (all day wearing) Group B (n=64): stabilization splint (nocturnal wearing) Group C (n=28): jaw exercise + heat application for 10 min.
Outcomes	Craniomandibular Index Pain (VAS) Sunbjective pain (Symptom Severity Index [SSI]) TMJ Scale
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection	Unclear risk	Quote: "...were randomly assigned..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding.
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Unclear risk	Missing data balanced in groups. Reasons not reported
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Truelove 2006

Methods	RCT. Single center; three parallel groups. Follow-up for 12 months.
Participants	200 patients: mean age group A=36 (±11), mean age group B=36 (±11), mean age group C=35 (±12); 86% women; 75.5% education more than high school; 8.5% race Nonwhite; mean number of yrs. with facial pain group A=5±5, mean number of yrs. with facial pain group A=6±9, mean number of yrs. with facial pain group A=5±6 Inclusion criteria: age 18-60 yrs.; RDC/TMD Axis I diagnosis of myofacial pain (Group Ia or Ib) with or without a concurrent diagnosis of arthralgia (Group IIIa) or disk displacement with reduction (Group IIa), as well as an RDC/TMD Axis II Graded Chronic Pain score of Grade I (low pain) or Grade II (high pain), both of which had no or minimal pain-related psychosocial interference. Exclusion criteria: any other RDC/TMD Axis I diagnosis (for example, arthritis, disk displacement without reduction); any systemic arthritis or other serious medical complications, full dentures; major psychological disorders; current satisfactory use of splint; no local language skills Location: USA
Interventions	Group A (n=64): usual treatment (self-care: jaw relaxation, reduction of parafunction, thermal packs, NSAIDs, passive opening stretches and suggestions about stress reduction) Group B (n=68): usual treatment + hard splint in centric occlusion nocturnal wearing and two additional hours daily while awake throughout the three-month and twelve-month follow-up Group C (n=68): usual treatment + soft splint in centric occlusion, nocturnal wearing and two additional hours daily while awakw throughout the three-month and twelve-month follow-up
Outcomes	Self report findings: CPI; pain duration; self reported TMD symptoms (TMJ clicking/popping sounds, TMJ grating sounds, TMJ locking/catching, tinnitus, jaw clenching-diurnal, jaw clenching-nocturnal, limitation in chewing). Clinical examination: range of motion (assisted and unassisted jaw opening); joint sounds; muscle and TMJ palpation pain (number of sites); RDC/TMD diagnoses
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “We generated randomization assignments using randomly selected block sizes of six, nine or 12 and stratified them by provider.”
Allocation concealment (selection bias)	Low risk	Quote: “We concealed randomization to all study personnel until after we obtained the subjects’ consent“
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The research dental hygienists conducting follow-up data collection were blinded to subject treatment group“

Incomplete outcome data (attrition bias)	Low risk	Quote: "…we took a conservative approach of carrying forward the last observation if the subject dropped out before month 12." Intent-to-treat analysis. Attritions reported and analyzed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Wieselmann-Penkner 2001

Methods	RCT. Single center; two parallel groups. Follow-up for 4 weeks.
Participants	20 patients: age (R=22-58); 65% women Inclusion criteria: bruxism; pain and tenderness to palpation of the masticatory muscles for at least 6 months pain Exclusion criteria: evidence of joint pathology Location: Austria
Interventions	Group A (n=10): Biofeedback-training (reduction of EMG activity with the help of visual feedback for 10 min masseter muscle and 10 min temporalis muscle with a pause of 3 min) Group B (n=30): Myomonitor-training (Transcutaneous Electrical Neuromuscular Stimulation [TENS] with pulses of approx. 0-5 msec duration at a frequency of 1-5 s, during a 5 min warming-up period (facial twitching), then gradually increased until the mandible performed symmetrical contractions and was left at this setting throughout a 20 min-period of rest)
Outcomes	Electromyographic (EMG) levels and skin conductance level (SCL)
Notes	Patients were defined as myofascial pain syndrome patients in the abstract of the article

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "…they were randomly assigned to the BFB or the myomonitor (MM)-treatment groups."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Unclear risk	Not addressed
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed
Incomplete outcome data (attrition bias)	Unclear risk	Not addresed
Selective reporting (reporting bias)	Unclear risk	No sufficient information
Other bias	High risk	No precise description of TMD diagnosis criteria

Wright 2000

Methods	RCT. Single center, two parallel groups. Follow-up for 4 weeks (2 weeks treatment)
Participants	61 patients: mean age= 31.75yrs.; 85% women Inclusion criteria: TMD muscle disorder diagnosis (RDC/TMD); at least 6 months of TMD pain; rated pain at least moderate in severity; the patient must live within a 90-minute drive from the clinic; no current treatment for TMD at the onset of the study; myogenous TMD.
Interventions	Group A (n=30): 2 30-min. sessions of posture training Group B (n=30): control group (no additional treatment) Cointerventions: both groups received TMD self-management instructions (rest recommendations, awareness of oral habits ; thermal packs; over-the -counter anti-inflammatory medication)
Outcomes	Modified SSI Maximum pain-free opening PPT
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The subjects were then randomized into two groups"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Quote: "The examiner was blinded to the assigned groups and the subjects in the treatment group..."
Incomplete outcome data (attrition bias)	High risk	One patient withdrew, however no information about the group at which allowed is available
Selective reporting (reporting	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Footnotes

Characteristics of excluded studies

Augustine 2008

Reason for exclusion	This study is not focused on TMD.

Craane 2012

Reason for exclusion	No myogenous TMD patients

Diracoglu 2009

Reason for exclusion	No myogenous TMD patients

Félicio 2008

Reason for exclusion	No myogenous TMD patients

Gavish 2002

Reason for exclusion	Not randomized

Grace 2002

Reason for exclusion	Non-random approach reported: "Systematic randomization" according to patient's admission

Haketa 2010

Reason for exclusion	No myogenous TMD patients

Laat 2003

Reason for exclusion	This study compares the same intervention with different durations

Sato 2008

Reason for exclusion	No myogenous TMD patients

Watanabe 2011

Reason for exclusion	This RCT evaluated clenching habits in bruxist patients.

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

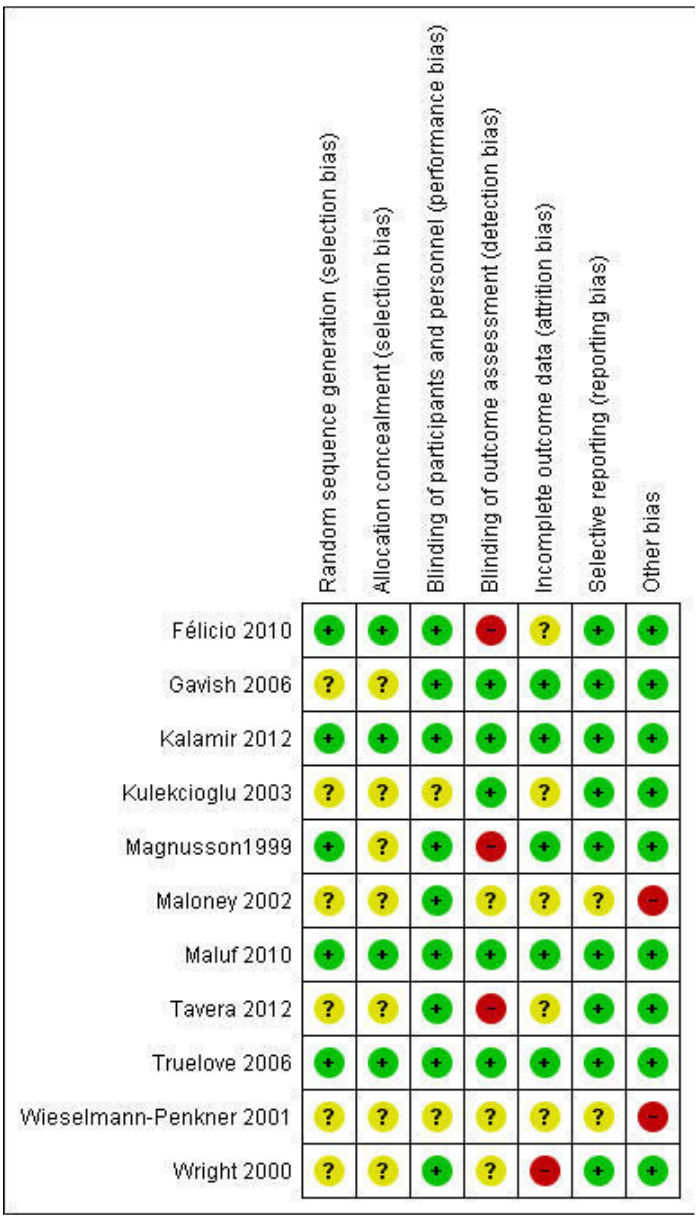

Figure 28: *Risk of bias summary*

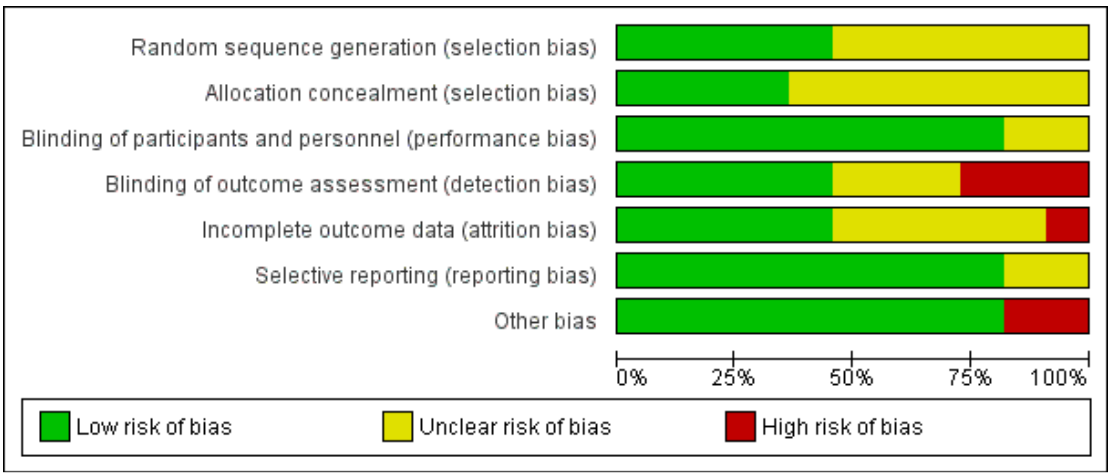

Figure 29*: Risk of bias graph: review authors' judgements*

References to studies

Included studies

Félicio 2010
Félicio CMde, Oliveira MMde, da Silva MAMR: Effects of orofacial myofunctional therapy on temporomandibular disorders. Cranio 2010;28:249-259 [PubMed: 21032979]

Gavish 2006
Gavish A, Winocur E, Astandzelov-Nachmias T, Gazit E: Effect of controlled masticatory exercise on pain and muscle performance in myofascial pain patients: A pilot study. Cranio 2006;24:184-190 [PubMed: 16933459]

Kalamir 2012
Kalamir A, Bonello R, Graham P, Vitiello AL, Pollard H: Intraoral myofascial therapy for chronic myogenous temporomandibular disorder: a randomized controlled trial. J Manipulative Physiol Ther 2012;35:26-37 [PubMed: 22079052]

Kulekcioglu 2003
Kulekcioglu S, Sivrioglu K, Ozcan O, Parlak M: Effectiveness of low-level laser therapy in temporomandibular disorder. Scand J Rheumatol 2003;32:114-118 [PubMed: 12737331]

Magnusson1999
Magnusson T, Syren M: Therapeutic jaw exercises and interocclusal appliance therapy. A comparison between two common treatments of temporomandibular disorders. Swed Dent J1999;23:27-37 [PubMed: 10371003]

Maloney 2002
Maloney GE, Mehta N, Forgione AG, Zawawi KH, Al-Badawi EA, Driscoll SE: Effect of a passive jaw motion device on pain and range of motion in TMD patients not responding to flat plane intraoral appliances. Cranio 2002;20:55-66 [PubMed: 11831346]

Maluf 2010
Maluf SA, Moreno BGD, Crivello O, Cabral CMN, Bortolotti G, Marques AP: Global postural reeducation and static stretching exercises in the treatment of myogenic temporomandibular disorders: a randomized study. J Manipulative Physiol Ther 2010;33:500-507 [PubMed: 20937428]

Tavera 2012
Tavera AT, Montoya MCP, Calderon EFGG, Gorodezky G, Wixtrom RN: Approaching temporomandibular disorders from a new direction: a randomized controlled clinical trial of the TMDes ear system. Cranio 2012;30:172-182 [PubMed: 22916669]

Truelove 2006
Truelove E, Huggins KH, Mancl L, Dworkin SF: The efficacy of traditional, low-cost and nonsplint therapies for temporomandibular disorder: a randomized controlled trial. J Am Dent Assoc 2006;137:1099-1007 [PubMed: 16873325]

Wieselmann-Penkner 2001
Wieselmann-Penkner K, Janda M, Lorenzoni M, Polansky R: A comparison of the muscular relaxation effect of TENS and EMG-biofeedback in patients with bruxism. J Oral Rehabil 2001;28:849-853 [PubMed: 11580823]

Wright 2000
Wright EF, Domenech MA, Fischer JR: Usefulness of posture training for patients with temporomandibular disorders J Am Dent Assoc 2000;131:202-210 [PubMed: 10680388]

Excluded studies

Augustine 2008
Augustine C, Makofsky HW, Britt C, Adomsky B, Deshler JM, Ramirez P, Douris P: Use of the Occivator for the correction of forward head posture, and the implications for temporomandibular disorders: a pilot study. Cranio 2008;26:136-143 [PubMed: 18468273]

Craane 2012
Craane B, Dijkstra PU, Stappaerts K, Laat Ade: Randomized controlled trial on physical therapy for TMJ closed lock. J Dent Res 2012;91:364-369 [PubMed: 22318373]

Diracoglu 2009
Diracoglu D, Saral IB, Keklik B, Kurt H, Emekli U, Ozcakar L, Karan A, Aksoy C: Arthrocentesis versus nonsurgical methods in the treatment of temporomandibular disc displacement without reduction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:3-8 [PubMed: 19272808]

Félicio 2008
Félicio CMde, Oliveira MMde, Ferreira CLP, Da Silva MAMR: Otologic symptoms of temporomandibular disorder and effect of orofacial myofunctional therapy. Cranio2008;26:118-125 [PubMed: 18468271]

Gavish 2002
Gavish A, Winocur E, Astandzelov-Nachmias T, Gazit E: Effect of controlled masticatory exercise on pain and muscle performance in myofascial pain patients: A pilot study. J Orofac Pain 2002;16:22-28 [Pubmed: 16933459]

Grace 2002
Grace EG, Sarlani E, Reid B: The use of an oral exercise device in the treatment of muscular TMD. Cranio 2002;20:204-208 [PubMed: 12150267]

Haketa 2010
Haketa T, Kino K, Sugisaki M, Takaoka M, Ohta T: Randomized clinical trial of treatment for TMJ disc displacement. J Dent Res 2010;89:1259-1263 [PubMed: 20739691]

Laat 2003
Laat Ade, Stappaerts K, Papy S: Counseling and physical therapy as treatment for myofascial pain of the masticatory system. J Orofac Pain 2003;17:42-29 [PubMed: 12756930]

Sato 2008
Sato S, Kawamura H: Evaluation of mouth opening exercise after pumping of the temporomandibular joint in patients with nonreducing disc displacement. J Oral Maxillofac Surg 2008;66:436-440 [Pubmed: 18280374]

Watanabe 2011
Watanabe A, Kanemura K, Tanabe N, Fujisawa M: Effect of electromyogram biofeedback on daytime clenching behavior in subjects with masticatory muscle pain. J Prosthodont Res 2011;55:75-81 [PubMed: 21130060]

3.6 Occlusal appliances for myofacial pain

Description of the intervention A: Occlusal appliance (splint)

Widely indicated by dentists, the splint therapy is the most commonly used treatment for TMD. It consists of the elaboration of a removable device named oral appliance, occlusal appliance, occlusal plane, or splint which supposedly stabilizes the dental occlusion. The classical fabrication of a splint implies the reproduction of the occlusal condition of the patient using models, which are later positioned in an articulator with the help of a facebow. The use of facebow, however, seems to be clinically irrelevant [520]; actually some authors proposed methods to avoid the mounted casts in order to simplify the laboratory processes [59]. The final objective is to generate a device theoretically able to modify the occlusal relationships.

Dentist specialized in TMD classify the occlusal appliances according to inherent qualities of the device, for instance the material, or according to the clinical indication. The simplest division refers to the material of confection for the splint, namely hard or soft. The typical dental material is acrylic, and the hard type is extensively indicated for myofacial pain.

According to the possibility of the teeth for displacement once the splint has been installed, the occlusal appliance are categorized in permissive and non-permissive or directive splints [129, 160]. Depending on the principal purpose they are divided in: bite planes, stabilization planes, repositioning planes, and pivot appliance. The next brief description of different splint types compiles concepts of the three before mentioned classifications:

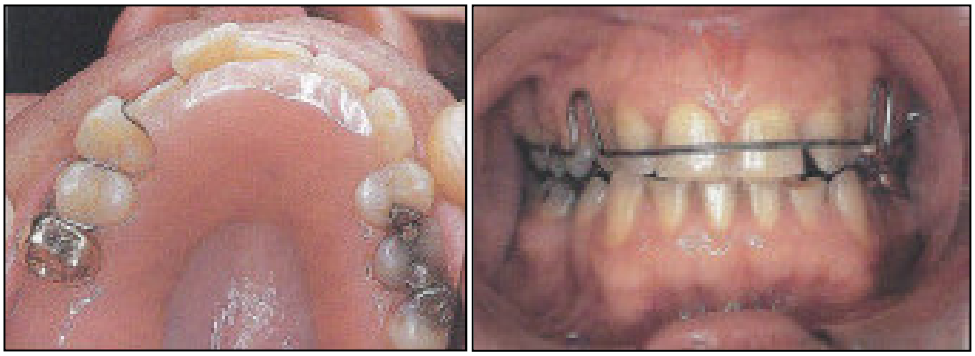

Figure 30. *Bite plane: Hawley splint (intraoral and frontal view)[51]*

- **Bite planes** (relaxation splints) (fig.30) are permissive splints in pursuit of the masticatory muscles deprogramming, removing, theoretically, the engrams, and increasing the vertical dimension. These planes are designed to be used only for a limited time, because they may cause permanent loss of the posterior occlusal contact. Although they generate marked changes in EMG-activity [501], they are not considered a treatment option for TMD, due to the chronicity of this condition. Examples are Sved plate or relaxation plane; Hawley splint; anterior jig; and Lucia jig, a prefabricated version of jig.

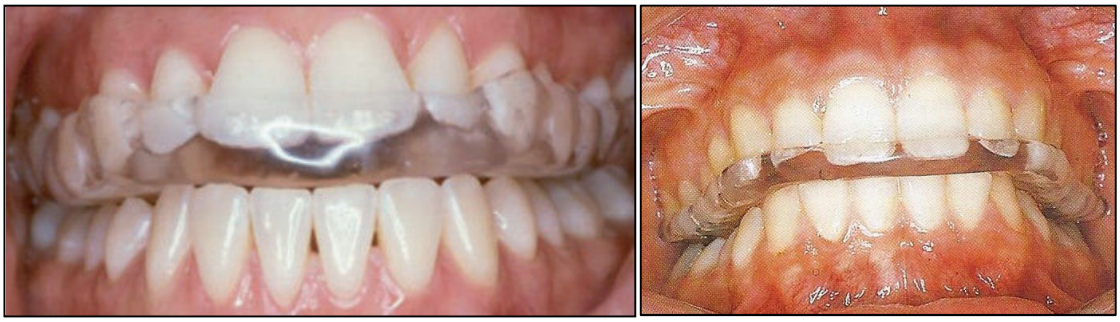

Figure 31. *Stabilization splint (left)* [Doepel 2012, included study]: *Michigan splint (right)* [51]

- **Stabilization splints** (fig.31) are permissive planes aimed to recover the occlusal stability, inducing muscular deprogramming and increase of the vertical dimension. This splint is the first election for bruxism and temporomandibular dysfunctions. Some kinds of stabilizations appliances are the flat plane, Michigan Tanner splint, superior repositioning, Shore splint, and centric relation splint.

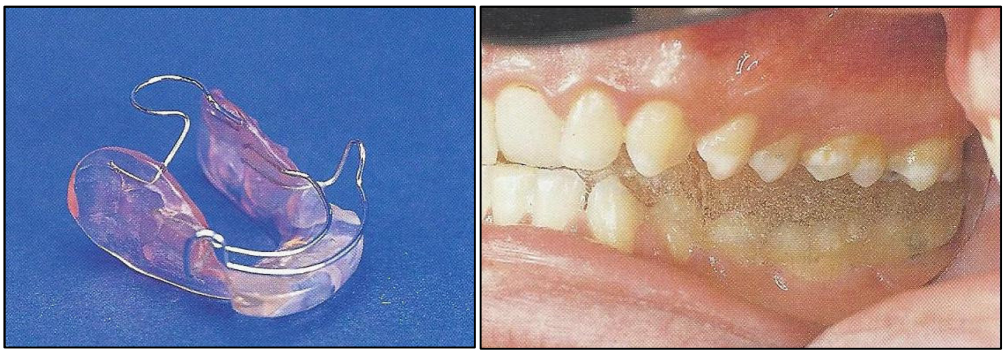

Figure 32. *Repositioning splint: Bionator (left);*
anterior repositioning splint in resilient material (right) [51]

- **Repositioning splints** (fig.32) are non-permissive splints, characterized for the mechanical retentions aimed to fix the relationship between the opposite

arches and the position of the condyle. Amongst these planes are the advancement appliance; partial posterior as MORA; centric relation plane; and some orthopedic devices such as Doppelplate, Bionator, Rick-a-nator, and modified Herbst.

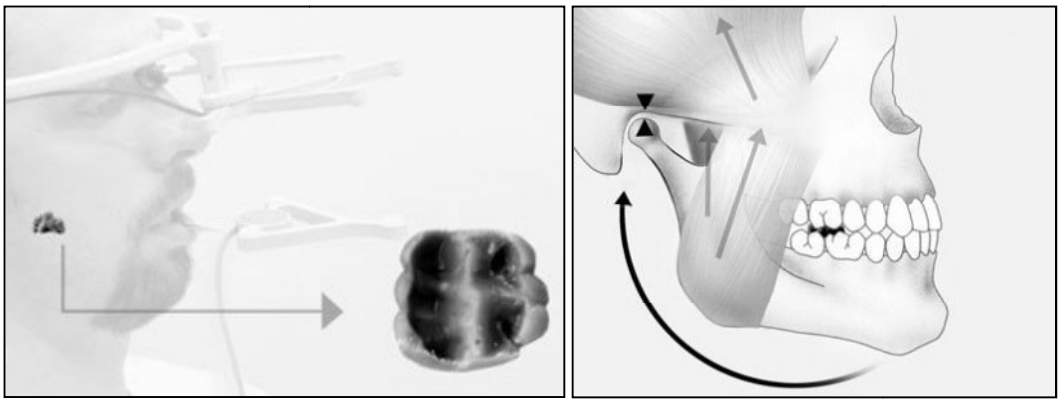

Figure 33: *effect of condylar upward torque using a posterior pivot* [513]

- **Distraction splints** (fig.33), also named pivot or pivoting appliances are non-permissive splints which intend occlusal decoupling (anterior pivot appliance) or load relieving (posterior pivot appliance).

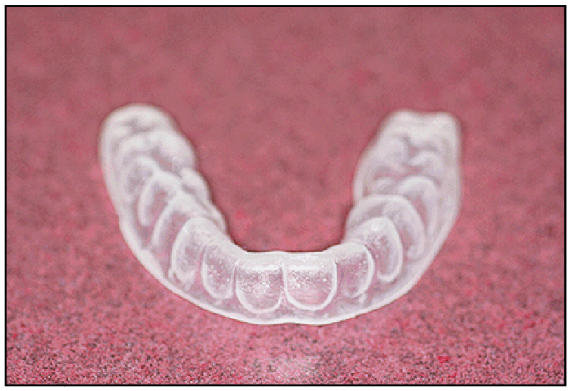

Figure 34*. resilient splint* [645]

- Some new acrylic materials, recently available in market, represent an intermediate or semi-permissive category, namely the **soft splints** (fig.34). Maybe a predecessor of soft splints, and also semi-permissive is the hydrostatic appliance. The active part of a hydrostatic appliance consisted of a water-filled acrylic allowing free jaw accommodation. The hydrostatic splint is currently commercialized with the name Aqualizer®.

Soft or resilient splints are semi-permissive splints allegedly effective for TMD [409, 411], but seldom indicated in Germany [437]. A recent high quality RCT does not attribute any clinical efficacy for short- and long-term TMD treatment [417, 419].

The clinical data about splint therapy is controversial. *Forssell* found in a systematic review only scarce evidence for the clinical efficacy of splint therapy [192]. Similarly, a meta-analysis concluded neither advantage nor disadvantages of the splint therapy when compared to other treatments, and only little evidence to be effective when contrasted to no treatment [29]. In other review no sufficient evidence was found to recommend occlusal appliances neither for TMD nor for bruxismus [305]. On the contrary, other reviews support the indication of occlusal appliances for myofacial pain and arthralgia. They suggest that the success of the splint therapy may be attributed to behavioural modifications [308].

Neff and *Gündel*, however, hold the view that the splint therapy would be useful only for disorders with dento-occlusal origin (according to the classification of TMD by *Sebald*). For the cases based on myogenic or arthrogenic causes, this oral appliance had a time-restricted effect or no effect at all [412].

Moreover, little evidence support the use of splint for bruxism, an allegedly risk factor for TMD. Some clinical studies did not found any improvement after a splint therapy for bruxism [38]. Likewise, *van Selms et al.* suggested that changes on nocturnal electromyographic activity of bruxer patients could be more assigned to psychological effects than the splint influence [587]. Even the use of oral appliances has not proved to produce any immediate significant change on the electromyographic activity of masticatory muscles [497, 474].

Nonetheless, extensive literature supports the use of occlusal appliances for TMD patients [51, 432, 284, 86]. The stabilization planes have shown to be more effective for myofacial pain than non-treatment or a control non-active intervention [166]. Besides, the stabilization splint was also related to improvement in the treatment of arthrogenous TMD [165]. In other study, patients with disc derangement acquired a better muscular bilateral equilibrium immediately after using splint [184]. Finally, many studies reported that the principal effect of therapies with occlusal appliances is pain relief.

How the intervention might work: Occlusal appliance

The exact therapeutic effect of the oral appliances is not yet understood. The multiple influences on the masticatory system may include the variation of the relationship between the dental occlusion and the mandible; the redistribution of jaw dynamic and chewing forces; changes on the condylar position related to the temporal glenoid fossa and articular disc; relaxation of the chewing musculature; etc. Some authors ruled out the primary belief that splint could increase the joint space diminishing the articular overloading [309, 394, 177]. Other hypothesis points out that the splint acts as reminder of oral habits, therefore reducing the parafunctional activity [215].
In general, the splint therapy targets a symptomatic reduction of the clinical pain, an improvement of the occlusal force distribution [311], reducing teeth wear and attrition [235], and the stabilization of occlusal contacts.

According to their clinical indication, there are three types of oral appliances [440]:

- **Relaxing – stabilization splint**: indicated for myopathy, oral habits (bruxism), insufficient occlusal support, and reestablishment of vertical dimension. By reason of the probably psychological origins of the oral habits, the use of stabilization splint for this purpose has a preventive roll, focused on the protection of the anatomical dental integrity.
Pre-fabricated splints are adjustable to resemble stabilization splints.
- **Distraction splint**: indicated for total anterior disc displacement without reposition, osteoarthritic structural changes on TMJ, and disc perforation. Distraction splints aim pain relief of the temporomandibular joint through vertical spacing of the articular cavity (approx. 0.6-1.0 mm expected). This effect has been retracted by many authors [513].
- **Repositioning splint** (decompression splint): indicated for partial lateral or anterior disc displacement with reposition. This therapy passes into orthodontics or prosthetic rehabilitation procedures, und it must be indicated only associated with painful symptomatology.

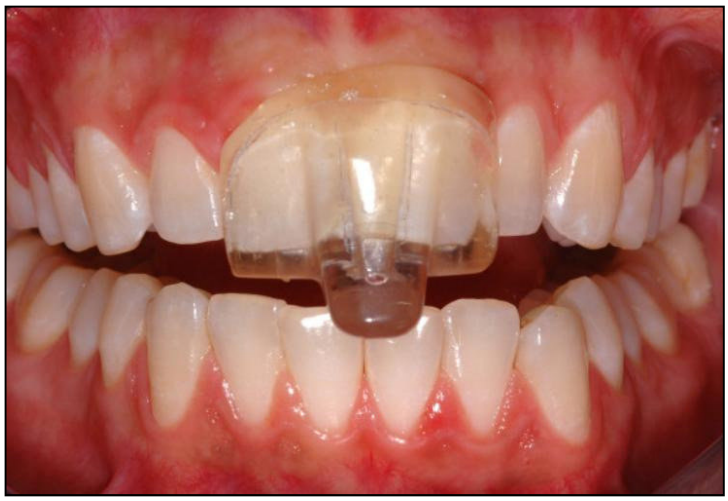

***Figure 35**. NTI-tss splint [644]*

Fabricants of specific splint designs offer their own explanations about the effectiveness of the devices. Some special functioning has been described for the Nociceptive Trigeminal Inhibitory (NTI-tss) splint (fig.35) adducing a direct effect over the neurosystem by activating the tension suspension system (tss). Besides, others claim a specific mechanism of action of the hydrostatic appliances based on the properties of the fluid inside the device inducing a redistribution of the occlusal forces.

Results of the search

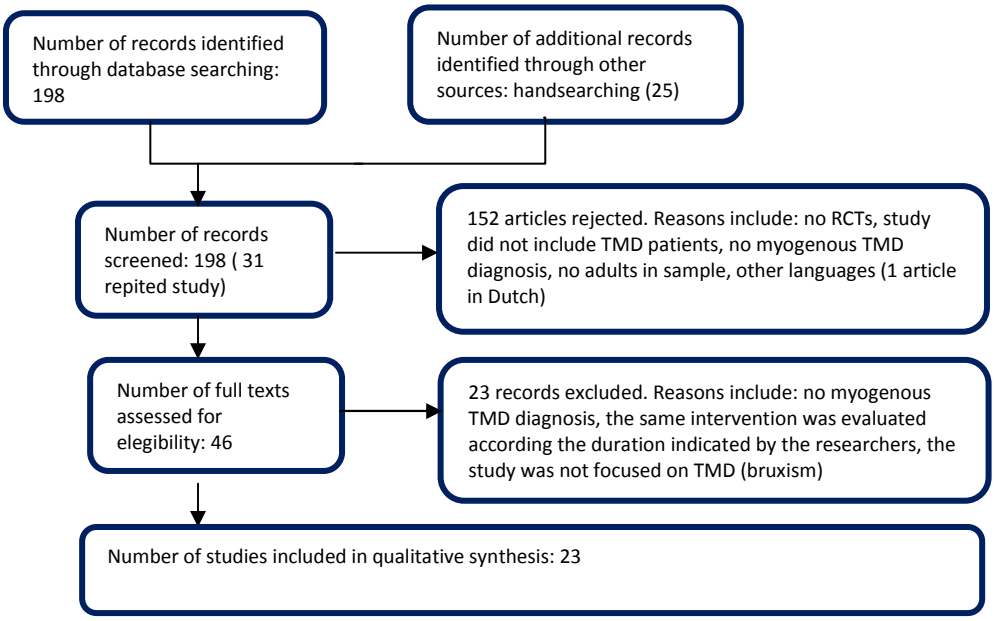

***Diagram 5**: Study flow diagram: Splint therapy for Myofacial Pain (1999-2012)*

Included studies

Coincidental to the before exposed clinical indications for occlusal appliances, after restriction of this review to studies including myofacial pain diagnoses, the included articles reported mainly on stabilization splint. During the period 1999-2012 we found only few reports considering other occlusal appliances types for myofacial pain, namely resilient splints, decompression splints, pre-fabricated splints, and Nociceptive Trigeminal Inhibitory (NTI) splints.

Stabilization splint was considered for intervention in twenty one (21) studies. *Alencar 2009* and *Wassell 2004* studied mandibular occlusal appliances. On the other hand, fourteen (14) studies indicated a maxillary (upper coverage) variation of splint therapy (*Carlson 2001*, *Conti 2012*, *Daif 2012*, *Doepel 2012*, *Ekberg 2004*, *Félicio 2010*, *Jokstad 2005*, *Magnusson 1999*, *Michelotti 2012*, *Öz 2010*, *Ozkan 2011*, *Raphael 2001*, *Tavera 2012*, *Truelove 2006*). The authors did not declare specific information in the description of the splint or images related to the splint position in both studies by *Dworkin 2002a*, *Dworkin 2002b* ("typically fabricated" intraoral flat plane occlusal appliance), in the study by *Kuttila 2002* ("flat stabilization splint"), in the study by *Litt 2010* ("flat-plane disoccluding splint"), nor in the study by *Magnusson 2004* ("stabilization appliance").

The effectiveness of exclusive use of stabilization splints was measured by *Carlson 2001*, *Daif 2012*, *Doepel 2012*, *Ekberg 2004*, *Félicio 2010*, *Kuttila 2002*, *Magnusson 1999*, *Magnusson 2004*, *Michelotti 2012*, *Öz 2010*, *Ozkan 2011*, *Tavera 2012*, and *Wassell 2004*.

All the rest of RCTs of stabilization splints complemented their action with psychosocial interventions, for instance self-care strategies, counseling and others. *Raphael 2001*, for example, confronted the clinical effectiveness of the stabilization splint plus self-care strategies with a non-occluding splint type.

Seven studies applied the combination stabilization splint, self-care strategies and counseling matching our definition of "usual treatment" which is further analyzed in the meta-analysis (Part 4). *Jokstad 2005* compared this "usual treatment" with a combination of NTI splint and the same self-care strategies and counseling. *Alencar 2009* indicated for all the three intervention groups (stabilization splint, resilient splint and a non-occluding splint) a cointervention consisting of self-care and counseling. *Conti 2012* designed one intervention

group using this formula of “usual treatment”, while the other two groups received the same counseling and self-care strategies, one of them also wearing NTI splints. Similarly, *Truelove 2006* opposed “usual treatment” to other two groups using the self-care strategies and counseling assigning to one of these groups also a soft splint. Both studies by *Dworkin* (*Dworkin 2002a, Dworkin 2002b*) compared the “usual treatment” with conservative treatments including counseling, self-care strategies and cognitive behavioral therapy (CBT) as a coadjuvant or as a therapy itself correspondingly. *Litt 2010* conducted a RCT dividing patients who received this "usual treatment" adding CBT and EMG-biofeedback to one of the groups.

Regarding other types of occlusal appliances, *Nilsson 2011* reported on resilient splints vs. a control non-occluding splint, while *Alencar 2009* compared the mentioned “usual treatment” with resilient splint and a non-occluding splint. NTI-tss splints were studied by *Jokstad 2005* and *Conti 2012*. Additionally, *Doepel 2012* tested pre-fabricated splints; and *Vicente-Barrero 2012* conducted a RCT comparing acupuncture to a decompression splint.

Excluded studies

The reasons for exclusion are presented in the section Characteristics of the excluded studies.

Effect of the intervention

Among the included studies, multiple comparisons were distinguishable. The author describes separately the principal effect of each splint.

Stabilization splint vs. no-treatment: *Daif 2012* measured EMG activity in two groups who were not identical at baseline. Besides, the clinical outcomes were summarized in a Helkimo diagnostic index. As a consequence no extractable information was available from this study. In the study by *Félicio 2010* clinical improvements were registered for the stabilization splint group and no changes for the no-treatment group, however no significant differences were detected for clinical signs of TMD at the follow-up control.

Stabilization splint vs. non-occluding appliance: No differences between groups with active or placebo splints in the study by *Alencar 2009* were possibly

attributable to the co-intervention consisting of self-care strategies and counselling (see stabilization splint vs. soft splint). In the study by *Ekberg 2004* the stabilization splint exhibited more effectiveness for overall symptomatic relief at 6 months- and 1-year follow-up. Unsatisfied patients in the control group were assigned after requirement to a mixed group to receive the splint therapy. At 1 year follow-up only the same outcome, overall symptomatic relief, brought differences. All the patients improved, with a 30% reduction of myofacial pain in 60% of patients in the stabilization splint group, 68% in the control group, and 63% in the mixed group at 1-year follow-up.

Kuttila 2002 observed a decrease on prevalence and intensity of secondary otalgia, TMD signs, and frequency of headaches within the group of patients using stabilization splint, but not in the control group. None of these outcomes differed significantly between groups.

Likewise, in the study by *Wassell 2004* the mandibular stabilization splint did not differ from the mandibular non-occluding plane decreasing actual pain and number of tender zones, and increasing the maximal mouth opening at 6-weeks follow-up. Non-responders were referred to other center for occlusal adjustment. The quality of this study was poor.

Stabilization splint vs. resilient splint: *Alencar 2009* observed general improvements for both therapies without significant differences (neither between them nor with non-occluding appliance).

Stabilization splint vs. pre-fabricated splint: *Doepel 2012* concluded that both splint act similarly reducing pain; and improving jaw limitation, depression and non-specific physical symptoms scores. 82.14% of the patients with myofacial pain wearing a pre-fabricated splint experienced 30% of pain reduction at 6 months, rising to 96.2% at 12-month follow-up; while the corresponding percentages of patients in the stabilization group were 91.6% and 95.45%.

Stabilization splint vs. NTI splint: in the study by *Conti 2012*, no differences were reported between both splint therapies in pain relief, with similar positive effects. Other measurements including pressure pain threshold and number of occlusal changes did not show important modifications. In spite the similar improvements in some clinical outcomes for both splints; *Magnusson 2004* claimed no

satisfaction of the half of the patients who received the NTI appliance at 6-months follow-up.

Stabilization splint vs. low level laser therapy (see review Low Level Laser Therapy for myofacial pain): in the study by *Öz 2010* splint raised the range of jaw motion and reduced pain as much as the LLLT. However, most patients in the splint group were symptomless after the treatment (85%) in comparison with 55% patients without pain after a shorter therapy with LLLT.

Stabilization splint vs. Physiotherapy (see review Physiotherapeutic treatments for myofacial pain): *Félicio 2010* reported improvements within the group of stabilization splint for clinical signs, severity of TMJ pain, and some components of an orofunctional evaluations related to TMJ noise, tooth sensitivity and appearance of the cheeks. However, the myofunctional therapy was more effective regarding other items of the myofunctional evaluation. Besides the myofunctional therapy presented better scores at 4-months follow-up of the ProTMD-Multi part II which measure clinical sign and symptoms of TMD.
In the study by *Magnusson 1999*, although both splint and jaw exercises showed improvements, the therapies did not distinguish one from each other about their effect on myofacial pain patients. However, the sample was very limited and only for the items of the anamnestic Helkimo index and the item muscle pain from the clinical dysfunction index at least 50% of the patients reported pain or discomfort at baseline. In similar manner, the study by *Tavera 2012* exhibited the same effectiveness for pain relief between stabilization splint, jaw exercises and a third therapy using a portable ear's device.
These three studies failed to accomplish the item of blinding of outcome assessment.

Stabilization splint vs. Stabilization splint and pharmacological agents (see review Drugs for myofacial pain): *Ozkan 2011* reported that splint therapy was efficient in time to reduce pain, however the experimental group showed significant better improvements at 12 weeks follow-up reducing pain during jaw movements, number of trigger points and intensity of pain.

Stabilization splint vs. Psychosocial interventions (see review Psychosocial interventions for myofacial pain): *Carlson 2001* were equally effective for pain relief and pain interference, however jaw opening performance increased mostly after a physical self-regulation therapy. Affective distress and obsessive-compulsive scores decreased significantly for both groups, but not different one from each other. All the other psychological outcomes did not vary during the study time in any group.

Other psychosocial intervention in the study by *Michelotti 2012* consisted of counselling and self-care strategies including jaw exercises inspired in oral habit reversal. Interestingly this psychosocial intervention was as effective as the stabilization splint to increase the pain-free mouth opening, and across the time its effect on spontaneous muscle pain was significant as opposed to the no time-effect of the splint at the third month follow-up.

Stabilization splint plus self-care strategies vs. Non-occluding splint plus self-care strategies: in the RCT by *Raphael 2001* the type of splint was irrelevant to explain the improvements in average pain and muscle pain upon palpation. Only the (log) least pain report favoured significantly the active group at 6-weeks follow-up.

Usual treatment vs. Psychosocial interventions (see meta-analysis of "usual treatment" vs. Psychosocial interventions for myofacial pain and review Psychosocial interventions for myofacial pain): *Conti 2012* contrasted the clinical performance of a group receiving counseling and self-care strategies with a group under "usual treatment" (stabilization splint + self-care strategies + counselling, with or without additional medicaments). The results were not different in respect of the pain scores; however, about 88% of the patients with usual treatment halved the initial VAS pain, while only 33% of the counseling group reached this clinical goal.

Dworkin 2002a reported a better performance of the "usual treatment" when combined with CBT to reduce pain intensity and to increase coping abilities in patients with high scores of psychological distress according to the scores of Graded Chronic Pain (GCP). For patients with lower GCP, the parallel RCT conducted by *Dworkin 2002b* showed that a tailored "usual treatment" was less

effective than SC+CBT decreasing pain intensity, pain interference, and number of painful sites.

In other study by *Truelove 2006*, no greater advantages were noticed for any of the three treatments based on a common intervention of self-care strategies and counseling, thus without making difference the addition or not of a stabilization or a soft splint.

In the RCT by *Litt 2010* the "usual treatment" was more effective when reinforced by cognitive behavioural therapy and EMG-biofeedback in pain reduction; however no differences were reported between groups for psychological outcomes.

Usual treatment vs. NTI splint plus self-care strategies and counseling: *Jokstad 2005* found one approach as effective as the other. Both combination of splints and conservative treatment resulted in improvement in TMD- related pain, jaw muscle tenderness upon palpation, and jaw opening range.

Resilient splint vs. non-occluding splint: *Nilsson 2011* observed significant pain relief and improvements in jaw functioning equally for both groups at 6- and 12-months follow-up. It is remarkable that although the psychological outcomes depression and somatisation decreased significantly for both groups at the 6-months follow-up, these effects extended to the next semester only in the control group. Occlusal changes were registered in three patients of the control group and none of the experimental group. 50% of the patients wearing the resilient splint experienced a 30% reduction of pain scores, while 42% of the control group achieved this goal at 12-months follow-up.

Decompression splint vs. acupuncture (see review Acupuncture for myofacial pain): *Vicente-Barrero 2012* found significant improvements within group receiving the traditional Chinese acupuncture, but not in the splint group. Nonetheless no analyses between groups are available. This study however presents a poor quality, therefore the evidence becomes weak.

Quality of the evidence

The risk of bias of the included studies according to the Cochrane Collaboration is presented in fig. 36 and 37. Five studies failed in the item of blinding of outcome assessment which was considered relevant for this systematic review (*Félicio 2010*; *Magnusson 1999*; *Tavera 2012*; *Vicente-Barrero 2012*; *Wassell 2004*). According to the Delphi list 78.95% of the RCTs accomplished this item. Two of those trials were evaluated at high risk of bias in mostly of the criteria for both Collaboration's tool and Delphi list (*Vicente-Barrero 2012*; *Wassell 2004*). 21.74% of the trials showed selective reporting, and around 40% of the studies were at unclear or high risk of bias for the items allocation concealment and incomplete outcome data.

Two RCTs did not conduct any analyses, but published the original data (*Magnusson 1999*; *Magnusson 2004*)

The general positive accomplishment of the Delphi list was 58.0%. RCTs with score 6 or higher were 52.63% of the included studies.

Study	Allocation randomized	Allocation concealed	Groups similar at baseline	Inclusion criteria specified	Blind outcome assessment	Blinded care provider	Blinded patients	Point estimates and variability	Intention-to-treat analysis
Alencar 2009	Yes	Don't know	Yes	Yes	Yes	No	Yes	Yes	No
Carlson 2001	Yes	No	Yes	Yes	Yes	No	No	Yes	No
Conti 2012	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
Daif 2012	Yes	Don't know	No	Yes	Don't know	No	No	Yes (EMG only)	Don't know
Doepel 2012	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Dworkin 2002a	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Dworkin 2002b	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Ekberg 2004	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Félicio 2010	Yes	Yes	Yes (randomized groups)	Yes	No	No	No	Yes	Don't know
Jokstad 2005	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
Kuttila 2002	Yes	No	Yes	Yes	Yes	No	Yes	No	No
Litt 2010	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Magnusson 1999	Yes	Yes	Yes (data of original groups)	Yes	No	No	No	No (original data)	No
Magnusson 2004	Yes	Yes	Yes	Yes	Yes	No	No	No (original data)	No
Michelotti 2012	Yes	Don't know	Yes	Yes	Yes	No	No	Yes	No
Nilsson 2011	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes

Öz 2010	Yes	No	Yes	Yes	Yes	No	No	Yes	No
Ozkan 2011	Yes	Don't know	Yes	Yes	Don't know	No	No	Yes	Don't know
Raphael 2001	Yes	Don't know	Yes	Yes	Yes	No	Don't know	Yes	No
Tavera 2012	Yes	Don't know	Yes	Yes	No	No	No	No	No
Truelove 2006	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Vicente-Barrero 2012	Don't know	Don't know	Don't know	Yes	No	No	No	No	Don't know
Wassell 2004	Yes	Don't know	Yes	Yes	No	No	Don't know	Yes	No

Table 8. *Delphi list: Occlusal appliances for myofacial pain*

Characteristics of studies

Characteristics of included studies

Alencar 2009

Methods	RCT. Single center; three parallel groups. Follow-up for 90 days.
Participants	42 (out of 45) patients: mean age (analyzed) = 34 (R=18-65), mean age group A=39 (R= 24-65), mean age group B=33 (18-52), mean age group C=31 (18-51); 88.10% women. Inclusion criteria: age 18-65 years; diagnosis of myofascial pain with reproduction of the chief complaint with palpation of a trigger point in the masseter muscle; at least six natural teeth in each quadrant. Exclusion criteria: previous splint therapy; any obvious dental decay or periodontal disease; history of trauma in the pain area in less than 30 days; any systemic condition associated with widespread pain (e.g. fibromyalgia); medical history of current drug addiction; any other TMD diagnosis according to the Diagnosis Criteria of the AAOP such as TMJ osteoarthritis or capsulitis. Location: Brazil
Interventions	Group A (n=14): mandibular hard occlusal splint adjusted to create contact of the centric cusps against splint with anterior guidance, full time wearing during the first week and after this period, only nocturnal wearing + counseling Group B (n=14): mandibular soft occlusal splint adjusted to create contact of the centric cusps against splint (no possible anterior guidance), full time wearing during the first week and after this period, only nocturnal wearing + counseling Group C (n=14): non-occluding splint, full time wearing during the first week and after this period, only nocturnal wearing + counseling
Outcomes	Intensity, frequency and pain duration using the Modified Symptom Severity Index (Mod-SSI) Intensity of pain to palpation (4-point scale)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: “Selection bias was considered through a defined and concealed randomization process with rather and subject blind of group assignment. Patients were randomly assigned into one of the three experimental groups…”
Allocation concealment (selection bias)	Unclear risk	Quote: “…concealed…” (s. random sequence generation)
Blinding of participants and personnel (performance bias)	Low risk	Participant but not personnel blind. Incomplete blinding, but outcome is not likely to be be influenced by this lack. Quote: “…subject blind of group assignment… “Splint installation, adjustment and follow-up were carried out by a researcher who knew to which group the patients belonged.”

Blinding of outcome assessment (detection bias)	Low risk	Quote: "Another 'blind' researcher collected the data."
Incomplete outcome data (attrition bias)	Low risk	Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups Quote: "Three patients dropped out (one from each group) and the main reason for this was that they were feeling better, with no necessity to come back to the University."
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Carlson 2001

Methods	RCT. Single center; two parallel groups. Follow-up for 26 weeks.
Participants	44 participants [out of 56 enrolled]: mean age analysed sample=34.6; 77.27% women; average months of pain duration=52.3. Inclusion criteria: myofascial pain (Type 1a and Type 1b) according to the RDC/TMD: chief complaint originating from the masticatory muscles; pain for longer than 1 month; pain to palpation of at least 3 standard muscle sites. Initial medication usage was not altered during the study. Location: USA
Interventions	Group A (n=21 [13 completers]): standard dental care (splint as described by *Okeson* (401), nocturnal wearing + self-care strategies [e.g. soft diet, jaw relaxing]) Group B (n=23 [19 completers]): two 50min. sessions of physical self-regulation (strategies for seven domains: monitoring and reducing muscle parafunction in the head and neck region, proprioceptive awareness training to improve symmetric head and neck posture, instructions for improving sleep onset, position oriented relaxation training, physical activity, nutrition/fluid management, and diaphragmatic breathing training)
Outcomes	Pain measures: MPI; daily pain self-rating (VAS); pain severity (7 points-scale); life interference; life control Physical examination: opening with and without pain; muscle pain index; awareness of tooth contact. Psychological variables: SCL-90-R; affective distress (MPI); fatigue 0-10 scale); sleep dysfunction (Pittsburgh Sleep Quality Index)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:"Random assignment was accomplished by the use of a table of random numbers."
Allocation concealment (selection bias)	Unclear risk	Not reported in the article From correspondence: "The evaluators and the professionals delivering the treatment were not a part of the assignment procedures but the table was open for the researchers to re*view."*

Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “A board-certified dentist with postdoctoral training in orofacial pain who was not aware of the treatment protocol to which each participant was assigned performed all initial dental evaluations and administered the self-report measures after the dental evaluations."
Incomplete outcome data (attrition bias)	Low risk	Detailed explanations for withdrawals. Missing outcome data balanced, and reasons unlikely to be related to true outcome. From correspondence: “26 weeks-analysis included only the completers” “As treated” analysis in a recall of the patients
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Conti 2012

Methods	RCT. Single center, three parallel groups. Follow-up for 3 months
Participants	51 participants: mean age 37.16yrs; 88.23% women. Inclusion criteria: adults aged 18 yrs. or more; diagnosis of myofascial pain with or without opening limitation (RDC/TMD); pain intensity of at least 50mm in VAS. Exclusion criteria: dental pain or tender muscles due to systematic diseases; major psychological disorders; recent history of face and neck trauma; current TMD treatment; denture wearers. Location: Brazil
Interventions	Group A (n=21): Stabilization appliance only nocturnal wearing + counseling (habits and behavioral changes)+ education. Group B (n= 16): NTI appliance + counseling + education. Group C (n=14): counseling only
Outcomes	Pain intensity (VAS) Pressure Pain Threshold (PPT) Number of occlusal contacts
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:“…patients were randomly allocated” From correspondence: “Randomization was done using a computer program (Excel)"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	The same blinded examiner conducted the follow-up Quote: “using a “blind” design with no awareness of the individuals group"

Incomplete outcome data (attrition bias)	Unclear risk	Insufficient report of attrition
Selective reporting (reporting bias)	High risk	Not all the primary outcomes were appropriately reported
Other bias	Low risk	Free of other bias

Daif 2012

Methods	Single center, two parallel groups. Follow-up for 6 months
Participants	40 participants: age ranged 22-46yrs.; 57.7%women Inclusion criteria: TMD with myofascial pain diagnosed by the presence of a nonteeth-related chronic orofacial pain with localized areas of tenderness in the masticatory muscles Exclusion criteria: any systemic neurological or muscular diseases that may influence the EMG records; and presence of pathological changes involving the components of the TMJ Location: Egypt
Interventions	Group A (n=20): stabilization splint (nocturnal wearing for 6 months Group B (n=20): control no-treatment (education about TMD and acceptance of wait-list status)
Outcomes	EMG Helkimo Index
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:"...performed using a computer-generated random number list."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible binding
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed Comments: probably not done
Incomplete outcome data (attrition	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	No sufficient information
Other bias	High risk	No treatment control group received a non-standardized education session

Doepel 2012

Methods	RCT.Multicenter; two parallel groups. Follow-up for 12 months.
Participants	65 patients: mean age group A=37 (R=20-63); mean age group B=36 (R=18-71); 89.23% women; 80% Scandinavian, 13.85% other Europeans, 6.15%. Asian, mean months of duration of pain group A= 80, mean months of duration of pain group B= 50 Inclusion criteria: age ≥ 18 years; pain of muscular origin with or without limited opening according to the RDC/TMD; self-assessed worst myofascial pain of at least 4 on a graded numeric rating scale (NRS); duration of pain at least 3 months. Exclusion criteria: TMJ pain; complete dentures use; symptoms related to

	disease in other components of the stomatognathic system (e.g., toothache, neuralgia); whiplash diagnosis; diagnosed systemic muscular or joint disease (e.g., fibromyalgia, rheumatoid arthritis); history of psychiatric disorders; periodontal problems; use of complete denture; previous treatment with an occlusal appliance; presence of idiopathic orofacial pain Location: Sweden and Finland
Interventions	Group A (n=32): pre-fabricated appliance Relax® individually fitted with self-curing silicone, nocturnal wearing Group B (n=33): stabilization appliance, nocturnal wearing
Outcomes	Reduction of worst pain intensity (VAS) Graded Chronic Pain Scale Functional limitation (Jaw Function Limitation Scale [JFLS-20]) Pressure pain threshold (PPT) Overall improvement Depression (SCL-90-R) Somatization
Notes	*Doepel* (147) report salivary cortisol and IgA levels in a subset of the RCT sample. *Nilner* reported the short-term results from this RCT in 2008 (415)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Shuffling envelopes
Allocation concealment (selection bias)	Low risk	Quote: “One independent person (D2) at each clinic carried out the randomization by using 10 series of consecutively numbered, sealed, opaque envelopes. Each envelope contained a treatment specification. The last series included 6 envelopes (3 for each treatment modality). This randomization procedure was repeated until 66 patients were included in the study.”
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias)	Low risk	Quote: “A single examiner at each university, blinded to the treatment groups, performed all clinical examinations and gave information and counselling.”
Incomplete outcome data (attrition bias)	Low risk	ITT analysis. Dropouts reported. Missing data balanced in number and with similar reasons across groups
Selective reporting (reporting bias)	High risk	The outcomes are not completely coincident between the reports of short- and long-term
Other bias	Low risk	Free of other bias

Dworkin 2002

Methods	RCT. Single center; two parallel groups. Treatment for 4 months, follow-up for 12 months.
Participants	117 patients: mean age 38.8 (SD=10); mean age group A= 38.6 (SE=1.3), mean age group B=39.3 (SE=1.4); 82,91% women; education level higher than high school 72.65% Inclusion criteria: age 18-70 yrs.; facial pain in the masticatory muscles, TMJ, region in front of the ear or inside the ear; RDC/TMD Axis II GCP score of II High, III, or IV.

	Exclusion criteria: pain attributable to confirmed migraine or head pain condition other than tension headache; acute infection or other significant disease of the teeth, ears, eyes, nose, or throat; debilitating physical or mental illness; necessity for emergency TMD treatment; no local language skills Location: USA
Interventions	Group A (n=59 [56 completers]): comprehensive care ("usual treatment" + cognitive behavioral therapy (CBT) and methods employed in multidisciplinary management of chronic pain including exercises for jaw stretching and jaw muscle relaxation) Group B (n=58 [51 completers]): "usual treatment" (at the discretion of the attending dentist: intraoral occlusal appliance + physiotherapy + medication + patient education including self-care behaviors)
Outcomes	Characteristic pain Intensity (CPI) Pain interference score (0-10) Ability to control pain (0-6) Somatization (SCL-90-R) Depression (SCL-90-R) Helpfulness of treatment Satisfaction with treatment Unassisted jaw opening without pain (mm) Unassisted jaw opening with pain (mm) Maximum assisted opening (mm) Number of muscle sites tender to palpation (16 extraoral +4 intraoral sites)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...117 (62.9%) agreed to participate and were assigned randomly to... (one of the two groups)" From correspondence: according to a coauthor, the standard method for this research team corresponds to the blocked randomization using different block sizes.
Allocation concealment (selection bias)	Low risk	Not reported in the article. From correspondence: according to a coauthor, the standard method of randomization includes the concealment of the allocation to the personnel until start the trial.
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but the outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: "All clinical baseline and follow-up study data collection were performed by calibrated and reliable clinical examiners not participating in the RCT and blinded to the study group to which patients were assigned."
Incomplete outcome data (attrition bias)	Low risk	ITT analysis without imputations. From correspondence: "We did not do any imputation" Comparison of study completers and dropouts was conducted.
Selective reporting (reporting bias)	Unclear risk	The number of participants for each outcome is not clear. Quote: "…there are small differences in numbers of patients across some analyses"

Other bias	Low risk	Free of other bias

Dworkin 2002b

Methods	RCT. Single center; two parallel groups. Treatment for 2.5 months, follow-up for 12 months.
Participants	124 patients: mean age 37.5 (SE=1.09) [mean age group A= 37.4 (SE=4.2), mean age group B= 38.0 (SE=3.6)]; 84.68% women; education level higher than high school group A=91.8%, education level higher than high school group B=66.7% (groups differed significantly). Inclusion criteria: age 18-70 yrs.; self-report of pain in the masticatory muscles, TMJ, region in front of the ear or inside the ear, or report of stiffness or other symptoms of discomfort in the same orofacial region; RDC/TMD Axis II GCP score of 0, I or II-Low Exclusion criteria: pain attributable to confirmed migraine or head pain condition other than tension headache; acute infection or other significant disease of the teeth, ears, eyes, nose, or throat; presence of significant or debilitating chronic physical or mental illness; necessity for emergency TMD treatment. Location: USA
Interventions	Group A (n=61): self-care intervention (manual-based individual 3 session of self-care including cognitive-behavioral methods) Group B (n=63): “usual treatment” (at discretion of the attending dentist: physiotherapy, medications, occlusal appliance, and patient education including some components of self-care)
Outcomes	Characteristic pain Intensity (CPI) Graded Chronic Pain Scale (GCPS) Somatization (SCL-90-R) Depression (SCL-90-R) Helpfulness of treatment (0-10) Satisfaction with treatment (0-5) Unassisted jaw opening without pain (mm) Unassisted jaw opening with pain (mm) Maximum assisted opening (mm) Number of muscle sites tender to palpation (0-16) Increase of knowledge (0-10)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The standard methods used in this study for randomizing…” From correspondence: according to a coauthor, the “standard method” for this research team corresponds to the blocked randomization using different block sizes
Allocation concealment (selection bias)	Low risk	Not reported in article. From correspondence: according to a coauthor, the standard method of randomization includes the concealment of the allocation to the personnel until start the trial.
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack

Blinding of outcome assessment (detection bias)	Low risk	Quote: “All clinical baseline and follow-up study data collection were performed by calibrated and reliable clinical examiners not participating in the RCT and blinded to the study group to which patients were assigned."
Incomplete outcome data (attrition bias)	Low risk	Quote: “ …only the results of intent-to-treat analyses are reported." Analysis of non completers
Selective reporting (reporting bias)	Unclear risk	All expected outcomes were reported. Quote: “All analyses present results for patients for whom data are available although there are small differences in numbers of patients across some analyses” Comment: not possible to define the mentioned differences
Other bias	Low risk	Free of other bias

Ekberg 2004

Methods	RCT. Single center; two parallel groups. Follow-up for 10 weeks, follow-up for 12 months reported in two separate articles.
Participants	60 patients: mean age=29 (±12; R=14-56); mean age group A=31 (R=14-54), mean age group B=28 (R=14-56); 86.67% women; 80% Scandinavian, 6.67% other Europeans, 6.67% Asian, 6.67% Latin Americans; 18.33% Elementary school, 53.33% High school, 28.33% College; median duration of pain =27 months (R=1-420) Inclusion criteria: myofascial pain according to RDC/TMD, pain of muscular origin with or without limited opening, including a complaint of pain associated with localized areas of tenderness to palpation in masticatory muscles, combined with self-assessed myofascial pain of at least 40 mm on VAS. Exclusion criteria: temporomandibular joint (TMJ) pain verified by interview and clinical examination; previous treatment for TMD; use of complete dentures; history of psychiatric disorders or symptoms related to disease in other components of the stomatognathic system (e.g. toothache, neuralgia). Location: Sweden
Interventions	Group A (n=30): stabilization appliance in centric relation with canine-protected articulation; nocturnal wearing for 10 weeks Group B (n=30, at long-term 17 were assigned to other treatment): palatal non-occlusal appliance, nocturnal wearing for 10 weeks
Outcomes	Frequency of myofascial pain. Intensity of pain (VAS), pain at rest, pain during mandibular movements. Number of sites and degree of tenderness on masticatory muscles TMJ sounds Maximal opening capacity Awareness of clenching/grinding Improvement of overall subjective symptoms
Notes	The articles in 2003 (167) and 2004 reported information about the RCT at short- and long-term respectively. The paper in 2006 refers to the headache outcomes and possible influencing factors.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "…randomization by using 10 series of consecutively numbered, sealed, opaque envelopes. Each envelope contained a treatment specification. This procedure was repeated until patients were found for the study."
Allocation concealment (selection bias)	Low risk	Quote: "One independent person carried out the randomization by using 10 series of consecutively numbered, sealed, opaque envelopes."
Blinding of participants and personnel (performance bias)	Low risk	Not possible blinding, but this lack is unlikely to influence the outcomes
Blinding of outcome assessment (detection bias)	Low risk	Quote:"The first specialist (who performed the evaluation after treatment), thus, had no information as to which group the patients belonged."
Incomplete outcome data (attrition bias)	Low risk	No drop outs at short-term. Intent-to-treat analysis at long-term
Selective reporting (reporting bias)	Low risk	High consistency with previous report (Ekberg 2003 (167))
Other bias	Low risk	Free of other bias

Félicio 2010

Methods	RCT. Single center; four parallel groups. Follow-up for 120 days.
Participants	30 patients (randomized) + 10 healthy subjects (not randomized): mean age group A=31 (R=13-43), mean age group B=29 (R=17-64), mean age group C=34 (R=14-63), mean age group D=27 (R=18-68); 100% women. Inclusion criteria: long-lasting associated articular and muscular TMD based on the RDC/TMD, For control group: absence of TMD. Exclusion criteria: associated neurological or cognitive deficit, previous or current tumors or traumas in the head and neck region, and orthodontic treatment. Location: Brazil
Interventions	Group A (n=10): Oral myofunctional therapy (OMT) Group B (n=10): Occlusal splint Group C (n=10): Symptomatic control (no treatment) Group D (n=10): Asymptomatic control
Outcomes	Mandibular range motion TMJ function Muscle and TMJ tenderness to palpation Pain during movements. Perception regarding the disorder (Helkimo's Anamnestic Dysfunction Index and ProTMDMulti Protocol) Orofacial Myofunctional evaluation with scores (OMES Protocol)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "…using the GraphPad software"
Allocation concealment (selection bias)	Low risk	Not reported in article. From correspondence: central allocation managed by the leader author
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding
Incomplete outcome data (attrition bias)	Unclear risk	Quote: "All subjects with TMD and AC subjects selected were considered for analysis"
Selective reporting (reporting bias)	Low risk	The principal outcomes were completely reported.
Other bias	Low risk	Free of other bias

Jokstad 2005

Methods	RCT. Single center; two parallel groups. Follow-up for 3 months.
Participants	40 patients: mean age=37 (R=17-62), mean age group A=34, mean age group B=39; 87.5% women Inclusion criteria: adults; common symptoms of TMD (i.e. impaired range of movement, impaired TM-joint function, muscle pain, TM-joint pain, and/or pain on movement of the mandible); positive diagnosis according to RDC/TMD; possible benefit from splint therapy. Exclusion criteria: presence of complete or removable partial prostheses with distal extensions or other treatments for TMD during the study, and individuals with recent facial or cervical trauma. Location: Norway
Interventions	Group A (n=20): stabilization splint (Michigan type) with canine rise during lateral excursions, nocturnal wearing + counseling and muscle relaxation exercises Group B (n=20 [18]): Nociceptive Trigeminal Inhibition-tension suppression system (NTI-tss) splint, nocturnal wearing + counseling and muscle relaxation exercises
Outcomes	Pain VAS Maximal unassisted jaw opening Muscle and TMJ tenderness upon palpation Comfort with splint therapy
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The allocation was randomized and done consecutively by someone using a random number list"
Allocation concealment (selection bias)	Low risk	Quote: "This person was independent of the trial and unaware of the patient names or diagnoses, and was not involved at any stage in the clinical treatment phase. An allocation list kept by this person was used at the

		completion of the trial to verify that the patients had been correctly assigned into the allocated splint group. “
Blinding of participants and personnel (performance bias)	Low risk	Incomplete blinding, but the outcomes are not likely to be influenced by this lack. Quote:” One dentist (A.M.) provided all the treatments throughout the full clinical trial period, and was the only individual who knew the splint type–patient codes.”
Blinding of outcome assessment (detection bias)	Low risk	Assessment by a blinded physical therapist (s. performance bias)
Incomplete outcome data (attrition bias)	Low risk	Explanation for drop outs. Reasons for missing outcome data unlikely to be related to true outcome
Selective reporting (reporting bias)	Low risk	All expected outcomes were reported
Other bias	Low risk	Free of other bias

Kuttila 2002

Methods	RCT. Single center; two parallel groups. Follow up (treatment) for 10 weeks.
Participants	36 patients: mean age group A=45 (25-65); mean age group B=47 (25-65); 75% women. Inclusion criteria: secondary otalgia; TMD diagnosis following a clinical stomatognathic examination and a comprehensive interview, and then classified according to the American Academy of Orofacial Pain; active TMD treatment need according to *Kuttila* Exclusion criteria: primary otalgia;previous treatment for TMD; complete dentures wearers; history of psychiatric disorder; symptoms of neuralgias or toothache. Location: Finland
Interventions	Group A (n=18): stabilization splint in centric relation with canine guidance and without any mediotrusion contacts during lateral slides, nocturnal wearing for 10 weeks Group B (n=18 [16]): non-occluding palatal splint, nocturnal wearing for 10 weeks
Outcomes	Secondary otalgia symptoms (VAS) Tenderness on masticatory muscle, and on TMJ Joint sounds.
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: “…subjects were randomly allocated to the splint treatment group and the control group by randomizing the first splint type by lot and, thereafter, alternating stabilization splint and control splint treatment for the consecutive subjects”
Allocation concealment (selection bias)	High risk	Alternation (s. adequate sequence generation)

Blinding of participants and personnel (performance bias)	Low risk	Participants blinded. Incomplete blinding, but not likely to influence the outcomes Quote: "…(subjects) agreed to participate in the splint treatment study with a double-blind set-up".
Blinding of outcome assessment (detection bias)	Low risk	Quote:"…subjects were reexamined by the same clinician (MK) who examined them before the treatment without knowing the type of splint used."
Incomplete outcome data (attrition bias)	Low risk	Drop outs reported. Not considered for analysis. Reasons for missing data unlikely to be related to true outcome
Selective reporting (reporting bias)	High risk	Some outcomes in the results section were not previously specified
Other bias	Low risk	Free of other bias

Litt 2010

Methods	RCT. Single center; two parallel groups. 6 weeks treatment, follow-up for 12 months.
Participants	101 patients: mean age 39.4 (SD=12.1); 84.16% women; years of education=14.7 (SD=2.5); 79% Caucasian, 9% African-American, 9% Hispanic, 3% self-described as other; average duration of pain 6.7 (SD=6.6); mean pain intensity 3.5 on a scale to 6 (SD=1.3) Inclusion criteria: pain in TM area for at least 3 months, positive axis I diagnosis on RDC/TMD. Exclusion criteria: contraindication to TMD treatment; history of TMJ surgery; extensive anatomical destruction or deterioration of the TMJ; rheumatoid disease; neuropathic or odontogenic pain; psychosis; current use of antidepressants, anxiolytics or opioid pain medication; pregnancy; no local language skills. Location: USA
Interventions	Group A (n=49): standard treatment group (STD)(splint 4 weeks continuously and later only a night guard +soft diet+ naproxen sodium 550mg po BID during 5 weeks, alternatively extra strength acetaminophen in case of gastric ulcer disease) Group B (n=52): STD+ cognitive-behavioral treatment (rationale for treatment + relaxation training and self-efficacy enhancement + masseter EMG biofeedback assisted relaxation + habit modification + combating negative thoughts and catastrophization + stress management)
Outcomes	Pain interference score (MPI) Pain severity (MPI) Coping Somatization Depression Catastrophizing Influencing factors (mediators, moderators) Readiness Self efficacy
Notes	Principal data from the study by Litt (2010)(344). The report published in 2009 (343) refers to a subset of the sample.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "(groups were randomized)... using a computerized urn randomization procedure"
Allocation concealment (selection bias)	Low risk	Not reported Comment: high unpredictability for urn design
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Long-term data were obtained by in-person interviews (not blinded assessor).
Incomplete outcome data (attrition bias)	Low risk	ITT analysis. Reasons for missing outcome data unlikely to be related to true outcome. From correspondence: "There were no differences in reasons by treatment condition." The groups were balanced in numbers.
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Magnusson 1999

Methods	RCT. Single center; two parallel groups. Follow-up for 6 months
Participants	26 patients: mean age group A=37 (R=16-67); mean age group B=32 (R=20-50) Inclusion criteria: myogenous TMD patients; patients referred to specialist clinic where the main subjective symptom was tension-type headache and/or orofacial pain of non-neurogenic or non-dental origin; history of pain of at least one year. Exclusion criteria: previous TMD treatment; general disease affecting the masticatory system; obvious morphological or functional malocclusion. Location: Sweden
Interventions	Group A (n=14 [9]): Michigan stabilization appliance, wore during night Group B (n=12 [9]): therapeutic jaw exercises (stretching and proprioceptive neuromuscular facilitation)
Outcomes	Helkimo Clinical dysfunction index: Impaired mandibular mobility; impaired TMJ function; TMJ pain; muscle pain; pain on movement Helkimo Anamnestic Index: Joint sound; tiredness in jaws; difficulty in opening the mouth; pain when opening the mouth; pain in the face or jaws.
Notes	After 3 months, some of the patients (n=8) were assigned to a combined treatment.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients were randomly assigned to receive either jaw exercises or interocclusal appliance therapy" From correspondence: shuffled envelopes

Allocation concealment (selection bias)	Unclear risk	Not reported in article From correspondence: “When a patient fulfilled the inclusion criteria, we opened an envelope and checked what treatment the patient was to receive.”
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding
Incomplete outcome data (attrition bias)	Unclear risk	Reasons for missing data are unlikely related to true outcome, and are balanced in groups
Selective reporting (reporting bias)	Low risk	Include all expected outcomes. The authors follow a standardized functional examination in their research.
Other bias	Low risk	Free of other bias

Magnusson 2004

Methods	RCT. Single center; two parallel groups. Follow-up for 6 months.
Participants	28 (out of 30) patients: mean age group A analyzed =31 (R=16-70), mean age group B analyzed=32 (R=21-61); 75% women; mean duration of symptoms group A= 6 yrs (R=0.5-35 yrs.); mean duration of symptoms group B= 7 yrs (R=0.5-30 yrs.) Inclusion criteria: 16 yrs. or older; duration of symptoms of at least 6 months; at least 12 teeth in the upper jaw and 12 teeth in the lower jaw; moderate or severe clinical signs of dysfunction according to Helkimo clinical dysfunction index, pronounced subjective symptoms according to Helkimo anamnestic index, or frequent tension type headache. Exclusion criteria: ongoing TMD treatment or splint therapy during the last year; indication of other kind of therapy or a combination of treatments; front teeth with periodontitis or fixed partial dentures; pronounced pre- or postnormal occlusion; deep bite; language difficulties; psychic disorder. Location: Sweden
Interventions	Group A (n=14): stabilization appliance in retruded contact position (RCP) and in an area 0.5-1.0mm anterior to RCP with canine-guidance during lateral and protrusive movements; nocturnal wearing Group B (n=14 [10]): NTI appliance adjusted to a point contact to the central mandibular incisors in RCP and during protrusive movement, only the mandibular incisors contacted the device during lateral excursions; nocturnal wearing
Outcomes	TMJ sounds, jaw fatigue, difficulties in mouth opening, Muscle and TMJ pain upon palpation Range of mandibular motion, impaired mandibular mobility, impaired TMJ function Pain in face or jaws during jaw movements, and at rest Tension type headache
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “By lot, made by a dental assistant…were randomly allocated to receive...“
Allocation concealment (selection bias)	Unclear risk	Quote: “…made by a dental assistant…”

Blinding of participants and personnel (performance bias)	Low risk	Not possible blinding, but this lack is unlikely to influence the outcomes
Blinding of outcome assessment (detection bias)	Low risk	Quote: “This examination…was made by one and the same examiner (MH) who did not know which treatment the individual patient received”
Incomplete outcome data (attrition bias)	Low risk	No statistical analysis. Original data available. Drop outs reported
Selective reporting (reporting bias)	Low risk	Include all expected outcomes. The authors follow a standardized functional examination in their research.
Other bias	Low risk	Free of other bias

Michelotti 2012

Methods	RCT. Single center; two parallel groups. Follow-up for 3 months.
Participants	41 (out of 44) patients: mean age 31.2 (11.8); 88.57% women. Inclusion criteria: Myofascial pain Diagnosis (RDC/TMD), and absence of objective evidence of joint pathology or dysfunction. Muscle pain greater than 30mm VAS Exclusion criteria: Disc displacement with or without reduction, arthrogenous TMD with pain or RX alterations in TMJ; other orofacial conditions; other TMD treatments performed in the last 3 months; neurological or psychiatric disorders, or both; history of abuse of medication; use of splint in the preceding year Location: Italy
Interventions	Group A (n=23): Education only (self-care, home exercise group focused on habit-reversal techniques, education about TMD) Group B (n=18): stabilization Splint only
Outcomes	Pain intensity (VAS) Unassisted jaw opening without pain (mm) Headache (VAS) Pain during chewing (VAS)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Balance block randomization
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. Outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “second examiner, who was masked as to the patient’s treatment performed the baseline assessment and 3 months after…still masked…”
Incomplete outcome data (attrition bias)	Unclear risk	Data of drop outs vs. completers. Insufficient information about completers.
Selective reporting (reporting bias)	Low risk	All expected outcomes were reported
Other bias	Low risk	Free of other bias

Nilsson 2011

Methods	RCT. Single center; two parallel groups. Follow-up for 12 months.
Participants	80 patients: mean age group A=35 (±15) (R=14-67), mean age group B= 33 (±14)(13-68); 80.82% women; median months of pain duration group A=24 (R=3-360), median months of pain duration group B=24 (R=4-72) Subset of the sample: 48 patients (group A=21, group B=27): mean age 36 (R=14-64); 77.08% women Inclusion criteria: at least 3 month of reported TMD pain, verified by a history questionnaire and a clinical examination according to the RDC/TMD; at least 40 mm on VAS for worst TMD pain; full dentition with sustained molar support but third molars or two other missing teeth was accepted. Exclusion criteria: previous treatment with occlusal appliances, symptoms related to disease in other parts of the stomatognathic system (e.g. toothache, neuralgia); pain due to systemic disease (e.g. rheumatoid arthritis); fibromyalgia; whiplash-associated disorder; history of psychiatric disorders; no local language skills. Location:Sweden
Interventions	Group A (n=40 [36]): resilient appliance 4-mm thick adjusted to occlude with contacts in the molar, premolar, and canine regions Group B (n=40 [37]): palatal hard non-occlusal appliance
Outcomes	Characteristic Pain intensity (CPI) Physical functioning measured by Jaw disability checklist Emotional functioning measured by SCL-90-R Coping ability measured by 29-item Sense of coherence (SoC) Global improvement Adverse effects
Notes	This study published on 2011 shows the results at long-term of the RCT which is extensively explained on a written version (ISBN/ISSN 91-7104-311-X/0348-6672) published on 2010. The article of *Limchaicana 2009*(excluded study) reports on MRI findings in a subset of the sample. The paper of *Nilsson & Ekberg 2010*(416) shows results on the Sense of Coherence, and a complete overall of the RCT was reported in the article of *Nilsson 2010*(419)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:“The dental assistant randomized the patients in blocks of 10 to one of the two groups..."
Allocation concealment (selection bias)	Low risk	Quote: “To exclude involvement of the treatment, the independent dental assistant to each dentist (ECE, HN) allocated the patients… Each block included five concealed sheets with the text ‘resilient appliance’ and five with the text ‘control appliance"
Blinding of participants and personnel (performance bias)	Low risk	Participants and personnel not blinded, but the outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The same examiners evaluated the patients after treatment. Both examiners were blinded to group assignment.”
Incomplete outcome data (attrition bias)	Low risk	Intent-to-treat analysis

Selective reporting (reporting bias)	Low risk	High consistency into the different reports
Other bias	Low risk	Free of other bias

Ozkan 2011

Methods	RCT. Single center two groups. Treatment for 1 week/3months, follow-up for 12 weeks after completing treatment.
Participants	50 participants: mean age=30.38; 88%women Inclusion criteria: pain of muscular origin with or without limited opening, duration of pain at least 3 months including a complaint of pain associated with localized areas of tenderness to palpation in masticatory muscles, combined with self-assessed myofascial pain of at least 40 mm on VAS. Exclusion criteria: odontogenic reasons for the orofacial pain; evidence of bone pathology (rheumatoid arthritis, osteoarthrosis, condylar resorption) and TMJ pain; previous treatment for TMD; use of complete dentures; other causes of pain (e.g. trigeminal neuralgia, atypical facial pain) Location: Turkey
Interventions	Group A (n=25): stabilization splint (splint at night for a period of three months) Group B (n=25): stabilization splint + injections into trigger points (2 sessions with solution of 0.5 ml lidocaine + 0.5 ml saline; and a third session with 0.1 ml triamcinolone acetanide. 22 injections in masseter muscle, 13 injections in temporalis, and 20 injections in lateral pterygoid muscles).
Outcomes	Maximal incisal opening (MIO), Pain during mandibular movements, and at rest Number of trigger points in masticatory muscles Intensity of myofascial pain (VAS) Frequency of myofascial pain
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...and randomly assigned to two equal Group"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Unclear risk	No possible blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed
Selective reporting (reporting	Low risk	Include all expected outcomes
Other bias	Unclear risk	Interventions have different duration, but follow-up was considered since treatment was completed.

Raphael 2001

Methods	RCT. Single center; two parallel groups. Follow-up for 6 weeks.
Participants	63 (out of 68) patients: mean age analyzed group =33.7 (SD=10.9); 100% women; mean of years of education= 14.4 (SD=2.2); 78% self-identified White; mean pain intensity in the last two weeks before start of trial 4.5 (±1.8); mean pain duration 5 yrs. (30% ≤ 1yr; 19% ≥ 10yrs.) Inclusion criteria: women; myofascial pain diagnosis according to RDC/TMD (facial pain complaint, tenderness to palpation at three or more of 20 masticatory muscle sites), MFP patients meeting criteria for additional TMDs such as osteoarthritis of the TMJ were not automatically excluded, providing that their chief complaint was determined to be pain of muscle origin (as opposed to clicking sounds or difficulty opening their mouth); at least six maxillary and six mandibular posterior natural teeth (i.e. without crowns) that occluded; local language skills. Exclusion criteria: currently undergoing orthodontic treatment; previous treatment for TMD or bruxism with oral splint. Location: USA
Interventions	Group A (n=32): maxillary flat-plane hard acrylic splint, nocturnal wearing (during sleep) + conservative treatments (soft diet, moist heat/massage, exercise, OTC NSAIDs) Group B (n=31): palatal-only splint without interfering occlusion + conservative treatments
Outcomes	Pain to palpation, average pain, worst pain Mood (10-point scale), functional outcome (questionnaire), interference in daily activities (10-point scale) Depression SCL-90 Expectations for improvement (4-point scale) Bruxism self-report, and bruxism wear turnover reported in a subset of the sample (second report (462))
Notes	The article of *Raphael 2003* (462) reports about the severity of bruxism as a predictor of the splint efficacy in a subset of the sample.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: " …(subjects) were randomly assigned to treatment with either an active or palatal-only splint"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Unclear risk	Not addressed
Blinding of outcome assessment (detection bias)	Low risk	Quote: "To keep RDC clinicians blind…not the same clinician as the one who conducted the RDC examinations at baseline and at the six-week follow-up visit"
Incomplete outcome data (attrition bias)	Low risk	"As treated" analysis, with balanced groups
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Tavera 2012

Methods	RCT. Single center, three parallel groups. Follow-up for 3 months
Participants	152 enrolled [out of 175 randomized] participants: mean age=37.2; 84.03% women Included criteria: jaw pain or dysfunction; completed informed consent process; RDC/TMD diagnosis (at least one of the following: myofascial pain, arthralgia, disc displacement with reduction); presence of one or more of the following findings associated with pain as demonstrated with a VAS score of >4: increased (>60 mm) or decreased (<40 mm) range of interincisal jaw opening, pain upon any jaw movement, pain on digital palpation (~1 lb. pressure) of the periauricular area or external auditory meatal areas, pain on digital palpation (~1 lb. pressure) in two or more muscles of mastication, or joint sound with pain. Excluded criteria: diagnosis of rheumatoid arthritis, osteoarthritis, osteoarthrosis or another connective tissue disorder; a history of direct trauma to the jaw; use of an occlusal appliance to treat a TMD within the previous six months; prior TMJ or ear surgery; physical or behavioral disorder, which, in the opinion of the principal investigator, would interfere with the use of the device or compliance with the study protocol; unsuitable ear canal anatomy (e.g., congenital deformity) not allowing for fit of the study device; use of a narcotic pain medication in the last seven days, or aspirin or a nonsteroidal anti-inflammatory agent in the last 24 hours; a history of ear pain unrelated to TMJ; a history of ear drainage in the past two years; active ear drainage, swelling, or redness as observed on targeted physical exam; not an appropriate candidate for an intraoral splint due to missing or poor quality dentition or untreated pain of dental origin. Location: Mexico
Interventions	Group A (n=60): TMDes (*ear system*) device (all day wearing) Group B (n=64): stabilization splint (nocturnal wearing) Group C (n=28): jaw exercise + heat application for 10 min.
Outcomes	Craniomandibular Index Pain (VAS) Sunbjective pain (Symptom Severity Index [SSI]) TMJ Scale
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection	Unclear risk	Quote: "...were randomly assigned..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding.
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding
Incomplete outcome data (attrition bias)	Unclear risk	Missing data balanced in groups. Reasons not reported
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Truelove 2006

Methods	RCT. Single center; three parallel groups. Follow-up for 12 months.
Participants	200 patients: mean age group A=36 (±11), mean age group B=36 (±11), mean age group C=35 (±12); 86% women; 75.5% education more than high school; 8.5% race Nonwhite; mean number of yrs. with facial pain group A=5±5, mean number of yrs. with facial pain group A=6±9, mean number of yrs. with facial pain group A=5±6 Inclusion criteria: age 18-60 yrs.; RDC/TMD Axis I diagnosis of myofacial pain (Group Ia or Ib) with or without a concurrent diagnosis of arthralgia (Group IIIa) or disk displacement with reduction (Group IIa), as well as an RDC/TMD Axis II Graded Chronic Pain score of Grade I (low pain) or Grade II (high pain), both of which had no or minimal pain-related psychosocial interference. Exclusion criteria: any other RDC/TMD Axis I diagnosis (for example, arthritis, disk displacement without reduction); any systemic arthritis or other serious medical complications, full dentures; major psychological disorders; current satisfactory use of splint; no local language skills Location: USA
Interventions	Group A (n=64): usual treatment (self-care: jaw relaxation, reduction of parafunction, thermal packs, NSAIDs, passive opening stretches and suggestions about stress reduction) Group B (n=68): usual treatment + hard splint in centric occlusion nocturnal wearing and two additional hours daily while awake throughout the three-month and twelve-month follow-up Group C (n=68): usual treatment + soft splint in centric occlusion, nocturnal wearing and two additional hours daily while awake throughout the three-month and twelve-month follow-up
Outcomes	Self report findings: CPI; pain duration; self reported TMD symptoms (TMJ clicking/popping sounds, TMJ grating sounds, TMJ locking/catching, tinnitus, jaw clenching-diurnal, jaw clenching-nocturnal, limitation in chewing). Clinical examination: range of motion (assisted and unassisted jaw opening); joint sounds; muscle and TMJ palpation pain (number of sites); RDC/TMD diagnoses
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “We generated randomization assignments using randomly selected block sizes of six, nine or 12 and stratified them by provider.”
Allocation concealment (selection bias)	Low risk	Quote: “We concealed randomization to all study personnel until after we obtained the subjects’ consent“
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The research dental hygienists conducting follow-up data collection were blinded to subject treatment group“

Incomplete outcome data (attrition bias)	Low risk	Quote: "…we took a conservative approach of carrying forward the last observation if the subject dropped out before month 12." Intent-to-treat analysis. Attritions reported and analyzed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Vicente-Barrero 2012

Methods	RCT. Single center, two parallel groups. Follow-up fpr 30 days.
Participants	20 participants: mean age=39 (R=18-58); 85% women Inclusion criteria: Three-month or longer history of at least two of the following signs or symptoms: pain upon palpation of the temporomandibular joint (TMJ) or associated muscles of mastication, restriction or deviation of jaw movement, headache plus joint noise. Headache and joint noise were not considered when they occurred separately; legal age ;normal vertical dimension with complete or almost complete dentition. Exclusion criteria: Legal involvement such as traffic accidents, sick leave, etc.; dental malocclusion with variations from normal vertical dimension; malignancies or other diseases, especially those involving other joints; bone and/or degenerative diseases; headache associated with general organic conditions; fibromyalgia; mental disorders; previous treatment with acupuncture and/or decompression splint; previous surgery of the TMJ; orthodontic treatment at the time of the study; wearing a complete removable prosthesis; allergy to metal.
Interventions	Group A (n=10): acupuncture (15 30 min. sessions with local EX-HN5, SJ 21, GB2, SJ17, ST6 acupoints and distal LI-4, ST-36, SJ5 and GB34 acupoints) with steel 0.25 mm x 25 mm needles to a depth of 3-5mm epicutaneous. Group B (n=10): decompression splint (nocturnal wearing)
Outcomes	Mouth opening and lateral jaw-deviation (mm) Sensitivity to pressure on preauricular area, masseter muscle, temporal muscle and trapezius (pounds) Pain (VAS)
Notes	No comparison between groups.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding
Blinding of outcome assessment (detection bias)	High risk	The same operator was responsible for the examination before and after treatment.
Incomplete outcome data (attrition bias)	Unclear risk	Not sufficient information
Selective reporting (reporting bias)	High risk	Insufficient report of outcomes

Other bias	Unclear risk	Insufficient information

Wassell 2004

Methods	RCT. Multicenter; two parallel groups. Treatment for 12 weeks, follow-up for one year.
Participants	72 (out of 77) patients: mean age group A=37.9 (SD=12.6), mean age group B= 35.9 (SD=10.3); mean age analyzed men=35.1 (±8.7), mean age analyzed women=37.7 (±11.9); 87.5% women. Inclusion criteria: aged ≥ 18; pain in TMJ or muscles or both plus one or more of the following: joint sounds (clicking or crepitus), history of jaw locking or limitation of opening, muscle tenderness to palpation, TMJ tenderness to palpation; symptoms present for >4 weeks; sufficient teeth to support and occlude against a lower splint. Exclusion criteria: patients who were dentists; requiring immediate treatment (eg. trauma or acute disc displacement without reduction); no agreement of the patient to participate. Location: United Kingdom
Interventions	Group A (n=34)(n=27*): Stabilizing splint (mandibular splint with anterior guidance and anterior occlusal stops only),full-time wearing Group B (n=38, 17 assigned to other treatment at 6 weeks)(n=12*): Control non-occluding splint (lingual flange of acrylic from occlusal surfaces into the lingual sulcus), full-time wearing
Outcomes	Pain intensity (VAS); pain diary Number of tender muscles; number of headaches per week TMJ Clicking; aggregate joint tenderness Interincisal opening Beck Hopelessness test; Spielberger Trait Anxiety test.
Notes	*Second report at 1-year follow-up Treatment was offered by general dentists who had attended courses about occlusion. Some patients (excluded from analysis at 1-year follow-up) were referred for occlusal adjustment. The article by *Wassell et al. 2008* (604) reported in a subsample of this study an attempt to define improvers using the area under the curve (AUC) of VAS/time graphs of pain intensity.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “the random allocation of splints was predetermined for each GDP using a permuted block of ten. “
Allocation concealment (selection bias)	Low risk	Central allocation Quote: “All dentists were blind to the allocation until the patient was registered into the trial. Letters were then sent to doctors and dentists informing them of their patients' involvement.”
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding

Blinding of outcome assessment (detection bias)	Unclear risk	Quote: "…the patient completed the VAS in the waiting room to reduce bias." No blinding. The outcomes are not likely to be influenced by this lack.
Incomplete outcome data (attrition bias)	High risk	Some of the attritions were explained as nonresponders patients to be referred for specialist treatment.
Selective reporting (reporting bias)	High risk	Two outcomes were not completely reported. Results from psychological tests were not reported.
Other bias	High risk	Referral may mask not successful results from therapies

Öz 2010

Methods	RCT. Single center; two parallel groups. Follow-up for 3 months.
Participants	40 (out of 44) patients: mean age group A=31.25 (±8.23), mean age group B=34.52 (±12.82); 85.0% women; mean years of education group A=9.65 (±5.40); mean years of education group B=10.50 (±3.84); mean months of pain duration group A=8.2 (±2.40), mean months of pain duration group B=7.9 (±2.58) Inclusion criteria: age 18-60 yrs.; diagnosis of MP according to RDC/TMD; natural posterior occlusion; no TMD treatment in the last 2 years; orofacial pain for at least 6 months. Exclusion criteria: TMD of articular origin diagnosed according to RDC/TMD; psychiatric disorders, heart disease, or pacemakers; removable prosthesis or the absence of more than 1 tooth per quadrant and major malocclusion (anterior open bite, unilaterally maxillary lingual crossbite, overjet >6 mm, slide from the retruded contact position to intercuspal position >2 mm); pregnancy; symptoms that could be caused by other orofacial region diseases (eg, toothache, neuralgia, migraine); treatment or any medication for headache or bruxism during the previous year; local skin infections over the masseter muscle. Location: Turkey
Interventions	Group A (n=20): low-level laser therapy onto trigger points to 3J/cm^2 by applying 300-mW output power for 10 sec. from a 2-mm distance; 2 times per week for 10 sessions Group B (n=20): stabilization splint according to *Okeson* (432), full time wearing for 3 months
Outcomes	Pain location Pressure pain threshold (PPT) Functional examination according to RDC/TMD: Active and passive mouth opening, muscle tenderness to palpation
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "…were randomly divided into 2 groups. Patients in both groups were age and sex matched" "Randomization was done before the arrangements for the date of therapy were made." From correspondence: "they (the patients) were divided in two groups; men and women. Then men were grouped into 2 age groups; 18-40, 40-60. The men in 18-40 group were divided into two groups; one group for study, one

		group for control. By every procedure, the groups were equal in number and the selection was done on the name list randomly: first name for one group, second for the other. Each division was performed by different prosthodontists in the department. The names of them were not included in the study. The same procedure was done for the women group, too".
Allocation concealment (selection bias)	High risk	*Quote*: "Selection bias was considered through a defined and concealed randomization process" From correspondence: alternation (s. random sequence generation)
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. This lack is not likely to influence the outcomes
Blinding of outcome assessment (detection bias)	Low risk	Quote: "Assessment of the participants was conducted by an independent investigator who was unaware of the study."
Incomplete outcome data (attrition bias)	Unclear risk	"As treated" analysis. Balanced groups
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Other bias	Unclear risk	The evaluation of the interventions differed in time due to different treatment duration

Footnotes

Characteristics of excluded studies

Al Quran 2006

Reason for exclusion	Not randomized

Al-Saad 2001

Reason for exclusion	Not randomized

Baad-Hansen 2007

Reason for exclusion	Diagnosis: bruxism. 5 out of 10 patients presented TMD

Bakke 2008

Reason for exclusion	No myogenous TMD patients

Berguer 2008

Reason for exclusion	This study included conservative treatment as cointervention. The interventions compared were neurorefloxology vs. placebo

Conti 2006

Reason for exclusion	No myogenous TMD patients

Ekberg 1999

Reason for exclusion	No myogenous TMD patients

Ekberg 2002

Reason for exclusion	No myogenous TMD patients

Ekberg 2002b

Reason for exclusion	No myogenous TMD patients

Fayed 2004

Reason for exclusion	No myogenous TMD patients

Gavish 2002

Reason for exclusion	Not randomized

Ghanem 2011

Reason for exclusion	No myogenous TMD patients

Glaros 2007

Reason for exclusion	RCT. Same intervention, with different instructions: Splint avoiding vs. splint maintaining contact

Grace 2002

Reason for exclusion	Not randomized

Haketa 2010

Reason for exclusion	No myogenous TMD patients

Hamata 2009

Reason for exclusion	Stabilization splint in CR vs MIC

Inchingolo 2011

Reason for exclusion	No randomized

Limchaicana 2009

Reason for exclusion	Second report of RCT. (s. Nilsson 2011)

Machon 2011

Reason for exclusion	No myogenous TMD patients

Madani 2011

Reason for exclusion	No myogenous TMD patients

Maloney 2002

Reason for exclusion	All groups received splint. Comparison between complementary physical therapy

Mejersjo 2008

Reason for exclusion	No myogenous TMD patients

Minakuchi 2004

Reason for exclusion	No myogenous TMD patients

Naikmasur 2008

Reason for exclusion	Different duration of the interventions (soft splint)

Nakaoka 2009

Reason for exclusion	No myogenous TMD patients

Nilner 2008

Reason for exclusion	Secondary report of RCT Doepel 2012

Rizzati-Barbosa 2003

Reason for exclusion	Not randomized

Rohida 2010

Reason for exclusion	No myogenous TMD patients

Schiffman 2007

Reason for exclusion	No myogenous TMD patients

Schmitter 2005

Reason for exclusion	No myogenous TMD patients

Stiesch-Scholz 2002

Reason for exclusion	No myogenous TMD patients

Stiesch-Scholz 2005

Reason for exclusion	No myogenous TMD patients

Tecco 2010

Reason for exclusion	No myogenous TMD patients

Wahlund 2003

Reason for exclusion	adolescents

Wahlund 2003b

Reason for exclusion	adolescents

Winocur 2002

Reason for exclusion	Not randomized

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

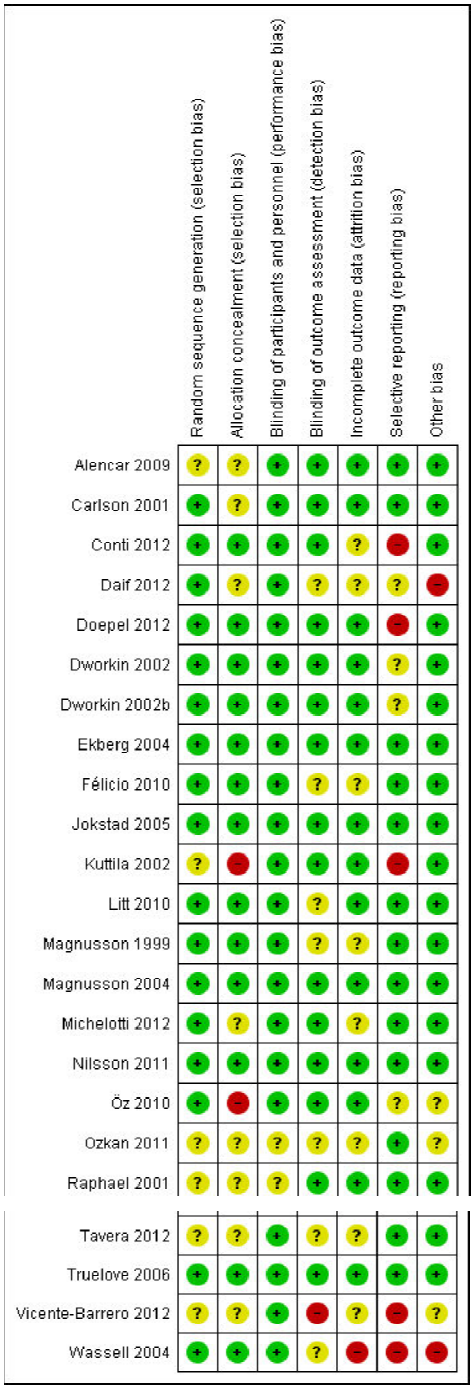

***Figure 36**. Risk of bias summary: review authors' judgements about each risk of bias item for each included study*

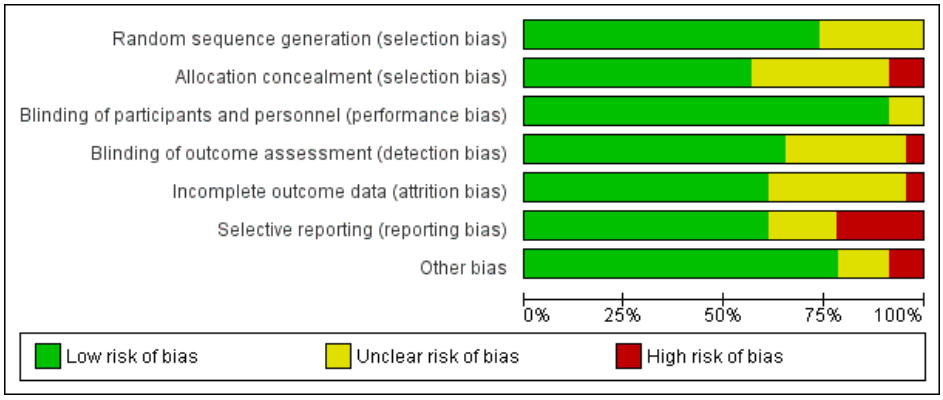

***Figure 37**. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies*

References to studies: Occlusal appliances for Myofacial Pain

Included studies

Alencar 2009
Alencar FJr, Becker A: Evaluation of different occlusal splints and counselling in the management of myofascial pain dysfunction. J Oral Rehabil 2009;36:79-85 [PubMed: 18976268]

Carlson 2001
Carlson CR, Bertrand PM, Ehrlich AD, Maxwell AW, Burton RG: Physical self-regulation training for the management of temporomandibular disorders. J Orofac Pain 2001;15:47-55 [PubMed: 11889647]

Conti 2012
Conti PCR, Alencar ENde, da Mota Correa AS, Lauris JRP, Porporatti AL, Costa YM: Behavioural changes and occlusal splints are effective in the management of masticatory myofascial pain: a short-term evaluation. J Oral Rehabil 2012;39:754-760 [PubMed: 22672361]

Daif 2012
Daif ET: Correlation of splint therapy outcome with the electromyography of masticatory muscles in temporomandibular disorder with myofascial pain. Acta Odontol Scand 2012;70:72-77 [PubMed: 21728748]

Doepel 2012
Doepel M, Nilner M, Ekberg E, Le Bell Y: Long-term effectiveness of a prefabricated oral appliance for myofascial pain. J Oral Rehabil 2012;39:252-260 [PubMed: 21985440]

Dworkin 2002a
Dworkin SF, Turner JA, Mancl L, Wilson L, Massoth D, Huggins KH, LeResche L, Truelove E: A randomized clinical trial of a tailored comprehensive care treatment program for temporomandibular disorders. J Orofac Pain 2002;16:259-276 [PubMed: 12455427]

Dworkin 2002b
Dworkin SF, Huggins KH, Wilson L, Mancl L, Turner J, Massoth D, LeResche L, Truelove E: A randomized clinical trial using research diagnostic criteria for temporomandibular disorders-axis II to target clinic cases for a tailored self-care TMD treatment program. J Orofac Pain 2002;16:48-63 [PubMed: 11889659]

Ekberg 2004
Ekberg E, Nilner M: Treatment outcome of appliance therapy in temporomandibular disorder patients with myofascial pain after 6 and 12 months. Acta Odontol Scand 2004;62:343-349 [PubMed: 15848979]

Félicio 2010
Félicio CMde, Oliveira MMde, da Silva MAMR: Effects of orofacial myofunctional therapy on temporomandibular disorders. Cranio 2010;28:249-259 [PubMed: 21032979]

Grace 2002
Grace EG, Sarlani E, Reid B: The use of an oral exercise device in the treatment of muscular TMD. Cranio 2002;20:204-208 [PubMed: 12150267]

Jokstad 2005
Jokstad A, Mo A, Krogstad BS: Clinical comparison between two different splint designs for temporomandibular disorder therapy. SODE 2005;63:218-226 [PubMed: 16040444]

Kuttila 2002
Kuttila M, Le Bell Y, Savolainen-Niemi E, Kuttila S, Alanen P: Efficiency of occlusal appliance therapy in secondary otalgia and temporomandibular disorders. Acta Odotol Scand 2002;60:248-254 [PubMed: 12222651]

Litt 2010
Litt MD, Shafer DM, Kreutzer DL: Brief cognitive-behavioral treatment for TMD pain: long-term outcomes and moderators of treatment. Pain 2010;151:110-116 [Pubmed: 20655662]

Magnusson 1999
Magnusson T, Syren M: Therapeutic jaw exercises and interocclusal appliance therapy. A comparison between two common treatments of temporomandibular disorders. Swed Dent J 1999;23:27-37 [PubMed: 10371003]

Magnusson 2004
Magnusson T, Adiels A-M, Nilsson HL, Helkimo M: Treatment effect on signs and symptoms of temporomandibular disorders--comparison between stabilisation splint and a new type of splint (NTI). A pilot study. Swed Dent J 2004;28:11-20 [PubMed: 15129601]

Michelotti 2012
Michelotti A, Iodice G, Vollaro S, Steenks MH, Farella M: Evaluation of the short-term effectiveness of education versus an occlusal splint for the treatment of myofascial pain of the jaw muscles. J Am Dent Assoc 2012;143:47-53 [PubMed: 22207667]

Nilsson 2011
Nilsson H, Vallon D, Ekberg EC: Long-term efficacy of resilient appliance therapy in TMD pain patients: a randomised, controlled trial. J Oral Rehabil 2011;38:713-721 [PubMed: 21434963]

Öz 2010
Öz S, Gokcen-Rohlig B, Saruhanoglu A, Tuncer EB: Management of myofascial pain: low-level laser therapy versus occlusal splints. J Craniofac Surg 2010;21:1722-1728 [PubMed: 21119408]

Ozkan 2011
Ozkan F, Cakir Ozkan N, Erkorkmaz U: Trigger point injection therapy in the management of myofascial temporomandibular pain. Agri 2011;23:119-125 [PubMed: 21935818]

Raphael 2001
Raphael KG, Marbach JJ: Widespread pain and the effectiveness of oral splints in myofascial face pain. J Am Dent Assoc 2011;132:305-316 [PubMed: 11258087]

Rizzati-Barbosa 2003
Rizzatti-Barbosa CM, Martinelli DA, Ambrosano GMB, Albergaria-Barbosa JRde: Therapeutic response of benzodiazepine, orphenadrine citrate and occlusal splint association in TMD pain. Cranio 2003;21:116-120 [PubMed: 12723857]

Tavera 2012
Tavera AT, Montoya MCP, Calderon EFGG, Gorodezky G, Wixtrom RN: Approaching temporomandibular disorders from a new direction: a randomized controlled clinical trial of the TMDes ear system. Cranio 2012;30:172-182 [PubMed: 22916669]

Truelove 2006
Truelove E, Huggins KH, Mancl L, Dworkin SF: The efficacy of traditional, low-cost and nonsplint therapies for temporomandibular disorder: a randomized controlled trial. J Am Dent Assoc 2006;137:1099-1107 [PubMed: 16873325]

Vicente-Barrero 2012
Vicente-Barrero M, Yu-Lu S-L, Zhang B, Bocanegra-Perez S, Duran-Moreno D, Lopez-Marquez A, Knezevic M, Castellano-Navarro J-M, Liminana-Canal J-M: The efficacy of acupuncture and decompression splints in the treatment of temporomandibular joint pain-dysfunction syndrome. Med Oral Patol Oral Cir Bucal 2012 doi:10.4317/medoral.17567 [PubMed: 22549668]

Wassell 2004
Wassell RW, Adams N, Kelly PJ: Treatment of temporomandibular disorders by stabilising splints in general dental practice: results after initial treatment. Br Dent J 2004;197:35-41 [PubMed: 15243608]

Winocur 2002
Winocur E, Gavish A, Emodi-Perlman A, Halachmi M, Eli I: Hypnorelaxation as treatment for myofascial pain disorder: a comparative study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;93:429-434 [PubMed: 12029281]

Excluded studies

Al Quran 2006
Al Quran FAM, Kamal Mudar S: Anterior midline point stop device (AMPS) in the treatment of myogenous TMDs: comparison with the stabilization splint and control group. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:741-747 [PubMed: 16731393]

Al-Saad 2001
Al-Saad M, Akeel RF: EMG and pain severity evaluation in patients with TMD using two different occlusal devices. Int J Prosthod 2001;14:15-21 [PubMed: 11842899]

Baad-Hansen 2007
Baad-Hansen L, Jadidi F, Castrillon E, Thomsen PB, Svensson P: Effect of a nociceptive trigeminal inhibitory splint on electromyographic activity in jaw closing muscles during sleep. J Oral Rehabil 2007;34:105-111 [PubMed: 17244232]

Bakke 2008
Bakke, Merete; Eriksson, Lars; Thorsen, Niels Max; Sewerin, Ib; Petersson, Arne; Wagner, Aase. Modified condylotomy versus conventional conservative treatment in painful reciprocal clicking--a preliminary prospective study in eight patients. Clin Oral Invest 2008;12:353-359 [Pubmed: 18548293]

Berguer 2008
Berguer A, Kovacs F, Abraira V, Mufraggi N, Royuela A, Muriel A, Gestoso M, Falahat F, Martin-Granizo R, Zamora J: Neuro-reflexotherapy for the management of myofascial temporomandibular joint pain: a double-blind, placebo-controlled, randomized clinical trial. J Oral Maxillofac Surg 2008;66:1664-1677 [PubMed: 18634956]

Conti 2006
Conti PCR, dos Santos CN, Kogawa EM, Castro Ferreira Conti ACde, Araujo CdosRPde: The treatment of painful temporomandibular joint clicking with oral splints: a randomized clinical trial. J Am Dent Assoc 2006;137:1108-1114 [PubMed: 16873326]

Ekberg 1999
Ekberg E, Nilner M: The influence of stabilisation appliance therapy and other factors on the treatment outcome in patients with temporomandibular disorders of arthrogeneous origin. Swed Dent J 1999;23:39-47 [PubMed: 10371004]

Ekberg 2002
Ekberg E, Vallon D, Nilner M: Treatment outcome of headache after occlusal appliance therapy in a randomised controlled trial among patients with temporomandibular disorders of mainly arthrogenous origin. Swed Dent J 2002;26:115-124 [PubMed: 12425225]

Ekberg 2002b
Ekberg E, Nilner M: A 6- and 12-month follow-up of appliance therapy in TMD patients: a follow-up of a controlled trial. Int J Prosthodont 2002;15:564-570 [PubMed: 12475163]

Fayed 2004
Fayed MMS, El-Mangoury NH, El-Bokle DN, Belal AI: Occlusal splint therapy and magnetic resonance imaging. Worl J Orthod 2004;5:133-140 [PubMed: 15615131]

Gavish 2002
Gavish A, Winocur E, Ventura YS, Halachmi M, Gazit E: Effect of stabilization splint therapy on pain during chewing in patients suffering from myofascial pain. J Oral Rehabil 2002;29:1181-1186 [PubMed: 12472855]

Ghanem 2011
Ghanem WA: Arthrocentesis and stabilizing splint are the treatment of choice for acute intermittent closed lock in patients with bruxism. J Craniomaxillofac Surg 2011;39:256-260 [PubMed: 20598897]

Glaros 2007
Glaros AG, Owais Z, Lausten L: Reduction in parafunctional activity: a potential mechanism for the effectiveness of splint therapy. J Oral Rehabil 2007;34:97-104 [PubMed: 17244231]

Haketa 2010
Haketa T, Kino K, Sugisaki M, Takaoka M, Ohta T: Randomized clinical trial of treatment for TMJ disc displacement. J Dent Res 2010;89:1259-1263 [PubMed: 20739691]

Hamata 2009
Hamata MM, Zuim PRJ, Garcia AR: Movement of the mandibular condyle and articular disc on placement of an occlusal splint. J Appl Oral Sci 2009;17:32-38 [PubMed: 21925908]

Inchingolo 2011
Jokstad A, Mo A, Krogstad BS: Clinical comparison between two different splint designs for temporomandibular disorder therapy. Eur Rev Med Pharmacol Sci 2011;15:1296-1300 [PubMed: 16040444]

Limchaicana 2009
Limchaichana N, Nilsson H, Petersson A, Ekberg E: Resilient appliance-therapy treatment outcome in patients with TMD pain correlated to MRI-determined changes in condyle position. Cranio 2009;27:185-193 [PubMed: 19697647]

Machon 2011
Machon V, Hirjak D, Lukas J: Therapy of the osteoarthritis of the temporomandibular joint. J Craniomaxillofac Surg 2011;39:127-130 [Pubmed: 20692843]

Madani 2011
Madani AS, Mirmortazavi A: Comparison of three treatment options for painful temporomandibular joint clicking. J Oral Sci 2011;53:349-354 [Pubmed: 21959663]

Maloney 2002
Maloney GE, Mehta N, Forgione AG, Zawawi KH, Al-Badawi EA, Driscoll SE: Effect of a passive jaw motion device on pain and range of motion in TMD patients not responding to flat plane intraoral appliances. Cranio 2002;20:55-66 [PubMed: 11831346]

Mejersjö 2008
Mejersjö C, Wenneberg B: Diclofenac sodium and occlusal splint therapy in TMJ osteoarthritis: a randomized controlled trial. J Oral Rehabil 2008;35:729-738 [Pubmed: 18482350]

Minakuchi 2004
Minakuchi H, Kuboki T, Maekawa K, Matsuka Y, Yatani H: Self-reported remission, difficulty, and satisfaction with nonsurgical therapy used to treat anterior disc displacement without reduction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;98:435-440 [PubMed: 15472659]

Naikmasur 2008
Naikmasur V, Bhargava P, Guttal K, Burde K: Soft occlusal splint therapy in the management of myofascial pain dysfunction syndrome: a follow-up study. Indian J Dent Res 2008;19:196-203 [PubMed: 18797094]

Nakaoka 2009
Nakaoka K, Hamada Y, Holmlund AB, Saito T, Arai G, Horiuchi T, Mishima A, Seto K: The changes of joint effusion on MRI and arthroscopic findings after visually guided TMJ irrigation correlated to the clinical outcome. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108: 99-104 [PubMed: 19201225]

Nilner 2008
Nilner M, Ekberg E, Doepel M, Andersson J, Selovuo K, Le Bell Y: Short-term effectiveness of a prefabricated occlusal appliance in patients with myofascial pain. J Orofac Pain 2008;22:209-218 [PubMed: 18780534]

Rohida 2010
Rohida NS, Bhad W: A clinical, MRI, and EMG analysis comparing the efficacy of twin blocks and flat occlusal splints in the management of disc displacements with reduction. World J Orthod 2010;11:236-244 [PubMed: 20877732]

Schiffman 2007
Schiffman EL, Look JO, Hodges JS, Swift JQ, Decker KL, Hathaway KM, Templeton RB, Fricton JR: Randomized effectiveness study of four therapeutic strategies for TMJ closed lock. J Dent Res 2007;86:58-63 [Pubmed: 17189464]

Schmitter 2005
Schmitter M, Zahran M, Duc J-MP, Henschel V, Rammelsberg P: Conservative therapy in patients with anterior disc displacement without reduction using 2 common splints: a randomized clinical trial. J Oral Maxillofac Surg 2005;63:1295-1303 [PubMed: 16122593]

Stiesch-Scholz 2002
Stiesch-Scholz M, Fink M, Tschernitschek H, Rossbach A: Medical and physical therapy of temporomandibular joint disk displacement without reduction. Cranio 2002;20;85-90 [PubMed: 12002834]

Stiesch-Scholz 2005
Stiesch-Scholz M, Kempert J, Wolter S, Tschernitschek H, Rossbach A: Comparative prospective study on splint therapy of anterior disc displacement without reduction. J Oral Rehabil 2005;32:474-479 [PubMed: 15975126]

Tecco 2010
Tecco S, Tete S, Crincoli V, Festa MA, Festa F: Fixed orthodontic therapy in temporomandibular disorder (TMD) treatment: an alternative to intraoral splint. Cranio 2010;20: 30-42 [PubMed: 20158007]

Wahlund 2003
Wahlund K, List T, Larsson B: Treatment of temporomandibular disorders among adolescents: a comparison between occlusal appliance, relaxation training, and brief information. Acta Odontol Scand 2003;61:203-211 [PubMed: 14582587]

Wahlund 2003b
Wahlund K: Temporomandibular disorders in adolescents. Epidemiological and methodological studies and a randomized controlled trial. Swed Dent J Suppl 2003;164:2-64 [PubMed: 14717039]

3.7 Psychosocial interventions for Myofascial Oral Pain

Description of the intervention: Psychosocial intervention

Psychosocial interventions are non-pharmacological therapies which highlight the psychological factor of chronic pain. Psychosocial interventions for TMD target psychobiological mechanisms and psychosomatic correlations in order to relieve pain and improve functionality. Two major strategies for TMD are the increase of the pain coping ability of the patient, and/or the intensification of the muscular activity awareness, controlling at the same time oral parafunctions (i.e. bruxism, thumb-sucking, onychophagia, and breathing disorders).

Very often experts in TMD recommend psychosocial interventions as coadjuvant for traditional treatments like splint therapy. Interestingly, simple interventions planned for a control group in clinical trials of TMD resulted in approximate ranges of success than the experimental intervention. This observation led to investigate the placebo effect, but later the real influence of the conservative approach involving self-care strategies and counselling.

Self care was first introduced in 1981 as a Medical Subject Heading (MeSH) under the definition: "Performance of activities or tasks traditionally performed by professional health care providers. The concept includes care of oneself or one's family and friends" [646]. The self-care strategies for TMD include different techniques to reduce the muscle overloading and symptomatology, for ex. relaxation training, jaw exercises. Advices and /or recommendations related to soft diet, application of hot and cold packs are frequently included in the self-care strategies for TMD.

The definition of counseling is widely variable depending on the subject in which is immerse, e.g. economics, education, ethics, legislation, etc. Counseling was introduced as a MeSH in 1966. The current definition according to the National Center for Biotechnology Information (NCBI) is "the giving of advice and assistance to individuals with educational or personal problems" [646].

In the case of TMD treatments, counseling is principally a resource to offer basic information about the possible etiology and pathogenesis of this condition, and the teaching of avoidance conduct potentially risky to worsen the associated symptomatology. Counseling can be regarded as a psychosocial

intervention, however as a part of the usual treatment for TMD represents a secondary intervention to the main effect of the occlusal splint.

Some of the self-care strategies are intrinsically related to counseling, e.g. guidance in reduction of parafunctional jaw activities. These two terms, self-care and counseling, are not well defined for the TMD treatment, and habitually are used indistinctly.

Among the multiple psychosocial interventions, some specific treatments have been proposed in focus to TMD, namely cognitive behavioral therapies, oral habit reversal (OHR) and hypnosis. The author describes here some considerations on these alternatives.

- **Cognitive Behavioral Therapies (CBT)** essentially aims to improve the coping capacity of the patient, modifying the perception of the patient about himself and his relationship with the symptoms of TMD. In general, a treatment of CBT can combine teaching sessions of copying strategies, stress management, relaxation and imagery, showing improvements in many different conditions associated with chronic pain [52]. CBT for TMD is mainly based on skills training interventions focus on modifying the patient's interpretation of pain, usually combined with educational approaches to provide information about the jaw function and TMD.

- Other psychosocial intervention proposed for treating TMD is the **Oral Habit Reversal (OHR)**, which derived from techniques to control tic disorders [95]. OHR has been indicated with some success in clinical series to modify damaging oral habits such as biting or chewing lips or cheeks [55] and bruxism [480]. An oral habit reversal treatment is focused on to counteract the action of noxious habit behaviors, which are repetitive, or stereotyped behaviors that have negative physical or social effects on the individual, in this case, the bruxism. The objective of this treatment is to replace a harmful behaviour by an alternative one, which competes as an adopted response for some habits, i.e. an innocuous habit take place of bruxism. They are usually combined with dental therapies.

Regarding the treatment of facial pain, *Gramling* observed improvements on all measures of relative pain in TMD patients treated with oral habit reversal (in a

group format), compared to those in the control group [225]. Along the same line, *Townsend* found a significant reduction of maladaptive oral habits occurred from pre- to post-treatment and significant reductions in life stress and pain interference in TMD patients treated with habit oral reversal in a minimal therapist contact [563]. This article by *Townsend* reports a RCT on 20 women aging 18-55 yrs. with pain in the temporomandibular surrounding musculature. The study compared a group treated with oral habit reversal in a minimal therapist contact format against a wait-list control group. The OHR group showed a significant decrease in the pain measurements, life interference and life stress, and a lower frequency of oral habits compared to the wait-list group in the short-term. At a follow-up of 16 months only of the OHR group, results on pain continued showing a tendency to improvement.

In respect of clinical pain relief, one study reported that OHR may be as effective as a behaviourally-modified splint therapy [214]. *Glaros* conducted a RCT with results on 8 women with myofacial pain, arthralgia or both diagnoses comparing the effects of the OHR with a splint therapy. Patients treated with OHR reported a significant effect on time meanwhile the group of splint therapy decreased values of pain without a statistical significance. Results on self-reported pain at 1 year follow-up however, are not interpretable due to the use of different units of measurement for this outcome.

Peterson suggests that habit reversal appears to be more effective in reducing the myofacial pain symptoms of TMD than in improving temporomandibular joint function. During clinical observations he found that the temporomandibular joint sounds were unexpectedly increased, although the pain was reduced [449].

- Some interest in the use of **hypnosis** to control damaging habits relaunched the last decade. One study [611] showed significant differences post-treatment among three treatment modalities: hypnosis, occlusal splint, and minimal intervention based on education. The group which underwent hypnosis decreased significantly values of pain. Moreover, hypnosis and splint therapy were more effective than the minimal treatment to reduce the muscle sensitivity, however there was no difference related to the range of jaw motion.

Abrahamsen et al. [5] studied the effects of hypnosis in a RCT of 40 women with myofacial pain. In comparison to a control group which received relaxation instructions only, the hypnosis group presented a higher rate of pain relief at the

end of the treatment. It is notable that the coping strategy of reinterpretation of pain was used as a fundamental element of the hypnosis therapy, and was effectively more reported for the interventional group, but it did not fulfill every consideration to be a mediator.

How the intervention might work: Psychosocial intervention

According to *Aggarwal* [14], psychosocial interventions for chronic orofacial pain target two different suspected mechanisms of pain generation: inactivity (avoiding behaviors), and over activity (emotional stress).

The first model appeals to avoiding behaviors and negative cognition in response to prolonged and persistent pain. This inactivity would induce an exacerbated symptomatology in the affected area.

On the other hand, the emotional stress model proposes that psychological factors trigger oral habits resulting in muscle hyperactivity and subsequent facial pain. In this sense, the bruxism for example can be considered to be an expression of high stress level and thus would require behavioral interventions, i.e. surface electromyographic biofeedback (sEMG), relaxation training, etc.

As regards of TMD therapies, some psychosocial interventions better related to the emotional stress model, including hypnosis and oral habit reversal among others, principally tackle the parafunctional habits.

Alternatively, there exists the possibility that psychosocial interventions target comorbid psychological disturbances, for instance depression or high somatisation, thus explaining the positive impact on TMD patients. It still remains this open question about the relevance of the psychological factors and the identification of the specific ones for TMD.

Results of the search

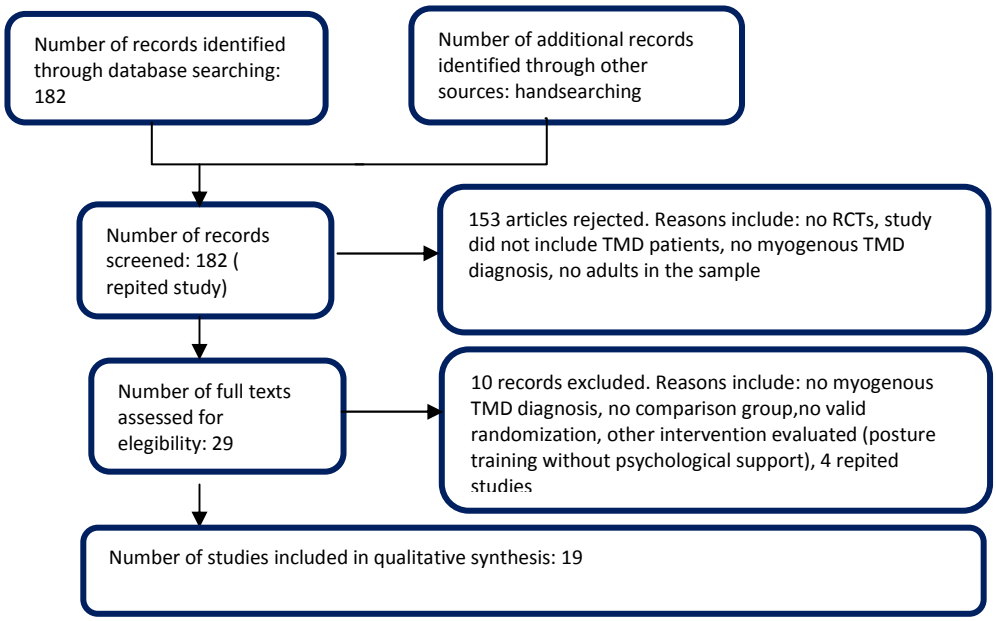

***Diagram 6**. Study flow diagram: Psychosocial interventions for the treatment of Myofacial Pain (1999-2012)*

Included studies

Multiple options of psychosocial interventions were reported during the last 13 years. The author didactically divided these interventions into four categories. The first one involves relative simple interventions oriented to enhance the self-control of the patient, i.e., counseling, self-care and their mutual reinforcement, and additionally their associations with other therapeutic agents. These interventions can be delivered for trained professionals other than psychologists. The second and third categories are psychotherapies which aim to improve coping abilities and behavioral management, namely cognitive behavioral therapies and hypnosis respectively, indicted alone or in combination with other treatments. The last category is a set of protocols closer to physiotherapeutic interventions which target harmful behaviors, increasing the awareness of muscular activity, e.g. physical self-regulation and EMG-biofeedback.

In the first category we found two studies on counseling: one study on counseling only (*Conti 2012*) and one trial on counseling plus placebo (*Alencar 2009*). Eight studies focused on self-care strategies with or without additional treatments or placebos: *Herman 2002*, *Kalamir 2012*, *Michelotti 2004*, *Michelotti*

2012, *Mulet 2007*, *Ritenbaugh 2012*, *Truelove 2006*, *Turner 2011*. Seven RCTs reported self-care strategies plus counseling in combination with splint therapy (see Meta-analysis of "Usual treatment" vs. Psychosocial interventions): *Carlson 2001*, *Conti 2012*, *Dworkin 2002a*, *Dworkin 2002b*, *Litt 2010*, *Truelove 2006*, *Turner 2006*. Three of them (*Dworkin 2002a*, *Dworkin 2002b*, *Turner 2006*) implemented an imbalance intervention consisting of self-care strategies, counseling and indication of occlusal appliances according to the prescription of the dentist. The studies by *Dworkin 2002a* and *Turner 2006* were especially concerned to the differences of two extra psychosocial interventions, viz. tailored self-care strategies and CBT.

In the second category, we detected seven trials on cognitive behavioral therapies: one CBT only (*Gardea 2001*), one CBT plus pharmaceutical placebo (*Calderón 2011*), two CBT plus EMG-biofeedback (*Gardea 2001*, *Gatchel 2006*), two CBT plus self-care strategies (*Ritenbaugh 2012*, *Dworkin 2002b*), and two CBT plus „usual treatment" (*Litt 2010*, *Dworkin 2002a*).

Hypnosis was reported in one RCT (*Abrahamsen 2009*). Finally, the last approach was represented by one study on Physical self-regulation (*Carlson 2001*), one Intraoral myofacial therapy (*Kalamir 2012*) and two trials on EMG-Biofeedback with and without CBT (*Gardea 2001*, *Gatchel 2006*)

Excluded studies

The reasons for exclusion are declared in the Characteritics of the excluded studies.

Effect of the intervention

Regarding counseling and self-care strategies (SC), the combination of both psychosocial interventions seems to lead to an enhancement of clinical success.

Michelotti 2004 compared a professional counseling (information about TMD and self-care of the jaw musculature) with SC structured around home-jaw exercises (diaphragmatic breathing, self-massage, thermal packs, and stretching and coordination jaw exercises). The authors did not find any differences between the groups at short-term. In the study by *Kalamir 2012*, the combination of SC with a routine of digital massages in the consultation room

for 5 weeks was more effective for pain relief at 1-year follow-up than the only routine of massages. Although this latter group obtained improvements alike the first one until the 6-months follow-up, the therapeutic effects increased onwards only for the combination with self-care strategies. The control non-treatment group showed no variation during the 12 months of observation.

Comparing counseling (education) with or without splint, *Conti 2012* observed similar reduction in pain scores; although the time to get improvements was shorter for stabilization splint (2-weeks follow-up) and NTI-splint (6-weeks follow-up) than for counseling only (3-months follow-up). Besides, the magnitude of pain reduction at 50% from baseline was reported for 88.2% of the patients in the stabilization group, 76.9% for the NTI splint, and only 33.3% of the counseling group. Other outcomes did not differ between groups, namely PPT, and number of occlusal contacts ($p>0.05$ declared by authors).

Alencar 2009 found equally efficacy in three different splint therapies combined with counseling and self-care strategies, including one stabilization splint, one resilient splint and one placebo palatal non-occluding plane. This fact suggests little relevance of the clinical impact of an oral appliance; however it is not possible to discard some influence of the non-occluding splint.

Michelotti 2012 observed that the intervention counselling and SC including jaw exercises inspired in oral habit reversal was comparable to effects of a splint therapy with a stabilization oral appliance. Besides, the time effect on spontaneous muscle pain of the intervention was only favourable for the psychosocial interventions at the third month follow-up.

In the study by *Mulet 2007* self-care strategies (SC) were as effective as a specific physiotherapy named 6x6 exercise program. Pain scores decreased significantly from baseline for both treatments, without differences between groups. Regarding physiotherapeutic evaluations, one of three postural measures varied distinctly for the interventions at 4-weeks follow-up (cranial angle SC=-1.49 degrees; SC+6x6=+1.76 degrees, $p<.01$). Moreover the head sway changed significantly different between groups. On the contrary, trunk sway and overall change of symptoms were similar for both groups.

When compared with Traditional Chinese Medicine (TCM), self-care strategies (SC) appeared to be less effective for patients with persistent higher scores of pain. However the community model by *Ritenbaugh 2012* should be analyzed thoroughly in different stages. In a first phase of this stepped care study,

patients with scores above the chosen cut-point (worst facial pain=7) were treated with TCM or SC. From this latter group, a clinical significant reduction (50% from baseline) of characteristic facial pain (CFP) and worst facial pain (WFP) was achieved by a 14,3% of the patients at 10-weeks follow-up, and were assigned to continue self-care strategies; they were not further analyzed. It is not verifiable if in the TCM group was present such a figure, because all patients just continued with the therapy until the end of the study. The patients in the self-care group who remained with scores higher than 5 of worst facial pain in the SC group were reallocated into two groups, one receiving TCM and other receiving CBT. From these two interventions, the combination of SC followed by a second phase of CBT exhibited less reported improvements than the group receiving TCM. However both combinations were superior to produce new changes in pain scores than the group of only TCM, considering that TCM group started this period about 1 point below in the measured scale (NGRS). We did not conduct extra analysis, because standard deviations were not available. Nonetheless, the authors found statistically significant benefits for TCM over SC in CFP, WFP and pain interference. The patients with higher scores of WFP who followed the complete period TCM treatment exhibited greater percentages of 30% pain reduction than the combinations of SC+TCM and SC+CBT (CFP=44, 36, 33 respectively). Apparently, the major impact of TCM was improving pain interference in both patients with higher and lower WFP scores (30% reduction pain interference=69% and 68% respectively). Other benefits were declared for TCM related to quality of overall well-being, sleep, and patient enablement, but not in psychological outcomes at short-term (18 weeks).

Pharmacological treatments were opposed to psychosocial interventions in the studies by *Herman 2002*, *Calderón 2011*, and *Turner 2011*. They observed no significant differences between the clinical results of SC with placebo or 0.5mg clonazepam, but higher pain relief for the combination of SC and 10mg cyclobenzaprine. The reduction of pain for the latter intervention doubled the scores of the other two groups which were identical. The adjusted scores of pain intensity to baseline, sex and gender exhibited a significant difference in favour of the cyclobenzaprine group. On the contrary as stated in the Cochrane review of Pharmacological interventions for pain in patients with chronic orofacial pain [14], we found no other bias in the study by *Herman 2002* since he

reported a baseline analysis without significant differences, and adjusted values in the results.

Turner 2011 evaluated the effects of an hormonal therapy (20 µg ethinyl estradiol and 100 µg levonorgestrel during 4 months) compared to two protocols of self-care strategies, one of them coincident to the menstrual cycle (targeted SC). Both SC interventions produced a decline in pain intensity, pain interference, and affective scores at 12-months follow-up meaningfully different from the hormonal therapy, but not different one of each other. At 1-year follow-up, 30% pain reduction was achieved by 67% of patients in the SC group, 70% of the targeted SC group, and only 35% of the pharmaceutical intervention. Patients in the targeted SC and SC groups had about 3 times more possibilities to report no pain interference when compared to the hormonal group (OR=3.2, 95%CI 1.1-9.1 for the targeted SC; OR=2.9, 95% CI 1.0-8.3 for the SC group). Among the process measures, beliefs of disability, harm and control, self-efficacy and perceived effectiveness of coping strategies obtained substantial improvements in both SC strategies. Nonetheless, catastrophizing, also a process measure, did not differ between groups at 12-months follow-up. The patients under psychosocial interventions did not report adverse effects, but the estradiol intervention produced 47% break-through bleeding or spotting, 11% increased appetite or weight gain, 11% moodiness, 8% breast tenderness, and 8% increased acne.

In the study by *Calderón 2011* 25mg amitriptyline and placebo were compared with and without additional CBT. At the 11th week, patients receiving amitriptyline with and without CBT, but not patients taking placebo, showed significant improvements in pain reduction within groups, however no differences between groups were identified. CBT was determinant between placebo interventions to improve depression scores at 11-weeks follow-up showing be more efficacious. Sleep quality and mean scores of Oral Health Impact Profile did change neither within nor between groups during this observation period. One patient was excluded because adverse effects (self-report visual symptoms).

Some studies reporting on „usual treatment“ (s. Meta-analysis “Usual treatment” vs. Psychosocial interventions) failed to demonstrate advantages of this multi-approach based on splint therapy to the only indication of psychosocial interventions. *Carlson 2001* did not observe differences between the “usual

treatment" (stabilization splint + self-care strategies and counseling) and a physical self-regulation program (defined by the authors as a psychosocial intervention), except for ranges of mouth opening.

Truelove 2006 did not find differences between self-care strategies and combined treatments with hard splint ("usual treatment") or soft splint.

In both studies by *Dworkin*, tailored "usual treatments" (UT) were confronted to psychosocial interventions. Patients referred to treatment for TMD were subject of two parallel studies, after being split by means of the scores in the Graded Chronic Pain (GCP). In patients with lower psychological distress (*Dworkin 2002b*), patients receiving self-care strategies plus CBT reported significant more pain relief, less pain interference, and reduction of the number of muscle tender points than an UT at 12-months follow-up.

In the study by *Dworkin 2002a,* patients with high psychosocial disabilities answered positively to "usual treatment" reinforced by CBT at the 6-months follow-up, however the effects on the outcomes characteristic pain intensity (CPI) and ability to control pain did not remain significantly different between groups after 1 year, by means of the continuous improvement of the UT group. Other outcomes like pain interference, range jaw movement and number of tender muscles differ neither at 6- nor 12-months follow-up.

In other RCT controlling the effect of adding CBT to "usual treatment" *Litt 2010* reported that although both interventions achieved pain reduction, it was greater for the combined treatment over the time. CBT and EMG-biofeedback seems to make no differences at 52 weeks-follow-up in respect of pain interference and depression. In addition, some moderators for CBT were analyzed, namely readiness for self-care (motivation), catastrophizing, somatization, coping, pain management self-efficacy, and optimism. Moderators "are baseline characteristics (that may or may not be theoretically identified) that interact with treatment to affect outcomes" [534]. It is noticeable that high readiness and low somatization was an influencing factor to explain more effectiveness for CBT regarding pain reduction within patients with similar baseline characteristics of the mentioned variables and also between different interventions. Besides, self-efficacy moderated only the UT+CBT intervention, thus patients with higher self-efficacy dropped pain over time significantly more than patients with lower scores. Other moderation effect was found for somatization on pain interference, which was positively related.

Moderation analyses only found predictors (when the interaction term with baseline characteristics is not statistically significant) on depression scores for all variables, and on interference for all variables but somatization.

The RCT by *Turner 2006* reported on the differences of adding CBT to "usual treatment". At 12-months follow-up the CBT+UT was significantly more successful in reducing scores of pain interference, characteristic pain intensity, and depression. 50% of pain reduction was achieved by 50% of the CBT+UT group, while 29% of the SC+UT group. The odds for reporting no pain interference for the CBT+UT quadrupled the expected for SC+UT (OR=4.2, 95%CI=1.7, 10.2). Along with these positive results, jaw functionality was improved for this group, expressed by better marks on the non-masticatory and masticatory MFIQ scales. Proportions of the participants with low in comparison with moderate/severe masticatory impairments adjusted to baseline were meaningfully more favorable for the CBT+UT group; however the non-masticatory scale was not significant between groups.

The authors defined some process measures including beliefs of disability, harm, control, and self-efficacy; catastrophizing and rumination. All of them were better evaluated at 1-year follow-up for the CBT+UT group. On the contrary, from unlike scales of coping strategies, only one was significantly different between groups, stating that relaxation was effectively used by the CBT group, but not task persistence, self statements or rest techniques. Furthermore, patients in the CBT+UT group decreased the prevalence of high BDI scores for depression, so that the odds ratio to get less than score 21 was four times higher for this group. Interestingly, when adjusted according to credibility all outcome and process measures raised statistical significance. Overall helpfulness and treatment satisfaction were more pronounced in the CBT+UT group, and only TMD knowledge did not differ between groups.

After a weighting of the final scores according to compliance of the treatment, *Gardea 2001* interpreted that except for cognitive behavioral therapies alone, the interventions (EMG-biofeedback and EMG-biofeedback plus CBT) were significantly better than no treatment in respect of characteristic pain intensity. Moreover, EMG-biofeedback plus CBT was for both disability scores and jaw functional limitations significantly more effective than no-treatment, likewise CBT was superior than no-treatment to improve jaw functionality. We cannot gauge the clinical usefulness for this kind of weighting, because no evidence is

available about the quantity of sessions necessary for these psychosocial interventions in the TMD treatment. The study by *Gatchel 2006* attempt to describe the effects of the same protocol combining CBT and EMG-biofeedback as an early intervention in patients with symptomatology related to TMD during less than 6 months. According to some authors, diagnosis of TMD is characterized by chronicity, which is addressed in most of the studies after 6 months of continuous signs and symptoms, but for others up to 3 months. We consider these results for both groups of patients with a mean of symptomatology of about 100 days. The authors found significant improvements in pain scores, coping abilities and depression (Beck Depression Inventory) for the active group also compared with a non-treatment group, which did not change during the 1-year follow-up. Furthermore, patients who were not intervened exhibited more psychological disturbances at the end of the trial, specifically generalized anxiety disorders and pain disorders.

Abrahamsen 2009 contrasted hypnosis to general relaxation and visualization home exercise. The overall pain intensity obtained from pain diaries dropped significantly within the hypnosis group, which reached 50.4% pain relief compared to -0.7% in the relaxation group. Therefore percentages of patients experiencing 30% pain reduction were 63% for the hypnosis group vs. 15% for the relaxation group. However, no relevant differences were found between groups using the McGill Pain Questionnaire which related pain to psychological descriptors. In contrast to the evaluation made by *Aggarwal* [14], we did not expected an exact correlation between the daily pain and the subjective pain, especially because the fluctuation of the TMD symptomatic. Besides, both outcomes showed reduction for the experimental group and not for the control group. The number of muscle tender upon palpation decreased equally for both groups; however the pain intensity in the masseter muscle was significantly higher in the hypnosis group. Likewise, the jaw opening and jaw limitation on oral activities improved similarly between groups. Patients in the hypnosis group used more the coping strategy reinterpreting pain sensations over the time, while both groups implemented diverting attention after treatment. Main effect for time was observed for somatization, anxiety scores and number of awakenings due to pain, decreasing in both groups from baseline.

Quality of the evidence

The risk of bias according to the Cochrane Collaboration of the included studies is presented in the figures 38 and 39. One study failed in the key criteria blinding of outcome assessment (*Gardea 2001*), and three studies were evaluated in this item as unclear risk of bias (*Calderón 2011*; *Litt 2010*; *Turner 2011*). According to the Delphi list 78.95% accomplished this item.

One study applied a weighting of the results according to the compliance of the treatment instead of using ITT analysis or imputations (*Gardea 2001*). 57.89% of the included RCTs conducted Intention-to-treat analysis.

In spite of the additional information from many authors, 47.47% of the included studies presented an unclear risk of bias for the criteria allocation concealment. According to the Delphi list 57.89% accomplished this item.

The general positive accomplishment of the Delphi list (table 9) was 69.56%. RCTs with score 6 or higher were 73.68% of the included studies.

Study	Allocation randomized	Allocation concealed	Groups similar at baseline	Inclusion criteria specified	Blind outcome assessment	Blinded care provider	Blinded patients	Point estimates and variability	Intention-to-treat analysis
Abrahamsen 2009	Yes	Don't know	Yes	Yes	Yes	No	No	Yes	No
Alencar 2009	Yes	Don't know	Yes	Yes	Yes	No	Yes	Yes	No
Calderón 2011	Yes	Yes	Yes	Yes	Don't know	Yes	Don't know	No	No
Carlson 2001	Yes	No	Yes	Yes	Yes	No	No	Yes	No
Conti 2012	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
Dworkin 2002a	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Dworkin 2002b	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Gardea 2001	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Gatchel 2006	Yes	Don't know	Yes	Yes	Yes	No	No	Yes	Yes
Herman 2002	Yes	Don't know	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kalamir 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes (control group)	Yes	Yes
Litt 2010	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes
Michelotti 2004	Yes	Don't know	Yes	Yes	Yes	No	No	Yes	No
Michelotti 2012	Yes	Don't know	Yes	Yes	Yes	No	No	Yes	No
Mulet 2007	Yes	Don't know	Yes	Yes	Yes	No	Yes	Yes	No

Ritenbaugh 2012	Yes	Yes	Yes (for each allocation)	Yes	Yes	No	No	No	Yes
Truelove 2006	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Turner 2006	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Turner 2011	Yes	Yes	Yes	Yes	Don't know	No	No	Yes	Yes

Table 9. *Delphi list: Psychosocial Interventions for myofacial pain*

Characteristics of studies

Characteristics of included studies

Abrahamsen 2009

Methods	RCT. Single center; two parallel groups. Data before and after treatment
Participants	40 (out of 43) participants: mean age=38 (SD=10.8), 100% women; mean duration of pain=11.9(9.9)yrs. Inclusion criteria: myofascial TMD pain according to the RDC/TMD, type Ia or Ib, and additionally type IIIab; daily pain intensity >3 on a NRS with a duration of 6 months or longer. Exclusion criteria: previous experience with hypnosis was not acceptable but experience with relaxation was allowed. Location: Denmark
Interventions	Group A (n=20): Hypnosis (4 individual 1hr session of hypnotic intervention aim to control or change pain perception) Group B (n=20): relaxation only (4 individual 1hr session of relaxation) Cointervention: previous splint or drug therapies were allowed to continue
Outcomes	Pain diary (NRS) McGill Pain Questionnaire Coping (Coping Strategies Questionnaire Muscle Pain Index (20 sites) Jaw opening without pain Maximum unassisted jaw opening Maximum assisted jaw opening Protrusion and laterotrusion Jaw Disability Index Characteristic Pain Pain Interference Somatization (SCL-90-R) Obsessive/compulsive symptoms (SCL-90-R) Coping (SCL-90-R) Depression (SCL-90-R) ANxiety (SCL-90-R) Sleep quality (Pittsburgh Sleep Quality Index) Self-medication Hypnotic susceptibility (Harvard Group Scale of Hypnotic Susceptibility)
Notes	A second report from this study about pain and blink reflexes was published by *Abrahamsen 2011* (6)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...patients were randomly assigned by drawing lots"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. However, The therapist who conducted the hypnosis was blinded to the hypnotic susceptibility of the patients during treatment.

Blinding of outcome assessment (detection bias)	Low risk	Quotes: "All data were entered by an assistant who was blinded to the treatment condition" "The clinicians performing the final RDC/TMD examinations were blinded to the hypotheses and group assignment."
Incomplete outcome data (attrition bias)	Low risk	Detailed report of drop outs. Balanced groups and similar reasons
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Alencar 2009

Methods	RCT. Single center; three parallel groups. Follow-up for 90 days.
Participants	42 (out of 45) patients: mean age (analyzed) = 34 (R=18-65); 88.10% women. Inclusion criteria: age 18-65 years; diagnosis of myofascial pain with reproduction of the chief complaint with palpation of a trigger point in the masseter muscle; at least six natural teeth in each quadrant. Exclusion criteria: previous splint therapy; any obvious dental decay or periodontal disease; history of trauma in the pain area in less than 30 days; any systemic condition associated with widespread pain (e.g. fibromyalgia); medical history of current drug addiction; any other TMD diagnosis according to the Diagnosis Criteria of the AAOP such as TMJ osteoarthritis or capsulitis. Location: Brazil
Interventions	Group A (n=14): mandibular hard occlusal splint Group B (n=14): mandibular soft occlusal splint Group C (n=14): non-occluding splint Indications for all groups: full time wearing of the respective splint during the first week and after this period, only nocturnal wearing Cointerventions: counseling for all groups
Outcomes	Muscle Pain Index (6 sites scored 0-3) Subjective Pain using the Modified Symptom Severity Index (Mod-SSI)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: “Selection bias was considered through a defined and concealed randomization process with rather and subject blind of group assignment. Patients were randomly assigned into one of the three experimental groups…”
Allocation concealment (selection bias)	Unclear risk	Quote: “…concealed…” (s. random sequence generation)
Blinding of participants and personnel (performance bias)	Low risk	Participant but not personnel blind. Incomplete blinding, but outcome is not likely to be be influenced by this lack Quote: “…subject blind of group assignment…” “Splint installation, adjustment and follow-up were carried out by a researcher who knew to which group the patients belonged.”

Blinding of outcome assessment (detection bias)	Low risk	Quote: ”Another ‘blind’ researcher collected the data.”
Incomplete outcome data (attrition bias)	Low risk	Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Calderón 2011

Methods	RCT. Single center, 4 parallel groups. 7 week treatment, follow-up for 4 weeks
Participants	47 participants [29 completers]: mean age= 35.6 years (range 17-52 years); mean pain duration=72.35 months (range 6-384 months); mean pain intensity=76.5mm VAS (range 42-100 mm). Inclusion criteria: history of orofacial pain for more than 6 months; pain occurring daily or almost daily for at least the month preceding enrolment; pain of at least moderate severity (i.e. at least 40 mm on a VAS) age ranging from 17-55 years. Exclusion criteria included major neurological or psychiatric disorders, glaucoma, history of intolerance to amitriptyline, pain secondary to trigeminal neuralgia, or pain attributable to other local, well defined condition. Location: Brazil
Interventions	Group A (n=11): amitriptyline 25 mg Group B (n=12): amitriptyline 25 mg and CBT Group C (n=11): placebo and CBT Group D (n=13): placebo only (control)
Outcomes	Pain intensity (VAS) Depression (BDI) Qulity of life (Oral Health Impact Profile (OHIP)) Sleep quality (Pittsburgh PSQI)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization scheme was generated using the web site ‘www.randomization.com’"
Allocation concealment (selection bias)	Low risk	Quote: "...a different person was designated to allocate the patients in their groups, for the medicine distribution and to lead the patients to the CBT"
Blinding of participants and personnel (performance bias)	Unclear risk	Quote:"...the researcher was blind to group distribution"
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed
Incomplete outcome data (attrition bias)	Low risk	Attritions balanced in number and reasons. "As treated" analysis

Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Carlson 2001

Methods	RCT. Single center; two parallel groups. Follow-up for 26 weeks.
Participants	44 (out of 56) participants: mean age analysed sample=34.6; 77.27% women; average months of pain duration=52.3. Inclusion criteria: myofascial pain (Type 1a and Type 1b) according to the RDC/TMD: chief complaint originating from the masticatory muscles; pain for longer than 1 month; pain to palpation of at least 3 standard muscle sites. Initial medication usage was not altered during the study. Location: USA
Interventions	Group A (n=21 [13 completers]): standard dental care (stabilization splint, nocturnal wearing + self-care strategies [e.g. soft diet, jaw relaxing]) Group B (n=23 [19 completers]): two 50min. sessions of physical self-regulation (strategies for seven domains: monitoring and reducing muscle parafunction in the head and neck region, proprioceptive awareness training to improve symmetric head and neck posture, instructions for improving sleep onset, position oriented relaxation training, physical activity, nutrition/fluid management, and diaphragmatic breathing training)
Outcomes	Life interference (MPI) Pain severity (MPI) Pain intensity (VAS) Ability to control pain Somatization (SCL-90-R) Depression (SCL-90-R) Anxiety (SCL-90-R) Affective distress (SCL-90-R) Unassisted jaw opening without pain (mm) Unassisted jaw opening with pain (mm) Muscle Pain Index (17 sites) Sleep quality (Pittsburgh) Awareness of tooth contact (min) Obsessive/compulsive (SCL-90-R) Fatigue (0-10)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:“Random assignment was accomplished by the use of a table of random numbers.”
Allocation concealment (selection bias)	Unclear risk	Not reported in the article From correspondence: “The evaluators and the professionals delivering the treatment were not a part of the assignment procedures but the table was open for the researchers to review.”
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.

Blinding of outcome assessment (detection bias)	Low risk	Quote*:* “A board-certified dentist with postdoctoral training in orofacial pain who was not aware of the treatment protocol to which each participant was assigned performed all initial dental evaluations and administered the self-report measures after the dental evaluations." Quote: „The orofacial pain evaluations were carried out by a dentist not aware of the protocols to which the participants were assigned.“
Incomplete outcome data (attrition bias)	Low risk	Detailed explanations for withdrawals. Missing outcome data balanced, and reasons unlikely to be related to true outcome. From correspondence: “26-weeks analysis included only the completers” “As treated” analysis in a recall of the patients
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Unclear risk	Free of other bias

Conti 2012

Methods	RCT. Single center, three parallel groups. Follow-up for 3 months
Participants	51 participants: mean age 37.16yrs; 88.23% women. Inclusion criteria: adults aged 18 yrs. or more; diagnosis of myofascial pain with or without opening limitation (RDC/TMD); pain intensity of at least 50mm in VAS. Exclusion criteria: dental pain or tender muscles due to systematic diseases; major psychological disorders; recent history of face and neck trauma; current TMD treatment; denture wearers. Location: Brazil
Interventions	Group A (n=21): Stabilization appliance only nocturnal wearing + counseling (habits and behavioral changes)+ education. Group B (n= 16): NTI appliance + counseling + education. Group C (n=14): counseling only
Outcomes	Pain intensity (VAS) Pressure Pain Threshold (PPT) Number of occlusal contacts
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:“…patients were randomly allocated” From correspondence: “Randomization was done using a computer program (Excel)"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.

Blinding of outcome assessment (detection bias)	Low risk	The same blinded examiner conducted the follow-up Quote: “using a “blind” design with no awareness of the individuals group"
Incomplete outcome data (attrition bias)	Unclear risk	Insufficient report of attrition
Selective reporting (reporting bias)	High risk	Not all the primary outcomes were appropriately reported
Other bias	Low risk	Free of other bias

Dworkin 2002a

Methods	RCT. Single center; two parallel groups. Treatment for 4 months, follow-up for 12 months.
Participants	117 patients: mean age 38.8 (SD=10); mean age group A= 38.6 (SE=1.3), mean age group B=39.3 (SE=1.4); 82,91% women; education level higher than high school 72.65% Inclusion criteria: age 18-70 yrs.; facial pain in the masticatory muscles, TMJ, region in front of the ear or inside the ear; RDC/TMD Axis II GCP score of II High, III, or IV. Exclusion criteria: pain attributable to confirmed migraine or head pain condition other than tension headache; acute infection or other significant disease of the teeth, ears, eyes, nose, or throat; debilitating physical or mental illness; necessity for emergency TMD treatment; no local language skills Location: USA
Interventions	Group A (n=59 [56 completers]): comprehensive care (“usual treatment” + cognitive behavioral therapy (CBT) and methods employed in multidisciplinary management of chronic pain including exercises for jaw stretching and jaw muscle relaxation) Group B (n=58 [51 completers]): “usual treatment” (at the discretion of the attending dentist: intraoral occlusal appliance + physiotherapy + medication + patient education including self-care behaviors)
Outcomes	Characteristic pain Intensity (CPI) Pain interference score (0-10) Ability to control pain (0-6) Somatization (SCL-90-R) Depression (SCL-90-R) Helpfulness of treatment Satisfaction with treatment Unassisted jaw opening without pain (mm) Unassisted jaw opening with pain (mm) Maximum assisted opening (mm) Number of muscle sites tender to palpation (16 extraoral +4 intraoral sites)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “...117 (62.9%) agreed to participate and were assigned randomly to... (one of the two groups)” From correspondence: according to a coauthor, the standard method for this research team corresponds to

		the blocked randomization using different block sizes.
Allocation concealment (selection bias)	Low risk	Not reported in the article. From correspondence: according to a coauthor, the standard method of randomization includes the concealment of the allocation to the personnel until start the trial.
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but the outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “All clinical baseline and follow-up study data collection were performed by calibrated and reliable clinical examiners not participating in the RCT and blinded to the study group to which patients were assigned."
Incomplete outcome data (attrition bias)	Low risk	ITT analysis without imputations. From correspondence: “We did not do any imputation” Comparison of study completers and dropouts was conducted.
Selective reporting (reporting bias)	Unclear risk	The number of participants for each outcome is not clear. Quote: “…there are small differences in numbers of patients across some analyses“
Other bias	Low risk	Free of other bias

Dworkin 2002b

Methods	RCT. Single center; two parallel groups. Treatment for 2.5 months, follow-up for 12 months.
Participants	124 patients: mean age 37.5 (SE=1.09) [mean age group A= 37.4 (SE=4.2), mean age group B= 38.0 (SE=3.6)]; 84.68% women; education level higher than high school group A=91.8%, education level higher than high school group B=66.7% (groups differed significantly). Inclusion criteria: age 18-70 yrs.; self-report of pain in the masticatory muscles, TMJ, region in front of the ear or inside the ear, or report of stiffness or other symptoms of discomfort in the same orofacial region; RDC/TMD Axis II GCP score of 0, I or II-Low Exclusion criteria: pain attributable to confirmed migraine or head pain condition other than tension headache; acute infection or other significant disease of the teeth, ears, eyes, nose, or throat; presence of significant or debilitating chronic physical or mental illness; necessity for emergency TMD treatment. Location: USA
Interventions	Group A (n=61): self-care intervention (manual-based individual 3 session of self-care including cognitive-behavioral methods) Group B (n=63): “usual treatment” (at discretion of the attending dentist: physiotherapy, medications, occlusal appliance, and patient education including some components of self-care)
Outcomes	Characteristic pain Intensity (CPI) Graded Chronic Pain Scale (GCPS) Somatization (SCL-90-R) Depression (SCL-90-R) Helpfulness of treatment (0-10) Satisfaction with treatment (0-5) Unassisted jaw opening without pain (mm) Unassisted jaw opening with pain (mm) Maximum assisted opening (mm) Number of muscle sites tender to palpation (0-16) Increase of knowledge (0-10)

Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The standard methods used in this study for randomizing…” From correspondence: according to a coauthor, the “standard method” for this research team corresponds to the blocked randomization using different block sizes
Allocation concealment (selection bias)	Low risk	Not reported in article. From correspondence: according to a coauthor, the standard method of randomization includes the concealment of the allocation to the personnel until start the trial.
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack
Blinding of outcome assessment (detection bias)	Low risk	Quote: “All clinical baseline and follow-up study data collection were performed by calibrated and reliable clinical examiners not participating in the RCT and blinded to the study group to which patients were assigned."
Incomplete outcome data (attrition bias)	Low risk	Quote: “ …only the results of intent-to-treat analyses are reported." Analysis of non completers
Selective reporting (reporting bias)	Unclear risk	All expected outcomes were reported. Quote: “All analyses present results for patients for whom data are available although there are small differences in numbers of patients across some analyses” Comment: not possible to define the mentioned differences
Other bias	Low risk	Free of other bias

Gardea 2001

Methods	RCT. Single center; four parallel groups. Treatment for 12 weeks, follow-up for 12 months.
Participants	108 patients: mean age group A=35.1 (±9.49), mean age group B=37.4 (±10.8), mean age group C=35.1 (±8.56), mean age group D=36.5 (±11.4); 83.33% women; mean years of education group A=16.0 (±1.9), mean years of education group B=15.3 (±2.40), mean years of education group C=16.1 (±1.79), mean years of education group D=14.8 (±2.07); 84.5% Caucasian, 7.13% Hispanic, 5.13%, African American, 3.25% Other; mean months of pain duration group A=110±115, mean months of pain duration group B=70.3±64.4, mean months of pain duration group C=70.2±70.7, mean months of pain duration group D=100±101 Inclusion criteria: range age 18-65; TMD diagnose according to RDC/TMD. Exclusion criteria: other significant physical condition (i.e. fibromyalgia, cancer, low back pain); ≥ 6 score DSM-IV Axis I diagnose; psychosis or active suicidal ideation; not meet RDC/TMD Location: USA

Interventions	Group A (n=24): Cognitive-behavioral skills training (CBST) Group B (n=27): Biofeedback Group C (n=29): Combined treatment (CBST+Biofeedback) Group D (n=28): no treatment
Outcomes	CPI, GCPS from RDC/TMD Axis I Limitations related to mandibular functioning Profile of mood states (POMS)
Notes	The previous report at short-term published by *Mishra et al*. (395) considers a smaller number of participants (n=94).

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...using the urn method of random assignment ..."
Allocation concealment (selection bias)	Low risk	Not addressed Comments: high unpredictability of urn design
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Low risk	Quote: "…follow up was conducted on an intent to-treat basis."
Selective reporting (reporting bias)	High risk	No complete consistency between short-term and long-term reports: some outcomes were incompletely reported.
Other bias	Unclear risk	Analysis was weighted by number of sessions (0-12) for follow-up outcomes

Gatchel 2006

Methods	RCT. Single center; two parallel groups. Follow-up for 12 months.
Participants	101 patients: mean age 37.76 (R=18.0-61.45), mean age group A=36.7 (±11.47), mean age group B= 39.08 (±11.17); 80.19% women; mean education years group A=15.11 (±2.05), mean education years group B=15.60 (±2.17); 78.21% Caucasian, 5.94% Hispanic, 7.92% African-American, 4.95% Asian, 2.97% other ethnic group. Inclusion criteria: age range 18-70; acute jaw or facial pain that had been present for less than six months; group 1a RDC/TMD diagnose (myofacial pain). Exclusion criteria: comorbid pain-exacerbating physical condition; previous history of jaw pain. Location: USA
Interventions	Group A (n=56): Cognitive-behavioral therapy (CBT) and biofeedback (BFB) Group B (n=45): no intervention
Outcomes	RDC/TMD Axis I: Pain (CPI) Median particle size (MPS) Back depression inventory mean (BDI), ways of coping mean (WOC) Mood and personality (SCID I and SCID II)

Notes	The second report presents financial data in a subsample (541). These outcomes are not relevant for the review.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote:"We randomly assigned 101 consecutive subjects..." "We randomly assigned the subjects to one of two groups..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote:"...follow-up contacts were conducted by one counsellor who had seen some of the subjects in the EI group at intake, thus allowing for potential interviewer bias...We made every attempt to keep our sole evaluator unbiased by using a structured assessment protocol that was audiotaped for fidelity checks."
Incomplete outcome data (attrition bias)	Low risk	Quote :"... we used an intent-to-treat statistical method to calculate the projected one-year follow-up results. To manage missing data, we used the last-observation-carried-forward approach in which missing values are replaced with the last previous nonmissing value“. (2 exclusions, 1 attrition)
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Herman 2002

Methods	RCT. Single center; three parallel groups. Follow-up (treatment) for 3 weeks.
Participants	41 patients: mean age group A=26.9 (SD=10.1), mean age group B=24.0(SD=4.8), mean age group C=30.3 (SD=8.6); 80.49% women. Inclusion criteria: age 18-65 yrs.; jaw pain upon awakening, occurring a minimum of 2 days per week; diagnosis of myofacial pain (axis 1 group I) according to RDC/TMD, concurrent diagnoses of TMJ arthralgia and disc displacement with reduction were allowed; self-report of an average jaw pain intensity in the past week of at least 4 on VAS; self-report of psychological stability (subjects taking antidepressants were considered stable if they reported no current depression, and had been on a stable regimen of psychotropic medications for 3 months. Exclusion criteria: any dental, orofacial problem or TMD not meeting the definition of myofacial pain as defined by the RDC/TMD; self-report of persistent depression or an unstable regimen of psychotropic medication of less than 3 months as indicated by their history; jaw pain of potential systemic (e.g. fibromyalgia, widespread pain); clinical or radiographic evidence of osseous, odontogenic, or TMJ pathology; report of liver dysfunction, alcoholism, glaucoma, history of seizures, impaired renal function, use of monoamine oxidase inhibitors, acute recovery phase of myocardial infarction, arrhythmia, heart block or conduction disturbances, congestive heart

	failure, hyperthyroidism, pregnancy, or any other contraindications to clonazepam or cyclobenzaprine (including drug allergies). Location: USA
Interventions	Group A (n=13): self-care program + Clonazepam 0.5mg daily Group B (n=15): self-care program + placebo (lactose filler) Group B (n=13): self-care program + Cyclobenzaprine 10mg daily
Outcomes	Symptom Severity Index (SSI) for jaw pain TMJ pain and temple pain Pittsburgh Sleep Quality Index (PSQI)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Subjects were allocated to their treatment group by means of a randomized block design with the blocking variable being the current use of psychotropic medications“
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	Participants and personnel blinded Quote: “The capsules were formulated to have the same appearance (…) Neither the treating doctor nor the subject was aware of the treatment assignment until completion of the intervention.”
Blinding of outcome assessment (detection bias)	Low risk	Not addressed. Comments: probably done (s. performance bias)
Incomplete outcome data (attrition bias)	Low risk	Quote: “The final sample consisted of 33 women and 8 men with no subject dropouts or withdrawals”
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Kalamir 2012

Methods	RCT. Single center; three parallel groups. Follow-up for 6 months.
Participants	93 patients: mean age group A=35 (6.7), mean age group B=34 (6.1), mean age group C=35 (5); 53.76% women. Inclusion criteria: age range 18-50 yrs; daily history of periauricular pain with or without joint sounds for at least 3 months; voluntary participation, and a willingness to contribute long-term follow-up data; myogenous TMD sufferers (RDC/TMD); minimum baseline graded chronic pain scale (GCPS) scores of 3/10 on each of the three symptom outcome measures. Exclusion criteria: previous attendance at the practitioner’s clinic, edentulous; history of malignancy in the last 5 yrs; other physical contraindications such as active inflammatory arthritides, fractures, dislocations, or known instability of the jaws or neck; metabolic diseases; connective tissue and rheumatic disorders; hematological disorders; severe depression or somatization according to axis II RDC/TMD. Location: Australia

Interventions	Group A (n=31): waiting-list control group Group B (n=31): intra-oral myofacial therapies (IMT) 2 weakly 15-min. sessions for 5 weeks Group C (n=31): IMT + self-care
Outcomes	Resting pain (11-point GPCS)* Pain at maximum opening Pain during clenching Inter-incisal opening range (mm.-calliper)
Notes	From correspondence: GCPS was defined as a 11-point likert-scale, not including any calculation with disability or pain interference scores

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "… using a web-based random number generator… and consecutively allocated each numbered participant file into 1 of 3 groups…" "…consecutive applicants were block randomized using a pregenerated schedule into 3 groups "
Allocation concealment (selection bias)	Low risk	Quote: "(receptionist)… prepared participant files, and consecutively numbered them for allocation. She was blinded to both the randomization schedule and assessments outcomes." These numbers were used to allocate the patients by an assistant blinded to assessments.
Blinding of participants and personnel (performance bias)	Low risk	Participants from control group blinded. Quote: "(control group)…were blinded to their control status during this time" Personnel blinded to randomization. Quote: "The practitioner (primary author) was blinded to the randomization schedule and assessment outcomes until the conclusion of the study"
Blinding of outcome assessment (detection bias)	Low risk	Quote: "All data collection was taken on the premises by appointment with the assessor, who was blinded to group allocation of the participants."
Incomplete outcome data (attrition bias)	Low risk	Quote: "...with 1 dropout in the control group after 6 months, citing impatience with"being in the wait-list" Other participants generally complied well with their scheduled appointments " The data were analyzed on an intention to treat basis, replacing missing values with baseline figures..."
Selective reporting (reporting bias)	Low risk	Australian Clinical Trials Register, registration no. ACTRN12610000329066 http://www.anzctr.org.au/trial_view.aspx?id=320772 High consistency with pilot report (279)
Other bias	Low risk	Free of other bias

Litt 2010

Methods	RCT. Single center; two parallel groups. 6 weeks treatment, follow-up for 12 months.
Participants	101 patients: mean age 39.4 (SD=12.1); 84.16% women; years of education=14.7 (SD=2.5); 79% Caucasian, 9% African-American, 9% Hispanic, 3% self-described as other; average duration of pain 6.7 (SD=6.6); mean pain intensity 3.5 on a scale to 6 (SD=1.3) Inclusion criteria: pain in TM area for at least 3 months, positive axis I diagnosis on RDC/TMD. Exclusion criteria: contraindication to TMD treatment; history of TMJ surgery; extensive anatomical destruction or deterioration of the TMJ; rheumatoid disease; neuropathic or odontogenic pain; psychosis; current use of antidepressants, anxiolytics or opioid pain medication; pregnancy; no local language skills. Location: USA
Interventions	Group A (n=49): standard treatment group (STD)(splint 4 weeks continuously and later only a night guard +soft diet+ naproxen sodium 550mg po BID during 5 weeks, alternatively extra strength acetaminophen in case of gastric ulcer disease) Group B (n=52): STD+ cognitive-behavioral treatment (rationale for treatment + relaxation training and self-efficacy enhancement + masseter EMG biofeedback assisted relaxation + habit modification + combating negative thoughts and catastrophization + stress management)
Outcomes	Pain interference score (MPI) Pain severity (MPI) Coping Somatization Depression Catastrophizing Influencing factors (mediators, moderators) Readiness Self efficacy
Notes	Principal data from the study by *Litt 2010*(344). The report published in 2009 (343) refers to a subset of the sample.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "(groups were randomized)... using a computerized urn randomization procedure"
Allocation concealment (selection bias)	Low risk	Not reported Comment: high unpredictability for urn design
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Long-term data were obtained by in-person interviews (not blinded assessor).
Incomplete outcome data (attrition bias)	Low risk	ITT analysis. Reasons for missing outcome data unlikely to be related to true outcome. From correspondence: “There were no differences in reasons by treatment condition.” The groups were balanced in numbers.

Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Michelotti 2004

Methods	RCT. Single center; two parallel groups. Follow-up for 3 months.
Participants	70 patients: mean age group A=31.8 (±13.0), mean age group B=28.2 (±8.8); 88.57% women. Inclusion criteria: myogenous TMD; pain recurrent or constant for more than 3 months; spontaneous pain in the last week >30 on VAS. Exclusion criteria: objective evidence of TMJ pathology or dysfunction; RDC/TMD diagnosis group II or III; other orofacial pain conditions; other TMD treatments within the last 3 months; neurologic or psychiatric disorders; pain medication abuse. Location: Italy
Interventions	Group A (n=34 [23]): education only Group B (n=36 [26]): education + self-supportive exercise program (self-relaxation exercises with diaphragmatic breathing, self-massage of the masticatory muscles, application of moist heat pads, stretching and coordination exercises)
Outcomes	Treatment contrast (normalized mean of pain intensity and functional limitation scores) Pressure Pain Threshold (PPT)(kPa) for masseter, temporalis and achiles tendon Pain intensity (VAS) Pain on chewing (VAS) Pain-free maximal jaw opening (mm) Headache (VAS)
Notes	Preliminary report in Italian: *Michellotti et al. 2000* (386)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "…using balanced block randomization."
Allocation concealment (selection bias)	Unclear risk	Not reported Comments: blocked randomization in an unblinded study is considered at high risk of selection bias. However in this RCT, the outcome assessment was blinded.
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: "…outcome measures were collected by an examiner who did not provide any treatment to the patients and who was blind to the treatment group assignment"
Incomplete outcome data (attrition bias)	Low risk	Detailed explanation for dropouts Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	Include all expected outcomes

Other bias	Low risk	Free of other bias

Michelotti 2012

Methods	RCT. Single center; two parallel groups. Follow-up for 3 months.
Participants	41 (out of 44) patients: mean age 31.2 (11.8); 88.57% women. Inclusion criteria: Myofascial pain Diagnosis (RDC/TMD), and absence of objective evidence of joint pathology or dysfunction. Muscle pain greater than 30mm VAS Exclusion criteria: Disc displacement with or without reduction, arthrogenous TMD with pain or RX alterations in TMJ; other orofacial conditions; other TMD treatments performed in the last 3 months; neurological or psychiatric disorders, or both; history of abuse of medication; use of splint in the preceding year Location: Italy
Interventions	Group A (n=23): Education only (self-care, home exercise group focused on habit-reversal techniques, education about TMD) Group B (n=18): stabilization Splint only
Outcomes	Pain intensity (VAS) Unassisted jaw opening without pain (mm) Headache (VAS) Pain during chewing (VAS)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Balance block randomization
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. Outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “second examiner, who was masked as to the patient’s treatment performed the baseline assessment and 3 months after…still masked…”
Incomplete outcome data (attrition bias)	Unclear risk	Data of drop outs vs. completers. Insufficient information about completers.
Selective reporting (reporting bias)	Low risk	All expected outcomes were reported
Other bias	Low risk	Free of other bias

Mulet 2007

Methods	RCT. Single center; two parallel groups. Follow-up for 4 weeks.
Participants	42 [out of 45] patients: mean age 24 yrs.; group A (analysed)=23.4 (SD=2.1), mean age group B (analysed)=25.1 (SD=2.3); 95.24% women; 50.00% some college, 26.19% college graduate, 23.81% postgraduate work; 92.86% White, 7.14% Asian; mean (yrs.) duration of pain=5.4±3.9 Inclusion criteria: age 18-65; RDC/TMD diagnosis of myofacial pain; duplicated pain by palpation of the masticatory muscles; pain ≥ 4 on a 11-point scale during the previous month; persistent pain for at least 6

	months with pain frequency ≥ 3 days per week; forward head posture; if active mouth opening was limited, passive interincisal opening had to be at least 40mm. Exclusion criteria: systemic rheumatic diseases; fibromyalgia; other orofacial pain; dental pathology; TMJ disc displacement without reduction or osteoarthritis; cervical structural pathology; current intake of over-the-counter analgesics more than 3 days per week; current use of narcotics, hypnotic drugs, sedatives, or muscle relaxants; major psychiatric disease; unwillingness to accept allocation to the treatment group. Location: USA
Interventions	Group A (n=20): self-care (optimistic counseling, patient education, encouragement to rest the masticatory muscles, application of heat and ice, control of maladaptive behaviours , pain-free diet) Group B (n=22): self-care + 6x6 exercises (6 exercises 6 times a day and repeated 6 times each: rest position of the tongue, shoulder posture, stabilized head flexion, axial extension of the neck, control of TMJ rotation, rhythmic stabilization technique)
Outcomes	Self-report pain intensity in masticatory muscles (NGRS) Pain intensity in masticatory and neck muscles (5-point VRS) Pain intensity in cervical muscles (NGRS) Postural measures (distance shoulder-ear, neck angle, cranial angle). Overall change in symptoms at the end of treatment (5-point scale)
Notes	Patients received 50US$ compensation for participation.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:" A stratified randomization scheme using randomization tables matched treatment groups for gender distribution and medication use"
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	Quote: “Subjects were told that 2 exercise programs were being tested for their effectiveness in relieving their jaw pain. They were not told that their posture was being evaluated. Incomplete blinding, but the outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The primary investigator, who was blinded to the treatments received, collected these data“.
Incomplete outcome data (attrition bias)	Low risk	“As treated” analysis. Missing outcome data balanced in numbers across intervention groups.
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Ritenbaugh 2012

Methods	RCT. Multicenter; three parallel groups in sequential allocation. Follow-up for 18 weeks.
Participants	168 patients: in period 1 mean age group A=42.3 (±13.5), mean age group B=42.9 (±13.0); 86.1% women; 10.1% ≤ high school graduate, 38.0% some college, 26.6% college graduate, 25.3% postgraduate work; 83.55% White, 6.35% Nonwhite, 10.1% Unknown or not reported; 31.65% income <$25,000; 29.2% income $25,000-$50,000, 26.55% income $50,000-$100,000, 8.75% income>$100,000, 3.8% do not response income question; 10.15%duration of pain less than 1yr, 49.3%mean duration of pain 1-10 yrs, 40.55%more than 10 yrs of pain duration. In period 2 mean age group A=43.7 (±12.4), mean age group B=43.6 (±12.0); 87.05% women; 17.65% ≤ high school graduate, 27.4% some college, 23.85% college graduate, 30.95% postgraduate work; 84.65% White, 5.9% Nonwhite, 9.45% Unknown or not reported; 28.3% income <$25,000; 29.45% income $25,000-$50,000, 23.5% income $50,000-$100,000, 10.55% income>$100,000, 8.2% do not response income question; 5.9% duration of pain less than 1yr, 50.65%mean duration of pain 1-10 yrs, 43.45%more than 10 yrs of pain duration. Inclusion criteria: worst facial pain ≥ 5; age 18-70 yrs.; RDC/TMD diagnose; presence of 1 of 10 Traditional Chinese Medicine diagnoses (Liver "qi" stagnation; Liver blood "xu"; Liver "yin xu"; Liver Wind; "Qi" and blood stagnation due to injury; Heart blood "xu"; Spleen "qi xu" and Damp retention; Kidney "qi xu"; Kidney "jing xu"; Kidney "yin xu"; Kidney "yang xu"; Wind-Cold invasion); completion of the run-in (TMD class) process. Exclusion criteria: serious pathology of the temporomandibular joint (e.g. infection, rheumatoid arthritis, fracture); presence of cancer or acute infection of the teeth, ears, eyes, nose, or throat; individuals undergoing active orthodontic treatment; serious psychiatric conditions; surgical implants for treatment of TMD; bleeding disorders; other life threatening conditions (eg. cancer, uncontrolled severe hypertension); severe joint/disk displacement; use of full dentures; use of medications for which study herbs are contraindicated; current pregnancy or plans to become pregnant during active treatment Location: USA
Interventions	Group A (n=39 [36 period2]): Traditional Chinese Medicine (TCM) (20 sessions: insertion of up to 20 acupuncture needles to a depth of 0.25-1.25 inches at acupoints according to TCM diagnoses, and additionally acupoints for TMD treatment [ST7 and/or ST6, GB20 and/or GB21, "yintang", LI4, LV3] for 20-30 min. + herbal prescription + massage ["tuina"] on the neck and shoulders + lifestyle and nutrition counseling) Group B (n=40 [15 period2; 20 reallocated]): Self-Care (2 in-person education/training session and 3 phone call follow-ups, which include a first period and a second period: In Period 1: education about biopsychosocial model, TMD etiology, and self-management + guided reading with structured feedback to explore participant's understanding of and identification with major themes + relaxation and stress management training + self-monitoring of signs and symptoms + "personal TMD self-care plan" + supervised practice and reinforcement of prescribed self-care treatments + maintenance and relapse prevention of the "personal TMD self-care". In Period 2: resiliency intervention [CBT]) Group C (n=88 [27 period2; 56 reallocated]): Self-care. Not randomized group (report of worst pain below the cut-point [predefined as WFP = 7in the Period1, and WFP=5 in the Period2]) Cointervention: all groups received education about TMD + jaw relaxation techniques (run-in phase)

Outcomes	Based on RDC/TMD characteristic pain index (average of worst, usual and actual pain) Pain interference on daily activities, social activities, and ability to work Sleep quality (1-item summary sleep measure) Brief depression measure (PHQ2) Patient Enablement Instrument (PEI) Well being (Arizona Integrative Outcomes Scale [AIOS]) Medication (dosage and frequency) Graded Chronic Pain Score
Notes	Two groups were randomized, and other assigned according to the outcome worst facial pain (WFP): "Those with pain below the cut-point automatically went to SC and are denoted as group s" In a second period, patients of this group which remain wtth low levels of pain were excluded from the main analysis. *Elder et al*. (169) reported medication use in a subsample of this RCT.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Dynamic allocations to treatment groups at weeks 2 and 10 were accomplished by an automated design adaptive allocation procedure that sequentially balanced the SC and TCM groups with regard to WFP, gender, depression, and age as each person became eligible for allocation...Allocations were computer-generated..." Comments:This study used a sequential allocation
Allocation concealment (selection bias)	Low risk	Quote: “Dr. Aickin using a computer program to which he alone had access, thereby concealing the allocation process from all other project staff. Moreover, participants were allocated in blocks, and an undisclosed feature of the allocation program rendered accurate prediction of allocation extremely unlikely. Allocations were provided to the project managers after data collection and at the time when participants needed to be informed. Staff played no role in generating allocations nor had any potential to manage or affect the process.”
Blinding of participants and personnel (performance bias)	Low risk	Personnel but not patients were blinded. The outcomes are unlikely to be influenced by this lack. Quote: "Practitioners were not aware of the specifics of the study design, nor were they aware of any details of participant assessments prior to beginning treatments." "Per the design, participants could be assigned to SC because they were below the pain cut-point or could be allocated by minimization if they were above the cut-point. However, practitioners were not informed of these aspects of the design, nor of the source of individual assignments to SC." "Specific study staff had their access restricted to only the information that was needed for their roles, and they could not view other participant-related information. This permitted overall study management while maintaining blinding."

Blinding of outcome assessment (detection bias)	Low risk	Quote: “A single trained interviewer at the Tucson call center used a computer-assisted telephone interview (CATI) system to collect all of the short-term follow-up data at weeks 2, 10, and 18, the data used for the outcome analyses presented here. Calls were recorded for random quality assurance checks. The interviewer was kept unaware of study design details and blinded to individual participant treatment assignment. Participants were encouraged not to divulge any treatment-related information to the interviewer, and the interviewer was trained to avoid any such discussions.“
Incomplete outcome data (attrition bias)	Low risk	Quote: "The analysis of the first 2 dynamic allocations presented here was undertaken on an intent-to-treat basis. Missing data were rare and were not replaced by imputation."
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Truelove 2006

Methods	RCT. Single center; three parallel groups. Follow-up for 12 months.
Participants	200 patients: mean age group A=36 (±11), mean age group B=36 (±11), mean age group C=35 (±12); 86% women; 75.5% education more than high school; 8.5% race Nonwhite; mean number of yrs. with facial pain group A=5±5, mean number of yrs. with facial pain group A=6±9, mean number of yrs. with facial pain group A=5±6 Inclusion criteria: age 18-60 yrs.; RDC/TMD Axis I diagnosis of myofacial pain (Group Ia or Ib) with or without a concurrent diagnosis of arthralgia (Group IIIa) or disk displacement with reduction (Group IIa), as well as an RDC/TMD Axis II Graded Chronic Pain score of Grade I (low pain) or Grade II (high pain), both of which had no or minimal pain-related psychosocial interference. Exclusion criteria: any other RDC/TMD Axis I diagnosis (for example, arthritis, disk displacement without reduction); any systemic arthritis or other serious medical complications, full dentures; major psychological disorders; current satisfactory use of splint; no local language skills Location: USA
Interventions	Group A (n=64): usual treatment (self-care: jaw relaxation, reduction of parafunction, thermal packs, NSAIDs, passive opening stretches and suggestions about stress reduction) Group B (n=68): usual treatment + hard splint in centric occlusion nocturnal wearing and two additional hours daily while awake throughout the three-month and twelve-month follow-up Group C (n=68): usual treatment + soft splint in centric occlusion, nocturnal wearing and two additional hours daily while awakw throughout the three-month and twelve-month follow-up
Outcomes	Self report findings: CPI; pain duration; self reported TMD symptoms (TMJ clicking/popping sounds, TMJ grating sounds, TMJ locking/catching, tinnitus, jaw clenching-diurnal, jaw clenching-nocturnal, limitation in chewing). Clinical examination: range of motion (assisted and unassisted jaw opening); joint sounds; muscle and TMJ palpation pain (number of sites); RDC/TMD diagnoses
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “We generated randomization assignments using randomly selected block sizes of six, nine or 12 and stratified them by provider.”
Allocation concealment (selection bias)	Low risk	Quote: “We concealed randomization to all study personnel until after we obtained the subjects’ consent“
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The research dental hygienists conducting follow-up data collection were blinded to subject treatment group“
Incomplete outcome data (attrition bias)	Low risk	Quote: “…we took a conservative approach of carrying forward the last observation if the subject dropped out before month 12.” Intent-to-treat analysis. Attritions reported and analyzed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Turner 2006

Methods	RCT. Single center; two parallel groups. Follow-up for 12 months.
Participants	158 patients [148 analyzed]: mean age original sample=37.0 (±11.4), mean age group A=38.9 (±11.6); mean age group B=35.7 (±10.9); 86.49% women; 21.62% high school or less, 41.22% some college or vocational/technical, 37,16% college graduate; duration (months) of current pain group A=13.5 (R=4-18), duration (months) of current pain group B=17.5 (R=4-72) Inclusion criteria: age 18 yrs or older; RDC/TMD Axis I TMD diagnosis; facial pain for at least three months; GCPS II high, III or IV; local language skills; residence within a 2-h drive of the clinic. Exclusion criteria: need for further diagnostic evaluation; pending litigation or disability compensation for pain; current or previous CBT for pain; major medical or psychiatric conditions. Location: USA
Interventions	Group A (n=79 [72]): pain management training (standard CBT for pain and chronic TMD pain, including breathing, relaxation, fear-avoidance, and relapse prevention techniques) + “usual treatment” according to dentist prescription (intraoral occlusal appliance + jaw stretching exercises + patient education + medication) Group B (n=79 [76]): self-care management (control for the effects of natural history/time, TMD education, patient expectations, completing study measures, and attention, excluding CBT) + tailored “usual treatment”
Outcomes	Activity Interference Graded Chronic Pain Scale (GCPS) Characteristic Pain Intensity (CPI) Mandibular Function Impairment Questionnarie (MFIQ) (17-item) Depression (21-Item Beck Depression Inventory (BDI)) Survey of Pain Attitudes (SOPA): Disability, Harm and Control; TMD Self-Efficacy Scale (SES)(8-item) Catastrophizing: CSQ Catastrophizing scale, and four-item Rumination

	subscale of the Pain Catastrophizing Scale (PCS) Coping: 4 scales from the Chronic Pain Coping Inventory (CPCI): Rest, Task Persistance, Coping Self-Statements, and Relaxation Treatment credibility TMD knowledge Treatment helpfulness
Notes	The data were collected principally from the article by *Turner 2006* (578) which reports the results at short- and long-term of the RCT. The articles by *Wig 2004* (607), by *Turner, Mancl & Aaron 2005* (electronic diaries during treatment (575)), and by *Aaron 2006* (electronic diaries prior to intervention(2)) correspond to a subsample of the principal study. The article by *Turner, Brister et al. 2005* (576) is an epidemiological report of a combined sample from this study and other RCT. Finally, in the article by *Turner 2007* (577) a subset of the sample was compared to a new extra group of participants.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Blocked randomization was stratified by chronic pain grade and gender Quote: “Randomization assignments were generated by a biostatistician (LM) using randomly selected block sizes of two or four…“
Allocation concealment (selection bias)	Low risk	Quote: “Treatment assignments were recorded on slips of paper numbered consecutively within each stratum and sealed in envelopes sequentially numbered by stratum. Randomization assignment was concealed to all study personnel until envelopes were opened by research staff after subject consent was obtained.”
Blinding of participants and personnel (performance bias)	Low risk	From correspondence: “… subjects were blinded to the intervention they were receiving and personnel were blind to the randomization the intervention, but personnel delivering the intervention knew which intervention they were delivering.” Comments: incomplete blinding unlikely to influence the outcomes.
Blinding of outcome assessment (detection bias)	Low risk	Quote:“Participants were asked to complete questionnaires at home and return them in person or by mail…”
Incomplete outcome data (attrition bias)	Low risk	ITT analyses, attrition and exclusions reported and analyzed. Detailed report for imputations. The groups did not differ at baseline on any sociodemographic or outcome variable. However sensitivity analyses were conducted in order to adjust differences on two clinical TMD diagnoses, and treatment credibility and expectancies.
Selective reporting (reporting bias)	Low risk	Include all expected outcomes. High consistency between the different reports.
Other bias	Low risk	Free of other bias

Turner 2011

Methods	RCT. Single center, three parallel groups. Follow-up for twelve months
Participants	191 patients:mean age group A=29.1(7.4), mean age group B=25.4(5.7),mean age group C=28.6(6.9); 100% women; 11.33% high school or less, 34.67% some college, 54% college graduate; 77.67% Non-Hispanic White Inclusion criteria: female gender; age 18–45 years; a Research Diagnostic Criteria/Temporomandibular Disorders (RDC/TMD) Axis I TMD pain diagnosis; premenopausal; characteristic pain intensity 3 or higher; local language skills Exclusion criteria: lacking a menstrual cycle; pregnant, lactating, or planning to become pregnant in the next 7 months; unwilling to take a continuous OC; need for further diagnostic evaluation of facial pain; major medical or psychiatric conditions that would interfere with ability to participate. Additionally, study participants randomized to the COCT group underwent a gynecological examination and were withdrawn from the study if they had a medical contraindication for COCT (eg, history of or active thromboembolic disease; cerebrovascular or coronary artery disease; undiagnosed genital bleeding; estrogen-dependent cancer; acute liver disease; benign or malignant liver tumors; severe headaches or headaches with atypical neurological changes); smoked cigarettes and were 35 years or older; had used medication within the last 3 months that interfered with estrogen or progestin metabolism; had an abnormal pelvic examination, abnormal cytology (Pap smear), or undiagnosed uterine bleeding; or had no current mammogram and were 40 years or older. Location: USA
Interventions	Group A (n=60): self-management training Group B (n=57): targeted self-management training (2 1.5 hr. interperson sessions+ 6 15 min. telephone session) Group C (n=74): continous oral contraceptive therapy (2 1.5 hr. interperson session + 6 15 min. telephone session) Cointerventions: every study participant received a personalized list of recommended TMD self-care strategies
Outcomes	Pain intensity (CPI) Pain interference Subjective Pain (McGill Pain Questionnaire) Depression (BDI) Treatment helpfulness Pain beliefs: Disability, Harm, and Control (SOPA) Self-efficacy (SES) Catastrophizing (CSQ Catastrophizing scale) Perceived effectiveness of pain coping strategies
Notes	DIfferences at baseline of age were widely explored.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization... was stratified by participant's baseline chronic pain grade and recruitment source, with blocking ... Block sizes were equal to 3 or 6, and were chosen randomly with 2/3 and 1/3 probability, respectively"... "The randomization list was prepared using the ''sample'' function of the S-PLUS statistical software"

Allocation concealment (selection bias)	Low risk	Quote: "Treatment assignments were recorded on cards numbered consecutively within each stratum, and a study assistant not involved in the screening and randomization put the randomization assignments in sealed envelopes sequentially numbered by stratum. Randomization assignments were concealed to all study personnel with study participant contact until envelopes were opened by research staff at the time of randomization."
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed
Incomplete outcome data (attrition bias)	Low risk	ITT analysis and additional "as treated" analysis, adequate imputation methods reported extensively
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Footnotes

Characteristics of excluded studies

Grace 2002

Reason for exclusion	Not randomized

Jerjes 2007

Reason for exclusion	Not randomized

Komiyama 1999

Reason for exclusion	No valid randomization (non-parallel groups). From correspondence: *"The experiment were carried out for three years. The subjects automatically received the different intervention in each year (Data for CT was collected in first year period, data for IT-1 was in second year period, and IT2 was in third year period)"*

Minakuchi 2004

Reason for exclusion	No myogenous TMD diagnosis

Mishra 2000

Reason for exclusion	Secondary report of RCT Gardea 2001 (included study)

Stowell 2007

Reason for exclusion	Secondary report of RCT Gatchel 2006 (included study)

Turner 2005

Reason for exclusion	Secondary report of RCT Turner 2006 (included study)

Vuckovic 2010

Reason for exclusion	No comparison group

Wahlund 2003

Reason for exclusion	Only adolescents

Wahlund 2003b

Reason for exclusion	Only adolescents

Wright 2000

Reason for exclusion	The intervention was posture training (examined and treated by a physical therapist) without psychological support.

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

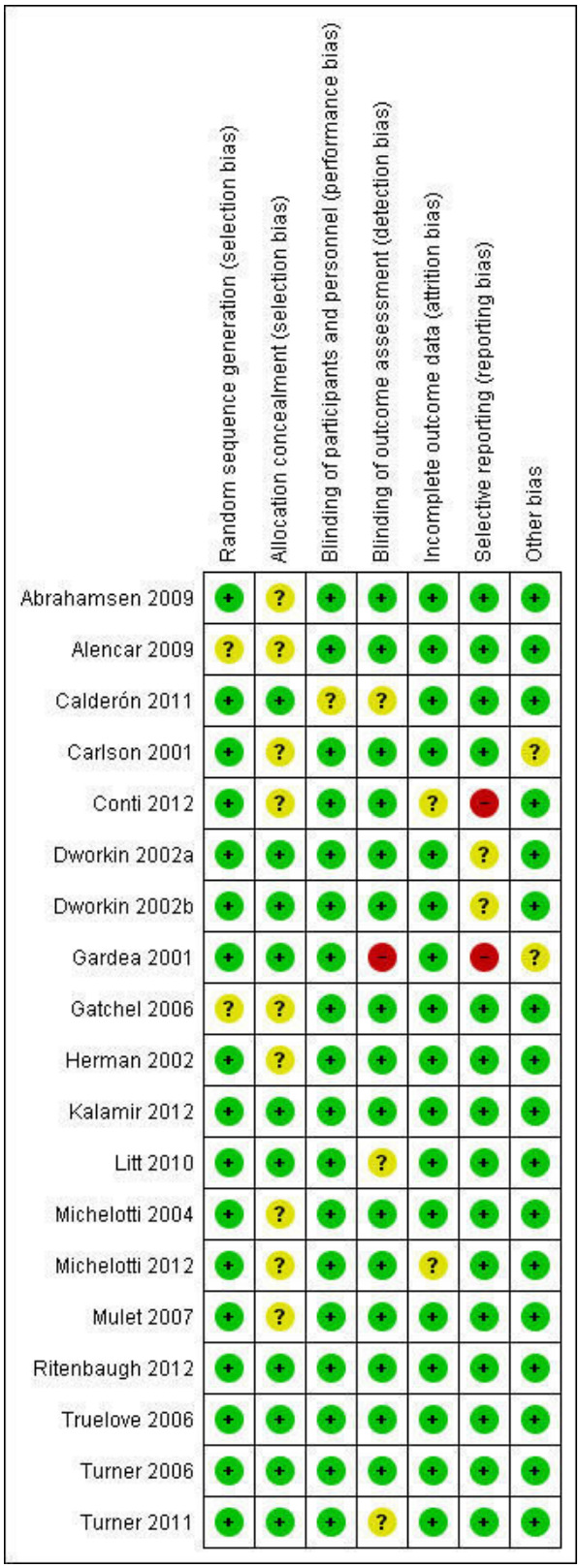

Figure 38. *Risk of bias summary: review authors' judgements about each risk of bias item for each included*

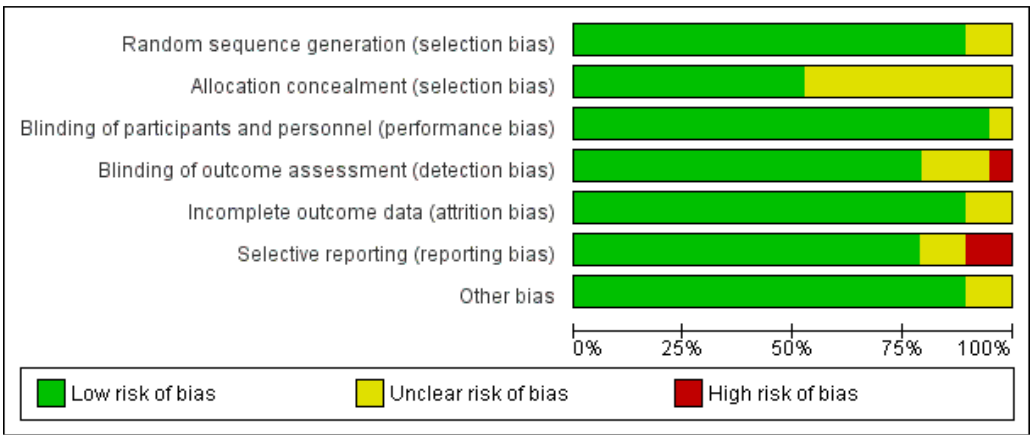

***Figure 39**. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.*

References to studies : Psychosocial Interventions for Myofacial Pain

Included studies

Abrahamsen 2009
Abrahamsen R, Zachariae R, Svensson P: Effect of hypnosis on oral function and psychological factors in temporomandibular disorders patients. J Oral Rehabil 2009;36:556-570 [PubMed: 19604319]

Alencar 2009
Alencar FJr, Becker A: Evaluation of different occlusal splints and counselling in the management of myofascial pain dysfunction. J Oral Rehabil 2009;36:79-85 [PubMed: 18976268]

Calderón 2011
Calderón PDosS, Tabaquim, MdeLM, Oliveira LCde, Camargo APA, Ramos Netto TdeC, Conti PCR: Effectiveness of cognitive-behavioral therapy and amitriptyline in patients with chronic temporomandibular disorders: a pilot study. Braz Dent J 2011;22:415-421 [PubMed: 22011899]

Carlson 2001
Carlson CR, Bertrand PM, Ehrlich AD, Maxwell AW, Burton RG: Physical self-regulation training for the management of temporomandibular disorders. J Orofac Pain 2001;15:47-55 [PubMed: 11889647]

Conti 2012
Conti PCR, Alencar ENde, da Mota Correa AS, Lauris JRP, Porporatti AL, Costa YM: Behavioural changes and occlusal splints are effective in the management of masticatory myofascial pain: a short-term evaluation. J Oral Rehabil 2012;39:754-760 [Pubmed: 22672361]

Dworkin 2002a
Dworkin SF, Turner JA, Mancl L, Wilson L, Massoth D, Huggins KH, LeResche L, Truelove E: A randomized clinical trial of a tailored comprehensive care treatment program for temporomandibular disorders. J Orofac Pain 2002;16:259-276 [PubMed: 12455427]

Dworkin 2002b
Dworkin SF, Huggins KH, Wilson L, Mancl L, Turner J, Massoth D, LeResche L, Truelove E: A randomized clinical trial using research diagnostic criteria for temporomandibular disorders-axis II to target clinic cases for a tailored self-care TMD treatment program. J Orofac Pain 2002;16:48-63 [PubMed: 11889659]

Gardea 2001
Gardea MA, Gatchel RJ, Mishra KD: Long-term efficacy of biobehavioral treatment of temporomandibular disorders. J Behav Med 2000;24:341-359 [PubMed: 11523332]

Gatchel 2006a
Gatchel RJ, Stowell AW, Wildenstein L, Riggs R, Ellis E: Efficacy of an early intervention for patients with acute temporomandibular disorder-related pain: a one-year outcome study. J Am Dent Assoc 2006;137:339-347 [PubMed: 16570467]

Herman 2002
Herman CR, Schiffman EL, Look JO, Rindal DB: The effectiveness of adding pharmacologic treatment with clonazepam or cyclobenzaprine to patient education and self-care for the treatment of jaw pain upon awakening: a randomized clinical trial. J Orofac Pain 2002;16:64-70 [PubMed: 11889661]

Kalamir 2012
Kalamir A, Bonello R, Graham P, Vitiello AL, Pollard H: Intraoral myofascial therapy for chronic myogenous temporomandibular disorder: a randomized controlled trial. J Manipulative Physiol Ther 2012;35:27-37 [PubMed: 22079052]

Litt 2010
Litt MD, Shafer DM, Kreutzer DL: Brief cognitive-behavioral treatment for TMD pain: long-term outcomes and moderators of treatment. Pain 2010;151:110-116 [PubMed: 20655662]

Michelotti 2004
Michelotti A, Steenks MH, Farella M, Parisini F, Cimino R, Martina R: The additional value of a home physical therapy regimen versus patient education only for the treatment of myofascial pain of the jaw muscles: short-term results of a randomized clinical trial. J Orofac Pain 2004;18:114-125 [PubMed: 15250431]

Michelotti 2012
Michelotti A, Iodice G, Vollaro S, Steenks MH, Farella M: Evaluation of the short-term effectiveness of education versus an occlusal splint for the treatment of myofascial pain of the jaw muscles. J Am Dent Assoc 2012;143:47-53 [PubMed: 22207667]

Mulet 2007
Mulet M, Decker KL, Look JO, Lenton PA, Schiffman EL: A randomized clinical trial assessing the efficacy of adding 6 x 6 exercises to self-care for the treatment of masticatory myofascial pain. J Orofac Pain 2007;21:318-328 [PubMed: 18018993]

Ritenbaugh 2012
Ritenbaugh C, Hammerschlag R, Dworkin SF, Aickin MG, Mist SD, Elder CR, Harris RE: Comparative effectiveness of traditional chinese medicine and psychosocial care in the treatment of temporomandibular disorders-associated chronic facial pain. J Pain 2012;13:1075-1089 [PubMed: 23059454]

Truelove 2006
Truelove E, Huggins KH, Mancl L, Dworkin SF: The efficacy of traditional, low-cost and nonsplint therapies for temporomandibular disorder: a randomized controlled trial. J Am Dent Assoc 2006;137:1099-1107 [PubMed: 16873325]

Turner 2006
Turner JA, Mancl L, Aaron LA: Short- and long-term efficacy of brief cognitive-behavioral therapy for patients with chronic temporomandibular disorder pain: a randomized, controlled trial. Pain 2006;121:181-194 [PubMed: 16495014]

Turner 2011
Turner JA, Mancl L, Huggins KH, Sherman JJ, Lentz G, LeResche L: Targeting temporomandibular disorder pain treatment to hormonal fluctuations: a randomized clinical trial. Pain 2011;152:2074-2084 [PubMed: 21680092]

Excluded studies

Grace 2002
Grace EG, Sarlani E, Reid B: The use of an oral exercise device in the treatment of muscular TMD. Cranio 2002;20:204-208 [PubMed: 12150267]

Jerjes 2007
Jerjes W, Madland G, Feinmann C, El Maaytah M, Kumar M, Hopper C. Upile T, Newman S: Psycho-education programme for temporomandibular disorders: a pilot study. J Negat Results Biomed 2007;6:4 [PubMed: 17381840]

Komiyama 1999
Komiyama O, Kawara M, Arai M, Asano T, Kobayashi K: Posture correction as part of behavioural therapy in treatment of myofascial pain with limited opening. J Oral Rehabil 1999;26:428-235 [PubMed: 10373091]

Minakuchi 2004
Minakuchi H, Kuboki T, Maekawa K, Matsuka Y, Yatani H: Self-reported remission, difficulty, and satisfaction with nonsurgical therapy used to treat anterior disc displacement without reduction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;98:435-440 [PubMed: 15472659]

Mishra 2000
Mishra KD, Gatchel RJ, Gardea MA: The relative efficacy of three cognitive-behavioral treatment approaches to temporomandibular disorders. J Behav Med 2000;23:293-309 [PubMed: 10863679]

Stowell 2007
Stowell AW, Gatchel RJ, Wildenstein L: Cost-effectiveness of treatments for temporomandibular disorders: biopsychosocial intervention versus treatment as usual. J Am Dent Assoc 2007;138:202-208 [PubMed: 17272375]

Turner 2005
Turner JA, Mancl L, Aaron LA: Brief cognitive-behavioral therapy for temporomandibular disorder pain: effects on daily electronic outcome and process measures. Pain 2005;117: 377-387 [PubMed: 16153777]

Vuckovic 2010
Vuckovic N, Schneider J, Williams LA, Ramirez M: Journey into healing: the transformative experience of shamanic healing on women with temporomandibular joint disorders. Explore 2010;6:371-379 [PubMed: 21040886]

Wahlund 2003
Wahlund K, List T, Larsson B: Treatment of temporomandibular disorders among adolescents: a comparison between occlusal appliance, relaxation training, and brief information. Acta Odontol Scand 2003;61:203-211 [PubMed: 14582587]

Wahlund 2003b
Wahlund K: Temporomandibular disorders in adolescents. Epidemiological and methodological studies and a randomized controlled trial. Swed Dent J Suppl 2003;164:2-64 [PubMed: 14717039]

Wright 2000
Wright EF, Domenech MA, Fischer JRJr: Usefulness of posture training for patients with temporomandibular disorders. J Am Dent Assoc 2000;131:202-210 [PubMed: 10680388]

3.8 Discussion of the series of systematic reviews

In this series of systematic reviews, the author compiled only RCTs (high quality evidence) according to the GRADE system, setting apart quasi-randomized (moderate quality), observational studies (low quality), and unsystematic reports (very low quality).

The author was able to group the different treatments for myofacial pain into six categories, according to an approximate rationale about the treatment of TMD. In general, acupuncture, LLLT, and drugs aimed principally the symptoms of TMD and were evaluated at short-term. On the contrary, long-term effects were desirable for physiotherapy, splint therapy and psychosocial interventions.

The author summarizes and comments the principal findings for each therapy:

1. **Acupuncture (11 RCTs, n= 510):**

Eleven (11) RCTs in acupuncture were screened; however three of them did not provide valid information. Symptomatic relief was reported using acupuncture in trigger points, Microsystems of acupuncture, and traditional Chinese acupuncture. Nonetheless, only acupuncture in trigger points was superior to sham acupuncture (*Fernández-Carnero 2010*).

The studies by *Ritenbaugh 2008* and *Ritenbaugh 2012* showed superiority of the Traditional Chinese Medicine (including traditional Chinese acupuncture, herbal prescription and massages) over self-care strategies reducing pain. These studies were the only with designs that exceed the 30 patients, representing 64.31% of the total sample in this review of acupuncture. The participants in both trials of TCM were interested in experiencing alternative medicine.

Overall the RCTs on Acupuncture and LLLT presented weak designs, and most of them without follow-up periods. Both therapies principally tackle symptomatic at immediate or short term. In spite of recommendations indicating a minimal number of 6 sessions for the treatment of myofacial pain [481], one session therapy was applied in many of those RCTs.

Only the acupuncture into trigger points provided evidence about the superiority of acupuncture over sham acupuncture. Within the literature, these TrPs are allegedly equalized with classical acupoints [150]. Nonetheless, the treatment on classical acupoints did not prove to be effective for myofacial pain.

In a systematic review (1975-2004), acupuncture was found as effective as occlusal planes for TMD, however not better than sham acupuncture [189]. In a meta-analysis including four RCTs-also present in this work (*Goddard 2002*, *Schmid-Schwap 2006*, *Smith 2007*; *Shen 2009*), the authors suggested a greater efficacy of acupuncture in comparison with placebo [316, 313]. Nonetheless, the author declares reservations about the results of the study by *Smith 2007*, due to the obvious imbalance at baseline. This implies that the results of the mentioned review are overestimated.

On the other hand, it is possible that sham acupuncture may produce a real effect on the patients. This effect seems to be based on psychological expectations as suggested in the study by *Shen 2007*.

On the contrary, the Traditional Chinese Medicine, which was included into the group of acupuncture, proved to be more efficient than self-care strategies. However these results were observed in patients who were already interested in receiving alternative medicine. The profile of the patients receptive to non-Western medicine is particular. According to a survey in USA, TMD patients who resort to alternative medicine principally use it as a complement of conventional therapies. Those TMD patients qualifying the treatment as "very helpful" also reported higher levels of exercise and fewer sleep disturbances [131].

2. Low-level laser therapy (6 RCTs, n= 215)

All these studies applied different dosage from distinct characteristics of laser irradiation (wavelength and frequency). No one of the included studies reported any advantage over placebo condition or a comparison group. Three studies found similar results for LLLT and placebo, two trials did not conduct statistical analysis between these groups, and one study did not report differences between LLLT and splint therapy at short-term.

As mentioned above, the methodological deficits on LLLT reports were frequent. The studies of LLLT did not overcome placebo. The lack of consensus about laser dosage and application sites is notable. In a recently published RCT, LLLT for treatment of myofacial pain was allegedly more efficient to produce pain relief and improvement of jaw opening when compared to placebo. However the sample of the study was limited, and the time of follow-up was short [22].

3. Drugs (10 RCTs, n= 437)

We found medicines for the treatment of Myofacial pain using three routes of administration: infiltrations (botulinum toxin, and a combination of lidocaine and corticosteroids), oral administration (cyclobenzaprine, clonazepam, gabapentin and diazepam), and topical administration (topical methyl salicylate, and PingOn ointment).

Regarding infiltrations, two studies did not report differences between botulinum toxin and placebo, while in other RCT the toxin was superior to placebo regarding reduction of pain. Moreover, in another trial botulinum toxin was similar to fascial manipulation. On the other hand, the combination lidocaine and triamcinolone acetonide reinforced the results of splint therapy at short-term reducing pain intensity and number of trigger points.

Among the oral medications, gabapentin showed to be significantly more effective than placebo for pain relief. Contrarily, diazepam did not differ from placebo. In other study, cyclobenzaprine plus self-care strategies was meaningfully more effective to reduce pain than self-care strategies combined with clonazepam or placebo.

Both articles on topical medicaments exhibited better performance for the pharmacological agents than for placebo.

Except for the RCTs on botulinum toxin, all other medicaments were subject of one single study. The high heterogeneity of the included studies covers not only the administration route, but also the type of medicament and the mechanism of action. However two principal effects were apparently expected namely pain relief, and muscle relaxation.

The evidence for the effectiveness of drugs in TMD patients is insufficient [341]; however the use of drugs for symptomatic relief often appears included into multimodal therapies. The controversies about the efficacy of medications, especially the non-steroidal anti-inflammatory, is not exclusive for TMD, but for all chronic pain conditions. In one RCT among patients with myofacial pain comparing Ibuprofen and Diazepam, only the latter showed effectiveness reducing symptoms. The authors suggested that pain in these patients is not related to inflammation processes [525].

The infiltration of Botulinum Toxin has received much attention as an alternative treatment for non-respondents to conservative strategies. Nonetheless, at the moment there is no agreement on the dosage for TMD treatment [532].

4. Physiotherapeutical interventions (11 RCTs, n= 699)

The most frequent physiotherapeutical intervention was jaw exercises. However among four RCTs, jaw exercises did not prove better results than splint therapy, global posture training, counseling only, or the ear device TMD*es.*

One study focused on orofacial myofunctional therapy exhibited greater improvements for this therapy than for splint therapy and a control group, specifically in muscle and TMJ pain severity. Additionally, some myofunctional parameters -which are not included within the therapeutical goals of the splint therapy-, were better evaluated after treating patients with this myofunctional therapy. This study showed some methodological flaws.

Combined therapies including jaw exercises were ambivalent. In one study, jaw exercises plus LLLT compared to jaw exercises plus placebo showed greater effects on jaw movements range, but not in pain reduction, for which the outcomes were similar.

In other study, jaw exercises as a part of self-care strategies plus counseling were similarly effective than other interventions using this same therapeutical combination, but adding splints (one hard, and other group receiving a soft splint). In other study, self-care strategies and counseling improved the clinical performance of a massage routine compared with the massages alone and a control group.

Other combined therapy showed greater efficacy to improve jaw opening ranges in patients with severe limitations of a splint therapy together with passive exercises using a mechanical device than with wooden depressors or nothing.

Finally, self-care strategies combined with posture training conducted by a physiotherapist showed greater improvements than a control group with only self-care strategies.

Regarding the therapies for long-term, no conclusive outcomes support any preference of one modality over the others.

Physiotherapeutical interventions for TMD tackle the muscle activity of the masticatory muscles and postural muscles. Jaw exercises and posture training display no conclusive, but potential effectiveness for TMD treatment [375, 377]

On the other hand, interventions on cervical musculature have shown positive effects on myofacial pain patients [314]. Accordingly, the included study using posture training found a significant correlation between the masticatory and neck symptomatology.

Other physiotherapeutical interventions such as TENS and ultrasound were excluded from this series due to the scarce quantity of RCTs reporting on TMD. Within the screened studies for our review, TENS appears as a complementary therapy to physiotherapy in the study by Wieselmann-Penkner 2001 with similar results to EMG-biofeedback. Nonetheless, the efficacy of TENS for chronic pain is refutable [96]

5. Occlusal appliances (23 RCTs, n= 1522)

Twenty one (21) RCTs investigated the stabilization splint, two reported on resilient splints, two on NTIs splints, one on prefabricated splint, and one trial on decompression splint.

The stabilization splint alone was not more effective than no treatment or non-occluding planes, except for one study reporting greater overall symptomatic relief (*Ekberg 2004*).

Likewise, stabilization splint was not superior to resilient splints or prefabricated splints. Clinical differences with the NTI splint were neither registered; however the patients wearing NTI splints were markedly less satisfied with the treatment.

The stabilization appliance was not significantly better than LLLT or physiotherapeutical interventions (myofunctional therapy, and jaw exercises) at short-time. The effects of stabilization splint were also similar to both psychosocial interventions, namely physical self-regulation and SC-co. One study reported that adding trigger point injections improved the results at short-term of the stabilization splint.

Regarding other splint types, the resilient splint did not show a better performance than a non-occluding splint.

Among the multiapproach therapies based on splint therapies, we found those using stabilization planes, NTI planes, and soft appliances.

The results of the RCTs on stabilization splint plus psychosocial interventions (including “usual treatment”) were not conclusive. Three studies reported improvements within groups, but not substantial differences with the comparisons groups (psychosocial interventions). On the other hand, “usual treatment” plus CBT was significantly more effective in pain reduction when compared to only “usual treatment”. When replacing the stabilization splint in the formula of “usual treatment” for other splint types (NTI, or resilient), the outcomes were similar.

In spite of their wide indication, the use of splints is not exempt of polemics. *Türp et al*. in a review of literature (1990-2003) did not find sufficient evidence to support stabilization splint for the treatment of myofacial pain over soft or non-occluding splints, physical therapy, or body acupuncture [568]. Similarly, a meta-analysis concluded that splints are more effective than no treatment, but they do not offer any advantages over other therapies [29]. Same conclusion was reported by other authors [193, 199]. These systematic reviews highlighted critical discussions about methodological approaches. The design topics embrace control groups, selection of outcomes and details of the splints.

Due to the lack of understanding of the possible mechanisms of action, the tests for effectiveness of the splints are erratic. In a study within myofacial pain patients under chewing effort, those wearing stabilization splint reported pain relief and less symptoms during the chewing test in comparison with a non-treatment group [206]. This observation is relevant when considering that most myofacial pain patients react with hyperalgesia after a chewing test [207].

The reports of EMG activity after using splints are some controversial. In bruxer patients the impact on EMG activity of a splint insertion is allegedly transient [237]. Notoriously, even the non-occluding planes seem to affect the neuromuscular activity of the masticatory muscles during sleep [238]. In one RCT, stabilization and palatal (placebo) splints were randomized within patients with sleep bruxism. Both groups experimented similar polysomnographic outcomes after a splint therapy for 4 weeks, without exhibiting relevant effects on the sleep bruxism activity, specifically number of episodes and burst per hour, or the total time of bruxism activity [585].

In one RCT among bruxers with muscle tenderness, the action of an occlusal appliance was not meaningfully different from other group receiving CBT in reduction of psychological impairment, use of stress-coping strategies, and

bruxism activity measured using a monitoring device. Nonetheless, the bruxism activity was continuously decreasing in the patients treated with splint. Contrarily, after an initial period of reduction, the levels of bruxism activity were approaching to baseline at the 6-months follow-up in the group of CBT [438].

Furthermore, there is no absolute consensus about the design of the splint or the usage time. Details of the splint design were reported in some of the included studies. Currently the thickness of the Michigan plane can be assumed as a reference for stabilization splints (2.5 – 3mm). Splints of 3 mm vertical thickness showed more efficacy reducing EMG activity than 6mm thickness in nocturnal bruxers [4]. Likewise, the Michigan appliance contemplates canine guidance, which was preferred within the included studies. Apparently, the disclusion mode (canine guidance or group function) may differentiate the action of splints on EMG activity [317].

There is no standardization for other types of splints, and consequently the rationale underlying its indication is more uncertain.

A review of NTI-tss appliances found 5 RCTs of different qualities. The NTI-tss appeared to be efficient to reduce EMG activity in bruxers in two RCTs, without a positive correlation with clinical symptoms. In patients with TMD, two RCTs (also included in our study: *Jokstad 2005*, *Magnusson 2004*) failed to demonstrate differences between NTI-tss and stabilization appliances. These authors concluded that NTI-tss can be indicated for bruxism and TMD treatment by increasing the vertical dimension or reducing EMG-activity during clenching or grinding [537]. Both effects are however not directly related with pain report in TMD patients.

Regarding the soft splints, the author did not find any evidence of clinical advantages for the treatment of TMD. In one RCT, soft splint was more effective than a palliative treatment and no treatment; however these results are obtained only at short-term [620]. In our review, soft splints were not effective at long-term, except when combined with counseling and self-care strategies.

6. Psychosocial interventions (19 RCTs, n= 1779)

Self-care strategies and counseling were the most frequently reported psychosocial interventions. Counseling consisted principally in theoretical explanations of the TMD etiology, education about the pathogenic agents and

advices on habits and risk factors to avoid. The author grouped into self-care strategies those actively targeting mandibular muscular activity with self-administered exercises (mainly oriented to muscular relaxation), and other home exercises aimed to promote the general physical relaxation.

One study did not find differences of the positive effects between TMD education and TMD education plus home-exercises at short term. In other study, the combined action of massages and counseling was superior to only counseling. On the other hand, other authors reported that counseling only is as effective but takes more time than the combined therapy of counseling and splint (stabilization or NTI-splint).

The self-care strategies as unique intervention were as effective as some physiotherapeutical interventions (6x6 exercise program). In one pharmacological trial, SC plus placebo was similar to SC plus clonazepam, but inferior to SC plus cyclobenzaprine. In other study, SCs resulted in a significant higher pain reduction than hormonal therapy with estradiol and levonorgestrel.

Self-care strategies together with counseling (SC-co) seem to produce the expected improvements in some patients with myofacial pain. One trial reported that adding a splint to self-care strategies did not change significantly the improvements obtained with SC-co only or SC-co plus a non-occluding (placebo) plane. In other study, self-care strategies plus counseling showed a similar positive effect than a stabilization splint only at short-term.

Interestingly, when splint therapy is administered together with SC-co ("usual treatment"), the outcomes are not different from other active interventions. One study reported similar efficacy for SC-co, "usual treatment" and the combined therapy resilient splint + SC-co. In other trial, "usual treatment" was not superior to a program of physical self-regulation

Nonetheless, within combined therapies, Cognitive Behavioral Therapy (CBT) bolstered the outcomes of "usual treatment" in 3 of the included RCTs.

The combination of SC and CBT produced a greater pain relief, and reduction of pain interference when compared to "usual treatment" in TMD patients with low psychological distress profile. However, in other RCT, SC + CBT were less effective than traditional Chinese Medicine in pain relief of patients with myofacial pain.

In one trial, CBT alone showed to be more effective than no-treatment reducing jaw dysfunctionality, but not pain. However, CBT only was inferior to EMG-

biofeedback and EMG-biofeedback plus CBT. The same authors reported in other study that EMG-biofeedback plus CBT improved pain scores, coping abilities and depression compared to a non-treatment control group.
Finally, only one trial informed of better clinical improvements of hypnosis in comparison to a relaxation program.

Among the psychosocial interventions, counseling and self-care strategies, CBT, hypnosis, and physiotherapy-based approaches were documented in this review. In a meta-analysis of psychosocial interventions for orofacial chronic pain, CBT was considered the most promising therapy; however the related evidence was weak and no recommendations were possible about mode or responsible of delivery, and number of sessions [14].
In a systematic review of CBT for TMD, two out of the five RCTs found by the authors [345] were considered in our review as repeated studies (specifically *Mishra 2000* / *Gardea 2001*; *Turner 2005* / *Turner 2006*), because they reported results in subsamples of the respective RCTs. Therefore, the author cannot agree with the results of this review.
In one RCT, CBT was similarly effective as hypnosis sessions in patients with TMD. For both groups, the high hypnotic susceptibility was a good predictor of pain reduction [536]. In the present review, hypnosis was reportedly useful to decrease symptoms through coping reinforcement. The evidence is limited to only one RCT, and consequently insufficient to get a conclusion. However, hypnosis has also been successfully used to modify habits. In one study among healthy volunteers, pain ratings after jaw clenching were modulated in persons with high hypnotic susceptibility [550].
The interventions based on neuromuscular modifications through active training of the awareness of muscular activity can be aimed specifically to masticatory muscles (control of harmful habits or local relaxation), or to general musculature (relaxation and/or posture). The EMG-biofeedback combined with CBT has been suggested as a valid alternative for TMD treatment [121], however conclusive reports are scarce. Preliminary data of a RCT evaluating CBT and OHR associated with EMG-biofeedback using a portable EMG device in comparison with a stabilization splint, showed improvements in both groups. The psychosocial intervention was more effective in reducing psychological symptoms (depression and somatization), however without statistical significance

[516]. According to the authors, the final results of this RCT will be published soon. In our review, the preliminary outcomes of this trial were not included due to the unspecified method for selection of the subsample.

PART 4

SYSTEMATIC REVIEW AND META-ANALYSIS: USUAL TREATMENT VS PSYCHOSOCIAL INTERVENTIONS FOR ORAL MYOFASCIAL PAIN

The part 4 contains a systematic review and meta-analysis of the "usual treatment" based on splint therapy compared to psychosocial interventions for the treatment of myofacial pain. The report was elaborated using the RevMan software.

This section presents the results of a collaborative research of the Department of Prosthetic Dentistry, Zentrum der Zahn-, Mund und Kieferheilkunde at the Johann Wolfgang Goethe University Frankfurt am Main and the Evidence Based Dentistry Unit of the Department of Oral and Maxillofacial Surgery at the Faculty of Dentistry, University of Chile.

Usual treatment vs psychosocial intervention for TMD

Review information

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Abstract

Background

TMD is the most frequent cause of orofacial pain. A lack of understanding of the etiology and pathogenesis of TMD leads to obfuscate the therapeutical targets. As a result, a great variety of treatments have been proposed during the last 70 years. The most prevalent form of TMD is the Myofacial pain which mainly affects the masticatory muscles. In this meta-analysis we compared the efficacy of two modern approaches for myofacial pain: a multimodal therapy based on occlusal appliances ("usual treatment"), and different psychosocial interventions.

Objectives

To assess the effects of "usual treatment" (based on splint therapies) and psychosocial interventions for the treatment of oral myofacial pain in adult patients.

Search methods

We searched for relevant articles according to a pre-defined search strategy within electronic databases (PubMed MEDLINE; The Cochrane Central Register of Controlled Trials (CENTRAL); EMBASE), ongoing trials databases (Current Controlled Trials; ClinicalTrials.gov) and we browsed through the abstracts of the different meetings of the International Association for Dental Research (IADR). Furthermore, we conducted manual search on the following journals for the last 6 months Cranio: The Journal of Craniomandibular practice; Journal of Oral Rehabilitation; and Deutsche Zahnärztliche Zeitschrift. No language limitations were applied.

Selection criteria

All Randomized Clinical Trials (RCTs) including comparisons between "usual treatment" based on splint therapy and psychosocial interventions for the treatment of TMD were analyzed.

Data collection and analysis

Two review authors independently extracted data, and assessed the risk of bias of included trials. In case of discordance, a third author was referred as arbiter. The authors of the selected articles were contacted for additional information.

Main results

In this meta-analysis, we analyzed 6 principal outcomes, namely self-report pain, pain interference, unassisted jaw opening without pain, muscle pain upon palpation, depression, and somatization. The outcomes Self-reported pain and Depression at long-term were significantly different for the comparisons tailored "usual treatment" vs. psychosocial interventions, favouring the latter (p=0.003, and p=0.04 respectively). These results have to be taken in account with some caution due to the limited number of studies.

Moreover, Muscle pain upon palpation and Somatization at short-term in the comparison UT vs PI showed a trend towards significance (p=0.08, p=0.09 respectively) also favouring PI over UT, however both effects did not remain in time. On the other hand, the outcomes were inclined toward PI in the second comparison for the outcomes Pain interference at long-term (p=0.08) and Depression at short-term (p=0.09). The effect of PI in Depression however resulted in a significant difference at long-term.

Authors' conclusions

We found no evidence to distinguish the clinical effectiveness between "usual treatment" and psychosocial interventions. However a no statistically significant trend towards greater improvements of psychological outcomes was seen for psychosocial interventions, while improvements of physical functioning were tendentious towards "usual treatment".

We suggest that next reports of TMD and related subdiagnosis should be reported according to a core outcomes set to afford comparisons. In this meta-analysis, we proposed a formula which allows to investigate the multifactoriality of TMD including pain (pain intensity, and pain interference), physical outcomes (muscle pain upon palpation and jaw opening without pain) and psychological outcomes (depression, and somatization).

Plain language summary

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[Summary text]

Background

Description of the condition

The temporomandibular disorder (TMD) is a complex term that involves different symptomatic definitions which affect the temporomandibular joint and the surrounding structures. Headaches, orofacial pain (chewing musculature, temporomandibular joint or both), ear affections (tinnitus), and alterations of jaw biomechanics (limitation or deviation of the mandibular trajectory) are characteristic signs of TMD that can appear in multiple combinations.

The prevalence of TMD reported in different literature reviews fluctuate around 10% over age 18 [566, 334], with a major percentage of affected women in the reproductive age. The symptomatic fluctuates along the years from adolescence to adulthood [355, 162], and seems to remit spontaneously in elderly individuals [249].

De Kanter [282] estimated treatment need in Dutch population at 3.1%, while *Rugh* and *Solberg* made an estimation of 5% [482] in United States of America, and *Micheelis* and *Reich* estimated at 3.2% in Germany [384]. In a meta-analysis, *Al- Jundi et al.* reported need for treatment in general adults at 15.6% for fixed effect model and at 16.2% for the random-effect model. Interestingly, the estimations were higher for studies based on clinical TMD signs than studies on self-report [34].

In the early 90s *Dworkin et al.* proposed the classification of Research Diagnostic Criteria for TMD (RDC/TMD). Thus far, it had been internationally recognized, is available in 21 languages [260], and recently it had been matched with medical imaging for the osseous diagnosis and disc displacement [19, 364]. The RDC/TMD consists in two complementary axes which compile information about clinical and psychosocial findings. According to the RDC/TMD axis I, there are principally three clinical diagnoses: group I for muscle disorders, group II for disc displacements, and group III for arthralgia, arthrosis and arthritis.

Epidemiological studies showed that the higher percentage of TMD patients is diagnosed with myofacial pain [612], i.e. group I of the RDC/TMD.

Not only different diagnosis in the medical field, but also dissimilar philosophy of treatment evidence the lack of understanding of this pathology. Particularly, the etiology of TMD is still controversial. Currently a multifactorial theory has received a great support among the scientific community. This theory draws attention to the interaction of psychological, neuromuscular and oral pathogenic factors.

Multiple possibilities have been proposed regarding the treatment of TMD. According to the integrity maintenance of the anatomical tissues, they are divided on reversible and irreversible therapies. Currently recognized standards of treatment for TMD prioritize reversible interventions over invasive ones. A first diagnosed patient should be treated by conservative and reversible therapies, such as patient education, medication, intraoral splints and behavioral treatments with different results. In failure case, it should be elected the modification of the anatomical environmental through surgery or other irreversible option such as occlusal adjustment.

In this meta-analysis, we analyzed the effects of two modern approaches to treat oral myofacial pain.

Description of the intervention

Description of the intervention A: Usual treatment (based on Splint therapy)

Pragmatically we defined the "usual treatment" as the most frequently reported combination of therapeutical methods to treat TMD. It is basically based on splint therapy and self-care strategies. Usually these self-care strategies are accompanied by dental professional counseling or analgesics.

Usual treatment vs psychosocial intervention for TMD

According to the European Academy of Craniomandibular Disorders and the Deutsche Gesellschaft für Funktionsdiagnostik und -therapie DGFDT (German Association for Function Diagnostics and Therapy), substantial improvement in TMD condition is possible through the recommended combination of splint therapy, counseling, and jaw exercises. Many authors support the concept of combinative therapies for the treatment of myofacial pain [79].

Widely indicated by dentists, the splint therapy is the most commonly used treatment for TMD. It consists of the elaboration of a removable device named oral appliance, occlusal appliance, occlusal plane, or splint; that stabilizes the dental occlusion.

The typical dental material employed for the confection of oral appliances is hard acrylic. The occlusion of the patient is transferred through a facebow to an articulator. However, the use of the facebow seems to be clinically irrelevant [520]. The occlusal appliance, according to the possibility of the teeth for displacement once installed, are categorized in permissive and non-permissive or directive splints according to *Dawson* [129]. Depending on the principal purpose they are divided in: bite planes, stabilization planes, repositioning planes, and pivot appliance.

Stabilization splints are permissive planes aimed to the recovery of the occlusal stability, muscular deprogramming, increase of the vertical dimension. This splint is the first election for bruxism and temporomandibular dysfunctions. Some kinds of stabilizations appliances are the flat plane, Michigan Tanner splint, superior repositioning, Shore splint, and centric relation splint.

Some new acrylic materials, recently available in market, represent an intermediate category, namely the soft splints, which also include the hydrostatic appliance, currently outdated. The soft splints are semi-permissive splints and are seldom indicated in Germany [437, 409]. A recent RCT did not attribute them any clinical efficacy for TMD treatment [417].

In this review, the usual treatment based on splint therapy is accompanied with self-care strategies. Self care was first introduced in 1981 as a Medical Subject Heading (MeSH) in the National Library of Medicine [646] (used for indexing the MEDLINE database) under the definition: "Performance of activities or tasks traditionally performed by professional health care providers. The concept includes care of oneself or one's family and friends". The self-care strategies for TMD include different techniques to reduce the muscle overloading and symptomatology, for ex. relaxation training, jaw exercises. Advices and /or recommendations related to soft diet, application of hot and cold packs are frequently included in the self-care strategies for TMD.

Additionally, the usual treatment may incorporate a coadjuvant agent which aims to reinforce the self-care strategies, including counseling or drugs indication.

The definition of counseling is widely variable depending on the subject in which is immerse, e.g. economics, education, ethics, legislation, etc. Counseling was introduced as a MeSH in 1966 conferring it a medical sense. The current definition according to the National Center for Biotechnology Information (NCBI) is "the giving of advice and assistance to individuals with educational or personal problems" [646].

In the case of TMD treatments, counseling is principally a resource to offer basic information about the possible etiology and pathogenesis of this condition, and the teaching of avoidance conduct potentially risky to worsen the associated symptomatology. Counseling can be regarded as a psychosocial intervention, however as a part of the usual treatment for TMD represents a secondary intervention to the main effect of the occlusal splint.

Some of the self-care strategies are intrinsically related to counseling, e.g. guidance in reduction of parafunctional jaw activities. These two terms, self-care and counseling, are not well defined for the TMD treatment, and habitually are used indistinctly.

The "usual treatment" may also include the indication of drugs, often nonsteroidal anti-inflammatory drugs (NSAIDs) or muscle relaxants, and occasionally antidepressants.

Description of the intervention B: Psychosocial intervention

Psychosocial interventions are non-pharmacological therapies which highlight the psychological factor of chronic pain. Psychosocial interventions for TMD target psychobiological mechanisms and psychosomatic correlations in order to relieve pain and improve functionality. Two major strategies for TMD are the increase of the pain coping ability of the patient, and/or the intensification of the muscular activity awareness [357], controlling at the same time oral parafunctions (i.e. bruxism, thumb-sucking, onychophagia, and breathing disorders).

The psychosocial interventions may be present in combination with the usual treatment. Under particular alignments of the review authors in order to specify the comparison groups, counseling and/or self-care were managed as psychosocial interventions only when they were the unique intervention.

How the intervention might work

Intervention A: Usual treatment based on occlusal splint

The mechanism of action of the "usual treatment" is probably the result of the combined action of each of its components.

The exact therapeutic effect of the oral appliances is not yet understood. The multiple influences on the masticatory system may include the variation of the relationship between the dental occlusion and the mandible; the redistribution of jaw dynamic and chewing forces; changes on the condylar position related to the temporal glenoid fossa and articular disc; relaxation of the chewing musculature; etc. It is noteworthy that some authors ruled out the primary belief that splints can increase joint space [309, 394, 177].

In general, the splint therapy targets a symptomatic reduction of the clinical pain, an improvement of the occlusal force distribution, reducing teeth wear, and the stabilization of occlusal contacts.

According to their clinical indication there are three types of oral appliances,namely, stabilization splint, distraction splint, and repositioning splint. Habitually, the stabilization splint is the first option for TMD treatments.

The stabilization or relaxing splint is indicated for myopathy, oral habits (bruxism), insufficient occlusal support, and reestablishment of vertical dimension. By reason of the probably psychological origins of the oral habits, the use of stabilization splint for this purpose has a preventive roll, focused on the protection of the anatomical dental integrity [440].

The splint has been reported as an effective therapy for TMD. Stabilization planes have shown to be more effective than control planes in a 6-12 months follow-up [166].

Neff and *Gündel*, however, hold the view that the splint therapy would be useful only for disorders with dento-occlusal origin (according to the classification of TMD by *Sebald*). For the cases based on myogenic or arthrogenic causes, this oral appliance had a time-restricted effect or no one at all [412]. Likewise, *van Selms et al.* suggested that changes on nocturnal electromyographic activity of bruxist patients could be more assigned to psychological effects than the splint influence [587]. Even the use of oral appliances has not proved to produce any immediate significant change on the electromyographic activity of masticatory muscles [497, 474, 311, 184].

The clinical data about splint therapy is controversial. *Forssell et al.* in a systematical review found only scarce evidence for the clinical efficacy of splint therapy [192]. In a review, no sufficient evidence was found to recommend occlusal appliances neither for TMD nor for bruxismus [305].

Recurring techniques of self-care strategies for TMD tackle the maintenance of the TMD

symptomatology. Dental TMD self-care involve dietary advices and /or recommendations, and use of thermal adjuvants as for example alternating application of hot and cold packs. Furthermore, the usual treatment may incorporate different techniques to reduce the muscle overloading, which is believed a factor of maintenance or causal agent of TMD. These strategies have proven to be sufficiently effective for the mentioned condition [154, 159].

The theoretic understanding of the possible etiology and pathogenesis of this condition allows an active participation of the patient in the relief of pain, maybe through improving coping abilities and/or helping the tissue regeneration when controlling inflammatory processes frequently linked to TMD symptoms. Counseling in this case, reinforces the self-care strategies. Similarly, the indication of medicaments points to the same objective.

Intervention B: Psychosocial intervention

According to *Aggarwal* [14], psychosocial interventions for chronic orofacial pain target two different suspected mechanisms of pain generation: inactivity (avoiding behaviors), and over activity (emotional stress).

The first model appeals to avoiding behaviors and negative cognition in response to prolonged and persistent pain. This inactivity would induce an exacerbated symptomatology in the affected area.

On the other hand, the emotional stress model proposes that psychological factors trigger oral habits resulting in muscle hyperactivity and subsequent facial pain. In this sense, the bruxism for example can be considered to be an expression of high stress level and thus would require behavioral interventions, i.e. surface electromyographic biofeedback (sEMG), relaxation training, etc.

Cognitive Behavioral Therapies (CBT) essentially aim to improve the coping capacity of the patient, modifying the perception of the patient about himself and his relationship with the symptoms of TMD. CBT for TMD is mainly based on skills training interventions focus on modifying the patient's interpretation of pain, usually combined with educational approaches to provide information about the jaw function and TMD.

As regards of TMD therapies, some psychosocial interventions better related to the emotional stress model, including hypnosis and oral habit reversal among others, principally tackle the parafunctional habits. The objective of this treatment is to replace a harmful behaviour by an alternative one, which competes as an adopted response for some habits, i.e. an innocuous habit take place of bruxism. They are usually combined with dental therapies.

Regarding the treatment of facial pain, *Gramling* observed improvements on all measures of relative pain in TMD patients treated with oral habit reversal (in a group format), compared to those in the control group [225]. Along the same line, *Townsend* found a significant reduction of maladaptative oral habits occurred from pre- to post-treatment and significant reductions in life stress and pain interference in TMD patients treated with habit oral reversal in a minimal therapist contact (MTC) [563].

In respect of clinical pain relief, *Glaros* reported that OHR may be as effective as a behaviourally-modified splint therapy [214]. However, *Peterson* suggests that habit reversal appears to be more effective in reducing the myofascial pain symptoms of TMD than in improving temporomandibular joint function. During clinical observations he found that the temporomandibular joint sounds were unexpectedly increased, although the pain was reduced [449].

Why it is important to do this review

Due to the high prevalence in every population studied, the high impact on the quality of life of the patients, and the necessity to define a therapeutical model for myofacial pain, which is the most prevalent form of TMD

prevalent form of TMD.

Objectives

To assess the effects of combined therapies based on splint therapy and psychosocial interventions for the treatment of oral myofascial pain in adult patients.

Methods

Criteria for considering studies for this review

Types of studies

Randomized controlled clinical trials (RCTs) conducted in patients with oral myofascial pain. Quasi-randomized and non-randomized trials, observational studies, narrative reviews, commentaries and letters to editors were excluded.

Types of participants

Adults diagnosed with temporomandibular disorders characterized as myofacial pain, with or without concomitant arthrogenous diagnoses.

Types of interventions

Intervention A: "usual treatment" based on splint therapy (stabilization splint plus self-care strategies and counseling, including or not drugs for symptomatic pain relief)

Intervention B: any type of psychosocial intervention (cognitive behavioral therapy, hypnosis, oral habit reversal, etc)

Types of outcome measures

The outcomes were chosen according to a previous random analysis of the most frequently reported outcomes in 5 trials of TMD. Considering the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) as reference for definition of outcomes for studies in TMD, we finally selected two outcomes for pain (self-reported pain and pain interference), two outcomes for clinical examination (unassisted jaw opening without pain and muscle pain upon palpation) and two outcomes for psychological parameters (somatization and depression).

Primary outcomes

- Self-reported Pain
- Unassisted jaw opening without pain (mm)

Secondary outcomes

Pain interference

Muscle pain upon palpation

Somatization

Depression

Search methods for identification of studies

We conducted electronic searches on 06.11.2012, and complemented the identification of studies with other resources. Details of the search strategy are available in Appendix 1, Appendix 2 and Appendix 3.

Electronic searches

We searched the following electronic databases to identify reports of relevant randomized clinical trials:

- PubMed MEDLINE
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*)
- EMBASE

Furthermore, we searched the following ongoing trials databases:

- Current Controlled Trials (http://www.controlled-trials.com/);
- ClinicalTrials.gov (http://www.clinicaltrials.gov/);

Searching other resources

We examined reference lists of relevant articles that were identified by the electronic searches for other pertinent articles to include in the review. Moreover, we browsed through the abstracts of the different meetings of the International Association for Dental Research (IADR) to identify possible relevant studies (http://iadr.confex.com/iadr/search.epl).

Finally, we conducted manual search on the following journals for the last 6 months for the purpose of explore for relevant articles:

- Cranio: The Journal of Craniomandibular practice
- Journal of Oral Rehabilitation
- Deutsche Zahnärztliche Zeitschrift

Data collection and analysis

Selection of studies

Every title and abstract obtained from the search strategy was tabulated in order to accomplish a first screening according to pre-established selection criteria. In a second stage, the pre-selected abstracts were assessed with a new form restraining criteria to increase the precision of the search. All the correspondent full texts of each article, that were obtained in the second screening, were regained and evaluated independently by two review authors. Disagreements were resolved by discussion with referral to a third review author if no consensus was reached. The process of screening is reported according to the QUORUM/PRISMA criteria [337] (Figure 1).

Data extraction and management

Two review authors extracted independently general data and outcomes results from each full text of all the selected studies. These data were compiled into a pre-designed form by duplicate. The partial results were shared and discussed with a third review author.

Assessment of risk of bias in included studies

All the included studies were evaluated adhering to the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011) [539]. The risk of bias of the included studies (full text version) was assessed independently by two review authors using the corresponding Cochrane Collaboration's tool. In case of discrepancies, the data were reviewed concurrently by both review authors and, if needed, a third review author was referred as arbiter.

The review authors were not blinded, because they were familiar with the literature. Besides, according to *Moher* blinding has not been considered an influencing factor in literature reviews [398].

We systematically contacted authors of trials in order to clarify methodological questions, except if every item of the risk of bias tool was positively fulfilled.

Measures of treatment effect

The measures of treatment effect that were used for evaluating the outcome in each trial were:

- Self-reported pain (VAS)
- Significant clinical improvement (33%)

Unit of analysis issues

The "usual treatment" intervention can be differentiated into two experimental designs: when is tailored to each patient and when applied uniformly in a group. These two modalities to administrate the usual treatment go by the hand of the personal beliefs of the authors, i.e., a tailored intervention is a research position respect of the needs of the TMD patients and is normally defined as "usual treatment" at discretion of the attending dentist. This particular circumstance force to separate the studies in different categories, due to the imbalance of the interventions, however the definition of "usual treatment" involves the same therapeutical components.

Dealing with missing data

We contacted the authors when necessary asking for additional information of incomplete data. A standard message with open questions was sent to the person addressed in the publication as the corresponding author.
The missing data of each trial was analyzed to discriminate missing data related directly to the intervention. The available data were adopted when the missing data occurred randomly and/or not linked to the intervention. In case of not random missing values of dichotomous or continuous data, worst-case scenario or imputation respectively, in agreement to the Cochrane Handbook [539].

Assessment of heterogeneity

The statistical heterogeneity was verified using the chi-square test at significance of 0.1. The I^2 statistic allowed the quantification of inconsistency across the studies demarcating four categories, namely unimportant (0%-40%), moderate (30%-60%), substantial (50%-90%), and considerable (75%-100%) heterogeneity amongst trials, according to the Cochrane Collaboration instructions [134]. The clinical and methodological heterogeneity was discussed based on the study design (patients, setting and interventions), and the risk of bias tool [248]. The assessment of heterogeneity was performed in subgroup analyses (see Subgroup analysis and investigation of heterogeneity).

Assessment of reporting biases

The outcome-reporting biases was investigated by searching protocols of the included RCTs [539]. Abstracts were also considered as a source of reporting bias. Publication bias was tested using the Egger test and making interpretations of the funnel plots for all outcomes [163].

Data synthesis

The included RCTs are described in a narrative overview, adding a meta-analysis of the comparison "usual treatment" vs. psychosocial interventions accomplished by working with RevMan 5.1. The outcome data with no obvious clinical heterogeneity and unimportant statistical heterogeneity amongst trials, i.e. I^2 value 0% to 40%, were compared using a fixed-effect model. We applied a random-effects model for outcomes without apparent clinical heterogeneity and the I^2 value greater than 40%. Finally, data with high heterogeneity were excluded.

Subgroup analysis and investigation of heterogeneity

Possible factors of heterogeneity across the results of the trials were anticipated and explored through subgroup analyses. Other sources of heterogeneity investigated include: modality of "usual treatment" (tailored or standardized) and type of psychosocial intervention (see Unit of analysis issues).

Sensitivity analysis

The exclusion criterion for this review was the high risk of bias. Since the blinding of outcome assessment was critical for the comparison of the interventions which are technically difficult to implement blinding of participants and personnel, a trial was regarded as at high risk of bias when the

blinding of outcome assessment domain or two or more other domains were judged to be at high risk of bias. The same criteria was applied to classify a trial as having unclear risk of bias. Otherwise, the trial was considered at low risk of bias.

Furthermore, possible outlier studies were subjected to sensitivity analysis in order to evaluate its effect on the results of the meta-analysis.

Main results

Description of studies

See: Characteristics of included studies, Characteristics of excluded studies, and Characteristics of studies awaiting classification

Results of the search

The search strategy of the six databases yielded 169 different titles of potential relevant clinical trials. After using two pre-established forms 135 articles were excluded because they were not randomized or because they did not match the intervention or condition of TMD, and 12 did not fulfill the characteristics of the type of participants (no adults or not myogenous TMD patients). Two independent reviewers assessed the full text of the selected 22 articles.

We contacted the authors of both studies awaiting for classification.The study of Huggins2004-Truelove 2004a was reported in two different abstracts at the 82.meeting of the International Association for Dental Research (IADR). With the available information was not possible to identify the definition of "usual treatment" and therefore not possible to include the results in any of the unit of analysis, however the authors declared the intention to publish a full text version. Regarding the other RCT awaiting for classification (Shedden Mora 2010), the authors already published two articles including subsamples which not represent the complete intervention groups. Nonetheless, the authors assured the final results will be available in an article to be published soon. 9 RCTs were finally excluded due to the reasons exposed in the section Characteristics of excluded studies. Thus, 12 trials (n=1122) were considered relevant to the meta-analysis. Among the included studies, 75% used the RDC/TMD as diagnostic tool. When available, the results were separate into short- (3 months or less) and long-term (more than 3 months).

Included studies

Out of the 12 included studies (n=1122), 7 studies (n=535) (Alencar 2009; Carlson 2001; Conti 2012; Crockett 1986; Litt 2010; Niemela 2012; Truelove 2006) applied a pre-defined "usual treatment" for all the patients in the intervention group. On contrast, 5 studies (n=587) (Dworkin 1994; Dworkin 2002a; Dworkin 2002b; Ferrando 2012; Turner 2006) used a tailored version, where the attending dentist decided independently the treatment for each patient, choosing among the therapeutical methods considered part of the "usual treatment". In this group of studies the dental treatment was not monitored.

The definition of usual treatment fitted for the first group with the following combinations: mandibular hard splint, counseling and self-care strategies (Alencar 2009); stabilization splint and self-care strategies (Carlson 2001); stabilization splint, self-care strategies (jaw exercises, soft diet) and counseling (education) (Conti 2012); splint therapy, counseling, and self-care strategies (jaw exercises) (Crockett 1986); splint, self-care strategies (soft diet) and analgesics (Litt 2010); splint, counseling and self-care strategies (jaw exercises) (Niemela 2012); and splint, self-care strategies and analgesics (Truelove 2006). In the second group of studies applying tailored intervention, the "usual treatment" corresponded to splint, self-care strategies (jaw exercises) and analgesics or muscle relaxants (Ferrando 2012); and occlusal splint, self-care strategies (jaw exercises, modification of dietary habits, use of cold and heat packs) and analgesics or muscle relaxants (Dworkin 1994; Dworkin 2002a; Dworkin 2002b).

The "usual treatment" for all these studies reported the indication of a hard stabilization splint (except for Turner 2006 who did not address any details of the dental treatment). The recommendations on

how to wear the splint varied from only nocturnal wearing (Carlson 2001, Conti 2012); nocturnal wearing plus 2 hours while awake (Truelove 2006); to full-time except for eating during the first period (1-4 weeks), and later only nocturnal wearing (Alencar 2009, Litt 2010). Two articles of the first group of studies did not specify the wearing time of the splint (Crockett 1986, Niemela 2012). The studies of tailored intervention did not define the time of using splint in concordance with the group definition (Dworkin 1994; Dworkin 2002a; Dworkin 2002b; Ferrando 2012, Turner 2006).

The psychosocial interventions were basically divided in two categories: only a psychosocial intervention or a combination of the "usual treatment" and the psychosocial intervention.

Counseling and self-care were considered a psychosocial intervention only when used as unique intervention (Conti 2012, Dworkin 2002b, Niemela 2012, Truelove 2006) or with a placebo splint (Alencar 2009). Other psychosocial interventions included in this review are physiotherapeutic oriented interventions as physical self-regulation (Carlson 2001), and EMG-biofeedback plus self-care strategies (Crockett 1986).

Due to ethical considerations, the indication of only cognitive behavioral therapies (CBT) is widely debatable in severe cases of TMD. CBT has proven to be effective for many psychological conditions; however there is no conclusive evidence about its effectiveness for TMD. Therefore, some authors designed a comparison group which embraces the psychosocial intervention (CBT) and the "usual treatment" together (Dworkin 1994; Ferrando 2012, Litt 2010; Turner 2006).

The samples of the studies comprehend at least a 75% of myofacial pain diagnosis at baseline: 100% in the following studies Alencar 2009, Carlson 2001, Conti 2012, Crockett 1986, Ferrando 2012, Truelove 2006, Dworkin 2002b; 96.0% in the trial by Turner 2006; 94.8% in the article Dworkin 2002a; 90.1% in Niemela 2012; and 77% in Litt 2010. TMD clinical diagnoses were not considered in one study (Dworkin 1994), however the relative large sample allows to presume findings similar to general epidemiological data.

Excluded studies

Among the excluded studies, 3 studies did not include myogenous TMD patients, however their results support the importance of self-care and counseling. Cunha 2012 (abstract) applied successfully a combined therapy of splint and counseling for TMJ arthralgia. Schiffman 2007 found comparable positive results between surgical interventions and conservative treatments (self-care, counseling and analgesics and muscle relaxants; and other experimental group carrying splint therapy, physiotherapy and CBT) for cases of TMJ closed lock. Finally, Minakuchi 2004 reported higher self-reported improvements in a group of patients with disc displacement without reduction treated with self-care strategies and analgesics than other similar group intervened with splint therapy, self-care strategies, analgesics and physiotherapy and a no-treatment control group.

Other excluded study (double report Gatchel 2006,and Stowell 2007) recruited only patients with acute TMJ symptomatology, not comparable with the chronicity of TMD diagnosis.

No one intervention group of the following studies did match our definition of "usual treatment": Glaros 2007 (only splint vs. oral habit reversal), Michelotti 2012 (only splint vs. self-care and counseling), Turk 1996 (splint, counseling and EMG-biofeedback vs. splint, counseling, EMG-biofeedback and CBT vs. splint, counseling, EMG-biofeedback and nondirective self-care strategies), and Wright 1995 (soft-splint vs self-care and analgesics vs. no treatment).

Risk of bias in included studies

See Figure 2 and Figure 3. We were in contact with all the authors of the included studies. This fact improved substantially the general and particular risk of bias of the analyzed RCTs.

We additionally include a Delphi list to evaluate the quality of the trials. Most of the items coincide with those from the Collaboration's tool. From this list we remark that in 50.0% of the included RCTs Intent-to-treat analyses were conducted. According to our modified evaluation using the Collaboration’s tool, 4 studies were at unclear risk of bias (Conti 2012; Crockett 1986; Dworkin 1994; Litt 2010), and the others were considered at low risk.

Allocation (selection bias)

Most of the included RCTs were written during the last two decades, which implies a high availability of statistical sources to conduct an adequate method of randomization. However, the concealment of the allocation was scarcely reported in the articles. The authors supported us with the required additional information. Consequently, we have 16.7% of unclear risk within the random sequence generation, and 41.7% unclear risk for the allocation concealment, and no one study evaluated as having high risk for this criteria.

Blinding (performance bias and detection bias)

Blinding regarding the performance bias is irrelevant for this sort of comparisons which are technically complex to be blinded. As a consequence, we considered the blinding of the outcome assessment especially important for our meta-analysis. Only 3 RCTs did not expressly report a method for blinding the outcome assessor. Out of these studies, 2 gave insufficient information. In the study by Litt 2010, long- but not short- term outcomes were assessed through interviews conducted in person. Nonetheless, we considered not having enough details to weigh the possible influence of this methodology since the data at long-term were coherent with the results on short-term.

Incomplete outcome data (attrition bias)

Only Conti 2012 and Niemela 2012 did not report sufficiently the reasons for attritions, however the number was informed.

Selective reporting (reporting bias)

The study by Conti 2012 did not report completely clinical data from the study, refering the reader to other similar study. The trials by Dworkin 2002a and Dworkin 2002b reported intent-to-treat analyses, but also as-treated analyses for some outcomes without defining minimal differences among the number of analyzed persons.

Other potential sources of bias

We found a low risk of bias for all the RCTs regarding this criteria.

Effects of interventions

Comparison 1. "Usual Treatment" vs Psychosocial Intervention

Primary outcomes: Self-reported Pain Intensity and Unassisted Jaw Opening without pain (mm)

- Self reported pain at short-term (less than 3 months):

Pain intensity at short-term was reported in all the included studies for this review using an homogeneous formula of "usual treatment" for the corresponding intervention (balanced intervention), i.e. 6 studies (Alencar 2009; Carlson 2001; Conti 2012; Crockett 1986, Niemela 2012; Truelove 2006) showing moderate heterogeneity I^2 =42% (P=0.13), and additionally one RCT by Litt 2010 using a combination of psychosocial intervention (PI) plus UT. Although some pain measurements included frequency and duration, the overall heterogeneity for the data of this outcome was not important (I^2 =36%; P=0.15), not differing for subgroups (I^2=0%; P=0.54)

There was no statistical significance for the difference between "Usual treatment" and Psychosocial Interventions (P=0.57), with only a slight standard mean difference favouring PI (SMD=0.08; 95% CI= -0.18, 0.33).

It is noticeable that the studies comparing UT vs. PI (Alencar 2009; Carlson 2001; Conti 2012; Crockett 1986; Niemela 2012; Truelove 2006) was close to neutral (SMD= 0.05; 95%CI= -0.26, 0.36), while the comparison of UT vs UT+PI (Litt 2010) was more auspicious for the latter (SMD=0.22; 95%CI= -0.20, 0.64), however without exhibiting significant differences (P=0.31).

Without considering the study that incorporated frequency or duration of pain (Alencar 2009) the heterogeneity increased (I^2=44%, P=0.11) showing that the difference between treatments slightly

increased to SMD= 0.06; 95%CI= -0.23, 0.34 (P=0.70). When comparing only actual reports of pain intensity (VAS or a media of a diary VAS) (Conti 2012; Crockett 1986; Niemela 2012) with a moderate heterogeneity (I^2=56%, P=0.11) the standard mean difference appears to a small extent more propitious for UT (SMD= -0.04; 95%CI= -0.65, 0.57), but remain not statistically meaningful (P=0.90). On the contrary, regarding studies using an average of the actual, worst and usual pain (Carlson 2001,Truelove 2006, Litt 2010; I^2=37%, P=0.20), the standard mean difference trend towards favouring PI (SMD=0.14; 95%CI= -0.18, 0.45), however the difference between interventions was again not significant (P=0.40).

- Self-reported pain at long-term (more than 3 months):

With a substantial heterogeneity (I^2=65%, P=0.06), 3 studies reporting averages of actual, worst and usual pain exhibited no significant differences in the overall effect of the interventions (P=0.35). This heterogeneity plunge to I^2=0% (P=0.91) when considering only the studies measuring this outcome with the Mutlidimensional Pain Inventory (MPI). The SMD was inclined to the PI interventions (SMD=0.23; 95%CI= -0.25, 0.71).

Nonetheless, the study by Litt 2010 showed P=0.05 for greater benefits of the combination UT+PI (SMD=0.47; 95%CI= 0.01, 0.93); approximately the same results in favour of PI in the study by Carlson 2001, both using MPI. Taking these 2 studies in a separate analysis, the results are statistically significant for the overall effect (P=0.02) with a mean difference=1.03 (95%CI=0.20, 1.86).

- Unassisted jaw opening without pain at short-term (less than 3 months):

4 studies provided data for this outcome at short-term (I^2=43%, P=0.17). However, the SD in the study by Truelove 2006 were not available. Therefore, the meta-analysis of the other trials (Carlson 2001; Crockett 1986; Niemela 2012) resulted in non-significant differences, with a mean difference= -1.66 (95%CI= -5.60, 2.28) given advantage to UT.

- Unassisted jaw opening without pain at long-term (more than 3 months):

Out of 2 trials, one provided only partial information (Truelove 2006). Thus the data by Carlson 2001 represented the outcome with an inclination to UT (MD= -2.50; 95%CI= -8.45, 3.45) without meaningful significance (P=0.41)

Secondary outcomes: Pain Interference, Muscle Pain upon palpation, Somatization and Depression

- Pain Interference at short-term (less than 3 months) and at long-term (more than 3 months):

Carlson 2001 and Litt 2010 (I^2=0%, P=0.63) reported more benefits at short-term when indicating interventions including PI (MD=0.37; 95%CI= -0.29, 1.02). The difference between groups was however not significant (P=0.28).

The same RCTs provided data for this outcome at long-term (I^2=0%, P=1.00). The results were once again not significant (P=0.60), diminishing the tendency pro PI (MD=0.20; 95%CI= -0.55, 0.95)

- Muscle Pain upon palpation at short-term (less than 3 months):

4 studies (Alencar 2009; Carlson 2001; Niemela 2012; Truelove 2006) reported muscle pain upon palpation using different scales, but without presenting heterogeneity (I^2=0%, P=0.66). Results trend towards significance (P=0.08) showing a standard mean difference inclined toward PI (SMD=0.21, 95%CI= -0.03, 0.44)

- Muscle Pain upon palpation at long-term (more than 3 months):

Contrarily to the short-term observations of this outcome, UT seems to be more beneficial than PI at long-term. 2 RCTs (Carlson 2001 and Truelove 2006) presenting moderate heterogeneity (I^2=36%, P=0.21), resulted in SMD= -0.06 (95%CI= -0.51, 0.39), however without statistical significance (P=0.80).

- Somatization at short- (less than 3 months) and long-term (more than 3 months):

Exclusively Carlson 2001 provided data for this outcome with a trend toward significance (P=0.09)

favouring PI (MD=0.23; 95%CI= -0.03, 0.49). No relevant changes were found at long-term (MD=0.30; 95%CI= -0.07, 0.67; overall effect P=0.11)

- Depression at short- (less than 3 months) and long-term (more than 3 months):

Only 2 RCT (Carlson 2001, Litt 2010) (I^2=0%, p=0.52) reported intervention effects on depression finding differences neither at short-term (SMD=0.19; 95%CI= -0.15, 0.54; overall effect P=0.27) nor at long-term (SMD=0.06; 95%CI= -0.32, 0.45; P=0.75) with some tendency toward PI.

Comparison 2. Tailored "Usual Treatment" vs. Psychosocial Interventions

Primary outcomes: Self-reported Pain Intensity and Unassisted Jaw Opening without pain (mm)

- Self-reported pain at short-term (less than 3 months):

5 studies provided data for pain intensity at short-term. One study could not be pooled due to incomplete information of the results (Dworkin 2002a). The four other studies (Dworkin 1994; Dworkin 2002b; Ferrando 2012; Turner 2006) showed a substantial heterogeneity (I^2=60%, P=0.06) with a non-significant overall effect (P=0.62) and a preference for PI (SMD=0.07; 95%CI= -0.22, 0.37)

When omitting the study by Ferrando 2012, the remaining studies, all measured using Characteristic Pain Intensity (CPI), experienced a sharp decline of heterogeneity to not important level (I^2=10%, P=0.33) and exhibited a mean difference favourable to UT (MD= -0.08; 95%CI= -0.50, 0.35), however without statistical significance.

- Self-reported pain at long-term (more than 3 months):

A significant difference was found for this outcome considering all the three included studies of *Dworkin* with heterogeneity I^2=0% (P=0.58). The study by Dworkin 2002a however could not be estimated due to incomplete information. PI+UT was significantly more effective (P=0.003) to reduce pain at long-term (MD=0.66; 95%CI= 0.23, 1.09).

- Unassisted jaw opening at short- (less than 3 months) and long-term (more than 3 months):

Dworkin 1994 reported means of the effects of the interventions at short-term, however not standard deviations. Identical situation occurred about the reports at long-term (Dworkin 1994; Dworkin 2002a; Dworkin 2002b). The data are not analyzable.

Secondary outcomes: Pain Interference, Somatization and Depression

- Pain Interference at short-term (less than 3 months):

Out of 4 studies, only for 2 the complete data were available. Presenting high homogeneity (I^2=0%, P=0.97), the studies by Dworkin 1994 and Ferrando 2012 reported a weak difference in favour to PI (SMD=0.02; 95%CI= -0.26, 0.30) without meaningful difference between interventions.

Turner 2006 reported this outcome in terms of percentage of patients who registered none pain interference at short- and long-term. These results were not compatible with those from other RCTs, and consequently not pooled.

- Pain interference at long-term (more than 3 months):

One trial provided incomplete data. The study by Dworkin 1994 showed a trend toward significance (P=0.08) with a mean difference in favour of PI (MD=0.66, 95%CI= -0.09, 1.41)

The odds of reporting no activity interference at 12 months in the study by Turner 2006, after adjusting for baseline interference, were four times greater in the UT+PI group than in the UT group (OR = 4.2; 95% CI = 1.7, 10.2). As mentioned before, this study was not pooled due to a different type of data.

- Muscle Pain upon palpation:

We did not find related studies for this outcome at short-term. Only Dworkin 2002a offers data for Muscle Pain upon palpation at long-term without statistical significance (MD=0.30, 95%CI= -1.66, 2.26; P=0.76)

- Somatization at short-term (less than 3 months):

Somatization at short-term was reported by Dworkin 1994 and Dworkin 2002a. From those, only the latter published complete data showing an inclination to PI, not meaningfully significant (MD=0.30; 95%CI= -0.24, 0.84; P=0.27).

- Somatization at long-term (more than 3 months):

Incomplete data in one study (Dworkin 1994) reduced the estimations of the analysis to only 2 RCTs by Dworkin (Dworkin 2002a; Dworkin 2002b) with substantial heterogeneity (I^2=62%, P=0.11). Probably, this high heterogeneity is linked to the psychological profile of the patients. In fact, those trials were parallel conducted by the same research team, who split the available participants according to the Chronic Pain Grade Scale (CGPS). This instrument includes the characteristic pain intensity (CPI) and the pain interference scale. It implies that the patients participating in the RCT by Dworkin 2002b showed at baseline less important impairments. Therefore, somatization scores may be interacting with the variable of pre-selection of the samples (CGPS). Mean difference leaned toward PI (MD=0.13; 95%CI= -0.46, 0.71) showing no statistical significance (P=0.68)

- Depression at short-term (less than 3 months):

Dworkin 1994 and Dworkin 2002a measured depression using SCL-R-90, however for only the latter the data are full available.Turner 2006 registered Depression using the Beck Depression Inventory (BDI) A trend toward significance was found for the overall effect of the interventions (P=0.09) with a standard mean difference of 0.22 (95%CI= -0.03, 0.47) in favour of PI.

- Depression at long-term (more than 3 months):

The three trials by Dworkin provided data for this outcome, however the complete information in the study by Dworkin 1994 was not available. The other two RCTs with null heterogeneity (I^2=0%, P=0.58) displayed a tendency towards PI (SMD=0.21; 95%CI= 0.00, 0.41), with statistical significance (P=0.04).

Discussion

In an ambitious attempt to shape a protocol of the current reported treatment for TMD, we grouped two principal categories of different studies, e.g. "usual treatment", and tailored "usual treatment". As a personal definition, "usual treatment" combined the action of an occlusal appliance and self-care strategies backed-up by counseling and sometimes drugs, especially analgesics.

Although other similar combination of therapies with splints was used in three of the included studies (Alencar 2009 and Truelove 2006 using soft splints; and Conti 2012 with NTI-splint) we only considered "usual treatment" when the stabilization plane was included, because of the evidence supporting its use was stronger than for other types of splints. Besides, the search strategy did not produce more results on these alternative combinations out of the mentioned above. Those outcomes will be commented further on the text.

Coincidentally with our review on splint therapy, the most indicated occlusal appliance within the screened trials was the hard stabilization splint. Seven included studies were in common when comparing the search strategies for splint therapy and for "usual treatment" (Alencar 2009; Carlson 2001; Conti 2012; Dworkin 2002a; Dworkin 2002b; Litt 2010; Truelove 2006).

The use of splints is not exempt of polemics by itself (see review "Occlusal appliances for Myofacial Pain"). It is hardly discussed what is the exact mechanism of action for the splint therapy. Even non-occluding planes have shown effects on TMD patients which go beyond the placebo effect.

Two of the excluded RCTs (Glaros 2007 and Michelotti 2012) compared psychosocial interventions to splint therapies. Both studies described similar improvements for PI and the stabilization splint. It implies however, that probably both interventions alone are not sufficient enough to solve the myofacial pain condition.

On the other hand, our endeavor to compile different psychosocial interventions was also challenging,

especially because the UT incorporates two basic PIs, namely self-care strategies and counseling. On account of this, we considered the intervention as PI when self-care strategies and counseling were applied alone, or when the combination of UT added a new psychosocial intervention different to them. The question raised is if additional PI or specific PI alone may exceed clinical improvements of the usual dental treatment. Do the psychological factors determine a greater clinical success?

Self-care strategies and counseling added to splint therapy regarding UT were principally directed to increase coping abilities of the patients. Theoretically, the principal aims were giving the participants a better understanding of the TMD condition (education has to be mentioned) and acting against symptoms through basic self-administrated physiotherapeutic interventions which could be reinforced by the indication of analgesics (Dworkin 1994; Dworkin 2002a; Dworkin 2002b; Ferrando 2012; Litt 2010; Truelove 2006) or muscle relaxants (Ferrando 2012).

In contrast, psychosocial interventions aimed to enhance the coping ability of the patient tackling psychological disturbances. We grouped together self-care strategies, CBT and EMG biofeedback. In a meta-analysis, the authors found weak evidence to indicate psychosocial interventions for orofacial pain. The included RCTs were at high or unclear risk of bias. However, CBT appeared as the most auspicious therapy among PIs which embraces also hypnosis, relaxation, and habit reversal [14].

In our review of psychosocial interventions, we found five trials comparing PI with interventions based on splint therapies. All of them were common to those here included (Dworkin 2002a; Dworkin 2002b; Litt 2010; Truelove 2006; Turner 2006).

Among the excluded studies of this meta-analysis, Turk 1996 used a multimodal therapy which consisted of intraoral appliance plus stress management and EMG-biofeedback. One experimental group received additionally supportive counseling, and the other group was treated with a customized CBT. Therefore, the comparison was based on the different effects of a generalized or a tailored psychosocial intervention. Both groups successfully improved the outcomes at 6-months follow-up. Contrarily, when comparing a generalized and a tailored intervention Turner 2006 reported that the tailored CBT group was meaningfully more efficient to reduce pain, depression, and medication use. Although the relevance and quality of the trial by Turk 1996, it did not match with any comparison group in the meta-analysis (due to the presence of a co-intervention consisting of EMG-biofeedback), and had to be excluded. This exclusion illustrates the arduousness behind the conceptualisation of an "usual treatment" when no previous consensus exists.

In four RCTs of this meta-analysis (Litt 2010; Dworkin 1994; Dworkin 2002a; Turner 2006) these PIs were accompanied with the same UT (tailored or not) applied to other comparison group. Therefore, within these studies, the effect of the specific PI, CBT for the three trials, is the differential factor between therapies. However, the comparison between these studies was not viable due to the imbalance represented by the tailored UT intervention (not every patient received the same therapy as done by Litt 2010).

In a recent meta-analysis of psychosocial interventions for chronic pain, CBT was found more effective than waiting list, but not against active controls. CBT is effective provided that this intervention is delivered by trained personnel. The main effects of CBT on chronic pain are over catastrophizing and disability [608].

In this meta-analysis, only the outcomes Self-reported pain and Depression at long-term were significantly different for the comparisons tailored "usual treatment" vs. psychosocial interventions, favouring the latter (p=0.003, and p=0.04 respectively). This comparison embraces the subgroup tailored "UT" vs. tailored "UT" + PI (CBT for all the included studies), and the subgroup tailored "UT" vs. PI (CBT in the only included study). These results have to be taken in account with some caution due to the limited number of studies.

Moreover, we found trend toward significance in 4 other outcomes. In the first comparison the results favoured PI at short term for the outcomes Muscle pain upon palpation (p=0.08), and Somatization (p=0.09). Both effects did not remain in time, similar to the observations in the meta-analysis by Williams 2012, and even Muscle pain upon palpation reverted its inclination toward UT. On the other

hand, the outcomes were inclined toward PI In the second comparison for the outcomes Pain interference at long-term (p=0.08) and Depression at short-term (p=0.09). The effect of PI in Depression however resulted in a significant difference at long-term.

When observing the different outcomes is possible to suspect a similar trend that relates "objective" clinical signs with "usual treatment", while "subjective" outcomes used to be more promising after psychosocial interventions, as much at short- as at long-term. For instance, the psychological outcomes (Depression and Somatization) and Pain interference showed in all comparisons a trend toward PI, while jaw opening was more favourable for UT. The outcome Muscle pain was also more auspicious for the UT at long-term in the first comparison (UT vs PI). Although the comparison of tailored UT vs PI for this outcome did not agree with our suggestions, it must be considered that in that case the data (no statistically significant) came from an unique RCT which is combination of PI+UT and we did not find any assessment at short-term. Therefore, more information from good qualities trials may help to elucidate if the lack of significance within our analyzes is related to the low statistical power, or it was only a random coincidence. Most probably, it also may indicate that psychosocial interventions alone do not address physical functioning of a myofacial pain patient.

Particularly interesting are the distinct measurements of pain in the first comparison (UT vs PI). We observed that considering only actual pain reports (VAS, or a mean of daily actual VAS) the results were inclined towards UT, on the contrary, registers of pain including memory reports (worst pain and usual pain during the last 3-4 weeks) exhibited a trend toward PI. Some authors have indicated that reports of memory of pain present an emotional component; for instance, it has been observed that, independent of the tool used to measure pain, the patients tend to overestimate past experiences of pain [356]. That implies that outcomes asking the patient recall past pain experiences probably present more accentuated scores within patients with higher somatization or catastrophizing levels.

In agreement with the tentative statement of Dworkin 2002a and Dworkin 2002b trials, it seems to be a relationship between the severity of psychological impairment and the effectiveness of "usual treatment". Concordantly, a review of literature concluded that TMD patients suffering major psychological disturbances benefit more of multimodal therapies than those patients without these problems [567]. They indicated that patients without major psychological disturbances, including those diagnosed with disc derangement, would be responsive to simple interventions, such as self-care strategies and counseling only.

Other multimodal therapies based on occlusal appliances were found in our review on splint therapy: *Raphael 2001* [458], *Jokstad 2005* [275] which were not compared to Psychosocial Interventions. The RCT by *Raphael 2001* set over two groups receiving self-care strategies, one also with stabilization splint against one with a non-occluding plane. Both groups improved ranges of pain similarly, except for the outcome (log)least pain that was significantly lower for the stabilization splint group. Likewise, the study by *Jokstad 2005* showed also that the type of splint was virtually irrelevant in terms of produce improvements when compared "usual" treatment with a multimodal combination of NTI-splint plus self-care strategies and counseling.

Many limitations are obvious in this study. The categorization we made can be subjected, especially in terms of the definition of self-care strategies and counseling. Moreover, the quantity of RCTs was relative scarce. Usually, the reports of TMD include multiple outcomes. This multiplicity of data makes difficult to find comparative points to evaluate the impact of a therapy. Out of 44 different outcomes available within the included studies, we analyzed only 6. The outcomes were chosen according to a previous random analysis of the most frequently reported outcomes in five trials of TMD. Perhaps, other outcomes may reflect a greater demarcation between the studied interventions.

Nonetheless, we suggest that future studies of TMD and related subdiagnosis should be reported with a minimal core of outcomes to enable comparisons. In agreement with the recommendations by *Turk 2003* [574], we addressed in our meta-analysis the three first domains for chronic pain trials (pain, physical functioning, and emotional functioning). A global assessment of the condition of the patient -encompassing these different domains- may help us to elucidate, if psychosocial interventions are

targeting physical functioning or not. Likewise more complete reports of the mentioned key outcomes may reveal if the low effects of "usual treatment" on psychological outcomes are related to the design of the intervention or are being underreported.

In addition, we collected data mainly, but not exclusively, from myofacial pain patients. We commented the diagnose situation in the section of results. Finally, in some RCTs the "usual treatment" intervention was customized to the personal necessities of the patients. We found only five RCTs using tailored "UT". Tailored interventions (second comparison) were not compared to balanced interventions (first comparison) in this meta-analysis due to the high heterogeneity between these different comparisons.

In spite of the apparently heterogeneity of the studies is not difficult to infer the philosophy of the authors on the study background. The comparison between groups points to a principally local treatment or a global psychosocial approach.

As suggested many times in this review, the comparison between the "usual treatment" and the psychosocial interventions encompasses a philosophical dilemma about the most correct approach for treatment, but even more interestingly about the etiology of TMD. As far as we are not able to identify the specific effect of each of the therapeutical strategies here mentioned -of the components of the UT, and of the different PIs-, we can not conclude anything in that regard.

In order to define a successful therapy, we should be concern about the expected outcome we want to improve. Considering that pain is the most common reason for consultation, we should subscribe to the current knowledge of pain which promotes to consider its multidimensionality. The psychological profile of the patient would be decisive to discriminate the most effective therapy for a personalized diagnosis of TMD.

Quality of the evidence

Thanks to the additional information from the authors, the risk of bias of the articles was notoriously improved. We asserted the changes in risk of bias evaluations since we systematically contacted every research team of the included RCTs and the studies awaiting for classification. To avoid compiling slanted information, benefiting only some studies over others, we asked for explanations of every item presenting unclear risk in the risk of bias tool of the Cochrane Library. We considered study design more relevant than study report in the sense of the followed rationale to tackle Myofacial pain. The quality of the evidence was therefore for our meta-analysis markedly better than for other reviews including some of the same RCTs, which is explained especially by the item allocation concealment. Moreover, we underestimated the item for blinding for participants and personnel due to the technical difficulties to implement it in this sort of comparison. For all the trials where the study design made impossible blinding patients and operators, we assessed low risk of bias.

Potential biases in the review process

Many factors made challenging to define the parameters for this review. First of all, the concept of "usual treatment" is not standard, however it reflects the real clinical situation. The nucleus of the "usual treatment" was pragmatically decided as the combination of splint and self-care strategies, nonetheless founded in the current literature and clinical experience.

Moreover, the psychosocial interventions include three principal groups: CBT, self-care and counseling, and physiotherapeutic oriented interventions (EMG-biofeedback, and physical self-regulation).

Finally, many of these studies are not restricted to patients with myofacial pain. Nonetheless, myofacial pain is the most common diagnostic for TMD patients and also for the included studies.

Authors' conclusions

Implications for practice

We found no evidence to distinguish the clinical effectiveness between "usual treatment" and psychosocial interventions alone. However a no statistically significant trend towards greater improvements of psychological outcomes was seen for psychosocial interventions, while improvements of physical outcomes were tendentious towards "usual treatment".

Implications for research

We suggest that next reports of TMD and related subdiagnosis should be reported according to a core outcomes set to enable comparisons. In this meta-analysis, we proposed a formula which allows to compare the multifactoriality of TMD including pain (pain intensity, and pain interference), physical outcomes (muscle pain upon palpation and jaw opening without pain) and psychological outcomes (depression, and somatization).

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Contributions of authors

Declarations of interest

The authors declare not to have any conflict of interests.

Differences between protocol and review

Published notes

Characteristics of studies

Characteristics of included studies

Alencar 2009

Methods	RCT. Single center; three parallel groups. Follow-up for 90 days.
Participants	42 (out of 45) patients: mean age=34 (R=18-65), 88.10% women. Inclusion criteria: age 18-65 years; diagnosis of myofacial pain with reproduction of the chief complaint upon palpation of a trigger point in the masseter muscle; at least six natural teeth in each quadrant. Exclusion criteria: previous splint therapy; any obvious dental decay or periodontal disease; history of trauma in the pain area in less than 30 days; any systemic condition associated with widespread pain (e.g. fibromyalgia); medical history of current drug addiction; any other TMD diagnosis according to the Diagnosis Criteria of the AAOP such as TMJ osteoarthritis or capsulitis. Location: Brazil

Interventions	Group A (n=14): mandibular hard occlusal splint Group B (n=14): mandibular soft occlusal splint Group C (n=14): non-occluding splint Indications for all groups: full time wearing of the respective splint during the first week and after this period, only nocturnal wearing Cointerventions: education, counseling and self-care instructions for all groups
Outcomes	Muscle Pain Index (6 sites scored 0-3) Subjective Pain using the Modified Symptom Severity Index (Mod-SSI)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: “Selection bias was considered through a defined and concealed randomization process with rather and subject blind of group assignment. Patients were randomly assigned into one of the three experimental groups…”
Allocation concealment (selection bias)	Unclear risk	Quote: “…concealed…” (s. random sequence generation)
Blinding of participants and personnel (performance bias)	Low risk	Participant but not personnel blind. Incomplete blinding, but outcome is not likely to be influenced by this lack Quote: “…subject blind of group assignment…” “Splint installation, adjustment and follow-up were carried out by a researcher who knew to which group the patients belonged.”
Blinding of outcome assessment (detection bias)	Low risk	Quote: ”Another ‘blind’ researcher collected the data.”
Incomplete outcome data (attrition bias)	Low risk	Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Carlson 2001

Methods	RCT. Single center; two parallel groups. Follow-up for 26 weeks.
Participants	44 (out of 56) participants: mean age analysed sample=34.6; 77.27% women; average months of pain duration=52.3. Inclusion criteria: myofascial pain (group Ia and group Ib) according to the RDC/TMD: chief complaint originating from the masticatory muscles; pain for longer than 1 month; pain to palpation of at least 3 standard muscle sites. Initial medication usage was not altered during the study. Location: USA

Interventions	Group A (n=21 [13 completers]): standard dental care (stabilization splint, nocturnal wearing + self-care strategies [e.g. soft diet, jaw relaxing]) Group B (n=23 [19 completers]): two 50min. sessions of physical self-regulation (strategies for seven domains: monitoring and reducing muscle parafunction in the head and neck region, proprioceptive awareness training to improve symmetric head and neck posture, instructions for improving sleep onset, position oriented relaxation training, physical activity, nutrition/fluid management, and diaphragmatic breathing training)
Outcomes	Life interference (MPI) Pain severity (MPI) Pain intensity (VAS) Ability to control pain Somatization (SCL-90-R) Depression (SCL-90-R) Anxiety (SCL-90-R) Affective distress (SCL-90-R) Unassisted jaw opening without pain (mm) Unassisted jaw opening with pain (mm) Muscle Pain Index (17 sites) Sleep quality (Pittsburgh) Awareness of tooth contact (min) Obsessive/compulsive (SCL-90-R) Fatigue (0-10)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Random assignment was accomplished by the use of a table of random numbers.”
Allocation concealment (selection bias)	Unclear risk	Not reported in the article From correspondence: “The evaluators and the professionals delivering the treatment were not a part of the assignment procedures but the table was open for the researchers to review.”
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “A board-certified dentist with postdoctoral training in orofacial pain who was not aware of the treatment protocol to which each participant was assigned performed all initial dental evaluations and administered the self-report measures after the dental evaluations."
Incomplete outcome data (attrition bias)	Low risk	Detailed explanations for withdrawals. Missing outcome data balanced, and reasons unlikely to be related to true outcome. From correspondence: “26 weeks-analysis included only the completers”

		"As treated" analysis in a recall of the patients
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Conti 2012

Methods	RCT. Single center, three parallel groups. Follow-up for 3 months.
Participants	51 participants: mean age 37.16yrs; 88.23% women. Inclusion criteria: adults aged 18 yrs. or more; diagnosis of myofascial pain with or without opening limitation (RDC/TMD); pain intensity of at least 50mm in VAS. Exclusion criteria: dental pain or tender muscles due to systematic diseases; major psychological disorders; recent history of face and neck trauma; current TMD treatment; denture wearers. Location: Brazil
Interventions	Group A (n=21): Stabilization appliance only nocturnal wearing + self-care strategies (relaxation techniques, diet modification, thermotherapy, massage in the painful area) and counseling (habits and behavioral changes + education). Group B (n= 16): NTI appliance + counseling and self-care strategies + education. Group C (n=14): counseling and self-care strategies only
Outcomes	Pain intensity (VAS) Pressure Pain Threshold (PPT) Number of occlusal contacts
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote:"…patients were randomly allocated" From correspondence:"Randomization was done using a computer program (Excel)"
Allocation concealment (selection bias)	Unclear risk	not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	The same blinded examiner conducted the follow-up Quote: "using a "blind" design with no awareness of the individuals group"
Incomplete outcome data (attrition bias)	Unclear risk	Insufficient report of attrition
Selective reporting (reporting bias)	High risk	Not all the primary outcomes were appropriately reported
Other bias	Low risk	Free of other bias

Crockett 1986

Methods	RCT. Single center, three parallel groups. Post-treatment evaluation
Participants	21(out of 33) participants: 100% women Inclusion criteria: complaint of pain with chronicity of at least 6 months; tenderness to palpation of masticatory muscles; limitation or deviation of jaw mobility; absence of radiographic evidence of joint pathology (disease or trauma); 19 years or older; local language skills. Exclusion criteria: major complaint related to joint tenderness, or associated with an organic condition Location: Canada
Interventions	Group A: dental program (occlusal splint + weekly physiotherapy sessions with hot/cold applications, and postural corrections and jaw exercises + recommendations (avoidance of chewy foods) Group B: biofeedback-enhanced progressive relaxation program (progressive muscle relaxation training program + EMGbiofeedback + home-practice exercises) Group C: Transcutaneous Electrical Nerve Stimulation (weekly 30-minutes sessions of TENS)
Outcomes	Pain to palpation (0-4) Worst pain (0-4) Subjective pain (McGill Pain Questionnaire) Weekly pain intensity (average daily pain over 3 weeks) Frequency of pain EMG Treatment expectancy Perception of therapist qualities Interincisal opening (mm)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were randomly assigned..."
Allocation concealment (selection bias)	Unclear risk	Not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Unclear risk	Not addressed
Incomplete outcome data (attrition bias)	Low risk	Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	All expected outcomes were included
Other bias	Low risk	Free of other bias

Dworkin 1994

Methods	RCT. Multicenter, two parallel groups. Follow up for 12 months.
Participants	139 (out of 185) participants: mean age 37±10.3years; 85% women; 96% Caucasian. 81% completed more than high school education. Inclusion criteria: referral for treatment of TMD with a self-report of facial ache or pain in the muscles of mastication, the TMJ, the region in front of the ear or inside the ear, other than infection. Exclusion criteria: pain attributable to confirmed migraine or head pain condition other than tension headache; acute infection or other significant disease of the teeth, ear, eye, nose or throat; or history of significant or debilitating chronic physical or mental illness; and patients requiring emergency TMD treatment Location: USA
Interventions	Group A (n=66): 2 sessions CBT in small group format (mode=4, range 2-7)(education, biobehavioral management of TMD, self-monitor TMD signs and symptoms, stress coping, introduction to CBT, progressive relaxation method, jaw muscles) preceding usual treatment. Group B (n=73): usual treatment (conservative treatment, splint, NSAIDs, passive and active jaw motion exercises, modification of parafunctional and/or dietary habits, and regular use of cold and heat packs)
Outcomes	Characteristic pain Intensity (CPI) Graded Chronic Pain Scale (GCPS) Pain interference score (0-10) Somatization (SCL-90-R) Depression (SCL-90-R) Helpfulness of treatment (0-10) Unassisted jaw opening without pain (mm) Maximum assisted opening (mm)
Notes	Two additional reports for same study were published: Turner 1995 described predictors in a stepwise regression, and Whitney 1997 analysed the randomization strategy

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomization schedule
Allocation concealment (selection bias)	Low risk	Comments: research team use standardized protocol (s. Dworkin 2002a)
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Unclear risk	Quote: "…by dental hygienist examiners blind to the subject's original random assignment"
Incomplete outcome data (attrition bias)	Low risk	Quote: "All subjects who dropped out from the study prior to completion of the 12-month follow-up were asked to complete an abbreviated questionnaire inquiring into the status of their pain and jaw function in order to allow intent to treat analyses of all subjects"

Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Low risk	Free of other bias

Dworkin 2002a

Methods	RCT. Single center; two parallel groups. Treatment for 4 months, follow-up for 12 months.
Participants	117 patients: mean age 38.8 (SD=10); mean age group A= 38.6 (SE=1.3), mean age group B=39.3 (SE=1.4); 82,91% women; education level higher than high school 72.65% Inclusion criteria: age 18-70 yrs.; facial pain in the masticatory muscles, TMJ, region in front of the ear or inside the ear; RDC/TMD Axis II GCP score of II High, III, or IV. Exclusion criteria: pain attributable to confirmed migraine or head pain condition other than tension headache; acute infection or other significant disease of the teeth, ears, eyes, nose, or throat; debilitating physical or mental illness; necessity for emergency TMD treatment; no local language skills Location: USA
Interventions	Group A (n=59 [56 completers]): comprehensive care ("usual treatment" + cognitive behavioral therapy (CBT) and methods employed in multidisciplinary management of chronic pain including exercises for jaw stretching and jaw muscle relaxation) Group B (n=58 [51 completers]): "usual treatment" (at the discretion of the attending dentist: intraoral occlusal appliance + physiotherapy + medication + patient education including self-care behaviors)
Outcomes	Characteristic pain Intensity (CPI) Pain interference score (0-10) Ability to control pain (0-6) Somatization (SCL-90-R) Depression (SCL-90-R) Helpfulness of treatment Satisfaction with treatment Unassisted jaw opening without pain (mm) Unassisted jaw opening with pain (mm) Maximum assisted opening (mm) Number of muscle sites tender to palpation (16extraoral +4intraoral sites)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...117 (62.9%) agreed to participate and were assigned randomly to... (one of the two groups)" From correspondence: according to a coauthor, the standard method for this research team corresponds to the blocked randomization using different block sizes.

Allocation concealment (selection bias)	Low risk	Not reported in the article. From correspondence: according to a coauthor, the standard method of randomization includes the concealment of the allocation to the personnel until start the trial.
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but the outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “All clinical baseline and follow-up study data collection were performed by calibrated and reliable clinical examiners not participating in the RCT and blinded to the study group to which patients were assigned."
Incomplete outcome data (attrition bias)	Low risk	ITT analysis without imputations. From correspondence: “We did not do any imputation” Comparison of study completers and dropouts was conducted.
Selective reporting (reporting bias)	Unclear risk	The number of participants for each outcome is not clear. Quote: “…there are small differences in numbers of patients across some analyses“
Other bias	Low risk	Free of other bias

Dworkin 2002b

Methods	RCT. Single center; two parallel groups. Treatment for 2.5 months, follow-up for 12 months.
Participants	124 patients: mean age 37.5 (SE=1.09) [mean age group A= 37.4 (SE=4.2), mean age group B= 38.0 (SE=3.6)]; 84.68% women; education level higher than high school group A=91.8%, education level higher than high school group B=66.7% (groups differed significantly). Inclusion criteria: age 18-70 yrs.; self-report of pain in the masticatory muscles, TMJ, region in front of the ear or inside the ear, or report of stiffness or other symptoms of discomfort in the same orofacial region; RDC/TMD Axis II GCP score of 0, I or II-Low Exclusion criteria: pain attributable to confirmed migraine or head pain condition other than tension headache; acute infection or other significant disease of the teeth, ears, eyes, nose, or throat; presence of significant or debilitating chronic physical or mental illness; necessity for emergency TMD treatment. Location: USA
Interventions	Group A (n=61): self-care intervention (manual-based individual 3 session of self-care including cognitive-behavioral methods) Group B (n=63): “usual treatment” (at discretion of the attending dentist: physiotherapy, medications, occlusal appliance, and patient education including a printed version of the instructions for the self-care strategies)
Outcomes	Characteristic pain Intensity (CPI) Graded Chronic Pain Scale (GCPS) Somatization (SCL-90-R) Depression (SCL-90-R) Helpfulness of treatment (0-10) Satisfaction with treatment (0-5) Unassisted jaw opening without pain (mm)

	Unassisted jaw opening with pain (mm) Maximum assisted opening (mm) Number of muscle sites tender to palpation (0-16) Increase of knowledge (0-10)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The standard methods used in this study for randomizing…” From correspondence: according to a coauthor, the “standard method” for this research team corresponds to the blocked randomization using different block sizes.
Allocation concealment (selection bias)	Low risk	Not reported in article. From correspondence: according to a coauthor, the standard method of randomization includes the concealment of the allocation to the personnel until start the trial.
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “All clinical baseline and follow-up study data collection were performed by calibrated and reliable clinical examiners not participating in the RCT and blinded to the study group to which patients were assigned."
Incomplete outcome data (attrition bias)	Low risk	Quote: “ …only the results of intent-to-treat analyses are reported." Analysis of non completers
Selective reporting (reporting bias)	Unclear risk	All expected outcomes were reported. Quote: “All analyses present results for patients for whom data are available although there are small differences in numbers of patients across some analyses” Comment: not possible to define the mentioned differences
Other bias	Low risk	Free of other bias

Ferrando 2012

Methods	RCT. Single center, two parallel groups. Follow-up for 3 months.
Participants	59 (out of 72) participants: mean age 38.98; 88.14% women Inclusion criteria: Myofascial pain diagnosis (RDC/TMD), intellectual ability to follow the evaluation process and psychologic intervention Exclusion criteria:Facial deformities, tumor or lesions of the oral mucosa; medical records of psychotic disorders Location: Spain

Usual treatment vs psychosocial intervention for TMD

Interventions	Group A (n=30): 6 1-hour session of CBT for chronic pain syndromes (psychoeducation, distraction, imagination techniques, assertiveness training, cognitive restructuring, activity planning, functional analysis of pain and modification to the contingencies, and hypnosis techniques) over 2.5 months + standard conservative therapy Group B (n=29): standard conservative therapy (splint, jaw exercises, NSAIDs and/or muscle relaxants). This intervention was neither uniform nor monitored, although patients were asked for accomplishment (50% experimental group, and 49% control group)
Outcomes	Pain intensity [Graded Chronic Pain Scale] (confirmed by author) Pain interference (MPI) Pain severity (MPI) Somatization (BS-18) Depression (BS-18) Anxiety (BS-18) Number of muscle sites tender to palpation (16extraoral +4intraoral sites) Pain frequency (n°days) Self-medication frequency (n°days) Subjective Pain (McGill Questionnaire) Emotional Distress(BS-18)
Notes	Post-treatment was evaluated 3 months after treatment, and follow-up was evaluated 9 months after post-treatment only in the experimental group Standard treatment is an imbalance intervention.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	External statistical program assigned a number
Allocation concealment (selection bias)	Low risk	s. sequence generation
Blinding of participants and personnel (performance bias)	Low risk	“(psychologists and practitioners) They were all blind”
Blinding of outcome assessment (detection bias)	Low risk	“the process of blind assessment…”
Incomplete outcome data (attrition bias)	Low risk	No ITT analysis, but analysis between drop outs and participants was done. Imputation of data:” To the initial value for the patient in the variable, the average change score of that variable for its group was added”
Selective reporting (reporting bias)	Low risk	All expected outcomes were reported
Other bias	Low risk	Free of other bias

Litt 2010

Methods	RCT. Single center; two parallel groups. 6 weeks treatment, follow-up for 12 months.
Participants	101 patients: mean age 39.4 (SD=12.1); 84.16% women; years of education=14.7 (SD=2.5); 79% Caucasian, 9% African-American, 9% Hispanic, 3% self-described as other; average duration of pain 6.7 (SD=6.6); mean pain intensity 3.5 on a scale to 6 (SD=1.3) Inclusion criteria: pain in TM area for at least 3 months, positive axis I diagnosis on RDC/TMD. Exclusion criteria: contraindication to TMD treatment; history of TMJ surgery; extensive anatomical destruction or deterioration of the TMJ; rheumatoid disease; neuropathic or odontogenic pain; psychosis; current use of antidepressants, anxiolytics or opioid pain medication; pregnancy; no local language skills. Location: USA
Interventions	Group A (n=49): standard treatment group (STD)(splint 4 weeks continuously and later only a night guard +soft diet+ naproxen sodium 550mg p.o. BID during 5 weeks, alternatively extra strength acetaminophen in case of gastric ulcer disease) Group B (n=52): STD+ cognitive-behavioral treatment (rationale for treatment + relaxation training and self-efficacy enhancement + masseter EMG biofeedback assisted relaxation + habit modification + combating negative thoughts and catastrophization + stress management)
Outcomes	Pain interference score (MPI) Pain severity (MPI) Coping (Pain Related Self-Statements, PRSS)(Miller Behavioral Style Scale, MBSS) Somatization (SCL90-R) Depression (CESD Depression score) Catastrophizing (PRSS) Readiness (Pain Stages of Change Questionnaire, PSCQ) Self efficacy (Chronic Pain Self-Efficacy Scale, CPSS)
Notes	Principal data from the study by *Litt* (2010). The report published in 2009 [343] refers to a subset of the sample.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "(groups were randomized)... using a computerized urn randomization procedure"
Allocation concealment (selection bias)	Low risk	Not reported Comment: high unpredictability for urn design
Blinding of participants and personnel (performance bias)	Low risk	No blinding, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding

Blinding of outcome assessment (detection bias)	Unclear risk	Long-term data were obtained by in-person interviews (not blinded assessor). The authors stated low influence on the outcomes: "The failure to detect between-condition differences on two of the three dependent variables, however, would suggest that experimenter bias was not operating to influence reporting of outcomes."
Incomplete outcome data (attrition bias)	Low risk	ITT analysis. Reasons for missing outcome data unlikely to be related to true outcome. From correspondence: “There were no differences in reasons by treatment condition.” The groups were balanced in numbers.
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Niemela 2012

Methods	RCT. Single center, two parallel groups. Follow-up for 1 month.
Participants	76 (out of 80) participants: mean age 43.65, 77.5% women Inclusion criteria: clinically diagnosed TMD as defined by the RDC/TMD; at least 20 years of age, and lack of general diseases (like rheumatoid arthritis) that may affect masticatory muscles or TMJs
Interventions	Group A (n=39): stabilization splint, counseling and masticatory muscle exercises Group B (n=37): counselling and instructions for masticatory muscle exercises
Outcomes	Pain intensity (VAS) Unassisted jaw opening without pain (mm) Number of muscle sites tender to palpation (20) TMJ pain (%) Laterotrusion, and Protrusion movements (mm)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“using computer generated random number to two groups”
Allocation concealment (selection bias)	Unclear risk	not addressed
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. Outcomes are not likely to be influenced by this lack.
Blinding of outcome assessment (detection bias)	Low risk	Quote: "...clinical examinations were conducted by the same dentist specialised in stomatognathic physiology (KS) who was unaware of the group status of the patients."

Incomplete outcome data (attrition bias)	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Low risk	Free of other bias

Truelove 2006

Methods	RCT. Single center; three parallel groups. Follow-up for 12 months.
Participants	200 patients: mean age=35.67 ; 86% women; 75.5% education more than high school; 8.5% race Nonwhite; mean number of yrs. with facial pain=5.33; Income $50,000 or greater 34.67% Inclusion criteria: age 18-60 yrs.; RDC/TMD Axis I diagnosis of myofascial pain (Group Ia or Ib) with or without a concurrent diagnosis of arthralgia (Group IIIa) or disk displacement with reduction (Group IIa), as well as a RDC/TMD Axis II Graded Chronic Pain score of Grade I (low pain) or Grade II (high pain), both of which had no or minimal pain-related psychosocial interference. Exclusion criteria: any other RDC/TMD Axis I diagnosis (for example, arthritis, disk displacement without reduction); any systemic arthritis or other serious medical complications, full dentures; major psychological disorders; current satisfactory use of splint; no local language skills Location: USA
Interventions	Group A (n=64): self-care strategies (jaw relaxation, reduction of parafunction, thermal packs, NSAIDs, passive opening stretches and suggestions about stress reduction) Group B (n=68) self-care strategies + hard splint in centric occlusion nocturnal wearing and two additional hours daily while awake throughout the three-month and twelve-month follow-up Group C (n=68) self-care strategies + soft splint in centric occlusion, nocturnal wearing and two additional hours daily while awake throughout the three-month and twelve-month follow-up
Outcomes	Characteristic pain Intensity (CPI) Unassisted jaw opening without pain (mm) Maximum assisted opening (mm) Number of muscle sites tender to palpation (16+4) TMJ pain (0-4) Pain frequency (hours) Pain/limitations during chewing (%) TMJ sounds/locking (%) Tinnitus (%) Jaw clenching (%)
Notes	The authors defined the intervention of self-care strategies as "usual treatment". To avoid confusion with the term used in this review, we named this intervention as self-care strategies.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “We generated randomization assignments using randomly selected block sizes of six, nine or 12 and stratified them by provider.”
Allocation concealment (selection bias)	Low risk	Quote: “We concealed randomization to all study personnel until after we obtained the subjects’ consent“
Blinding of participants and personnel (performance bias)	Low risk	No possible blinding. The outcomes are not likely to be influenced by this lack
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The research dental hygienists conducting follow-up data collection were blinded to subject treatment group“
Incomplete outcome data (attrition bias)	Low risk	Quote: “…we took a conservative approach of carrying forward the last observation if the subject dropped out before month 12.” Intent-to-treat analysis. Attritions reported and analyzed
Selective reporting (reporting bias)	Low risk	Include all expected outcomes
Other bias	Low risk	Free of other bias

Turner 2006

Methods	RCT. Single center; two parallel groups. Follow-up for 12 months.
Participants	158 patients (148 analysed): mean age original sample=37.0 (±11.4), mean age group A=38.9 (±11.6); mean age group B=35.7 (±10.9); 86.49% women; 21.62% high school or less, 41.22% some college or vocational/technical, 37,16% college graduate Inclusion criteria: age 18 yrs or older; RDC/TMD Axis I TMD diagnosis; facial pain for at least three months; GCPS II high, III or IV; local language skills; residence within a 2-h drive of the clinic. Exclusion criteria: need for further diagnostic evaluation; pending litigation or disability compensation for pain; current or previous CBT for pain; major medical or psychiatric conditions. Location: USA
Interventions	Group A (n=72 [79]): pain management training (standard CBT for pain and chronic TMD pain, including breathing, relaxation, fear-avoidance, and relapse prevention techniques) + “usual treatment” according to dentist prescription (intraoral occlusal appliance + jaw stretching exercises + patient education + medication) Group B (n=76 [79]): self-care management (“usual treatment” according to dentist prescription, TMD education and general health education, excluding CBT)
Outcomes	GCPS, GPI, activity interference Mandibular Function Impairment Questionnarie (MFIQ) (17-item) 21-Item Beck Depression Inventory (BDI)Survey of Pain Attitudes (SOPA): Disability, Harm and Control TMD Self-Efficacy Scale (SES)(8-item) CSQ Catastrophizing scale, and four-item Rumination subscale of the Pain Catastrophizing Scale (PCS) Four scales from the Chronic Pain Coping Inventory (CPCI): Rest, Task

	Persistance, Coping Self-Statements, and Relaxation Treatment credibility adapted to TMD treatment TMD knowledge Treatment helpfulness and credibility
Notes	The data are collected principally from the article by *Turner et al. 2006* [578] which reports the results at short- and long-term of the RCT. The articles by *Wig et al. 2004* [607], by *Turner, Mancl & Aaron 2005* [575] (electronic diaries during treatment) , by *Aaron et al.* [2] (electronic diaries prior to intervention) seem to be a subsample of the principal study. The article by *Turner, Brister et al.2005* [576] is an epidemiological report of a combined sample from this study and other RCT. Finally, in the article by *Turner et al.2007* [577] a subset of the sample was compared to a new extra group of participants.

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Blocked randomization was stratified by CPG and gender Quote: "Randomization assignments were generated by a biostatistician (LM) using randomly selected block sizes of two or four…"
Allocation concealment (selection bias)	Low risk	Quote: "Treatment assignments were recorded on slips of paper numbered consecutively within each stratum and sealed in envelopes sequentially numbered by stratum. Randomization assignment was concealed to all study personnel until envelopes were opened by research staff after subject consent was obtained."
Blinding of participants and personnel (performance bias)	Low risk	No blinding. The outcomes are not likely to be influenced by this lack
Blinding of outcome assessment (detection bias)	Low risk	Quote: "Participants were asked to complete questionnaires at home and return them in person or by mail…"
Incomplete outcome data (attrition bias)	Low risk	ITT analyses, attrition and exclusions reported and analyzed. Detailed report for imputations
Selective reporting (reporting bias)	Low risk	Include all expected outcomes. High consistency between the different reports.
Other bias	Low risk	Free of other bias

Footnotes

Characteristics of excluded studies

Cunha 2012

Reason for exclusion	Sample did not include myogenous TMD patients

Gatchel 2006

Reason for exclusion	Patients acute symptoms of TMD (symptoms less than 6 months)

Glaros 2007

Reason for exclusion	Intervention with splint did not include counseling or self-care strategies

Michelotti 2012

Reason for exclusion	Intervention with splint did not include counseling

Minakuchi 2004

Reason for exclusion	Sample did not include myogenous TMD patients

Schiffman 2007

Reason for exclusion	Sample did not include myogenous TMD patients

Shedden Mora 2012

Reason for exclusion	Subsample of study awaiting classification

Stowell 2007

Reason for exclusion	Patients acute symptoms of TMD (symptoms less than 6 months). Second report of Gatchel 2006.

Turk 1996

Reason for exclusion	Other intervention. Both evaluated groups received EMG-Biofeedback, thus to the "usual treatment" intervention was added EMG-biofeedback resulting in a different intervention.

Winocur 2002

Reason for exclusion	Not randomized

Wright 1995

Reason for exclusion	Other intervention (soft splint only vs. palliative care)

Footnotes

Characteristics of studies awaiting classification

Huggins2004-Truelove 2004a

Methods	RCT. Single center, three parallel groups. Follow up for 24 months.
Participants	272 participants: TMD patients
Interventions	Group A (n=91): Usual treatment (UT) Group B (n=93): UT+ Self-care Group C (n=88): UT+ Self-care + case manager

Outcomes	Characteristic pain Intensity (CPI) Pain interference score (0-10) Satisfaction with treatment (0-10) Unassisted jaw opening without pain (mm) Number of muscle sites tender to palpation (16+4) TMJ symptoms (0-16) Worry over TMD condition (0-10) Mandibular function (MFQ)
Notes	Only abstracts. Authors work on article

Shedden Mora 2010

Methods	RCT. Single center, two parallel groups. Preliminary report
Participants	26 participants: mean age group A=37.1 (14.4), mean age group B=35.9(13.7); 78.45% women;mean of pain duration group A=44.9(51.5) months, mean of pain duration group B= 48.4 (62.2) months; 80.55% completed high school Inclusion criteria: Age 18-70, diagnosis of myofascial pain with or without TMJ pain, according to RDC/TMD; symptoms at least 3 months; local language skills. Exclusion criteria: Unsuccessful splint treatment during the last 3 months, indication for treatment of disc derangement or arthralgia (diagnosis group II or III according to RDC/TMD), presence of other pain condition of predominantly severity, psychotic disorder, alcohol or substance abuse. Location: Germany
Interventions	Group A (n=15): 8 sessions Biofeedback-Based Cognitive Behavioral Treatment (individual sessions, each containing both cognitive behavioral and biofeedback elements. Treatment elements are education about the disorder, biofeedback training aimed at improving proprioceptive awareness and reversing parafunctional habits, relaxation techniques, and stress management. Furthermore patients receive portable biofeedback devices for EMG-biofeedback training during day and nighttime in order to reverse diurnal and nocturnal bruxing habits). Group B (n=11): Interocclusal splint therapy (Maxillary or mandibular occlusal splints are made of hard acrylic, daily and nocturnal wearing for 7 weeks. One week after initial insertion of the splint patients are requested to return for adjustment)
Outcomes	Characteristic pain Intensity (CPI) Pain interference score Somatization (SOMS-7) Depression (ADS-L) Satisfaction with treatment (0-5) Mandibular function (jaw disability index)
Notes	In a second report, EMG data of a subsample from this RCT were compared to healthy subjects (*Shedden Mora 2012*). According to the authors, the complete results from the RCT will be available in a future publication.

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

Alencar 2009

Alencar Jr F, Becker A. Evaluation of different occlusal splints and counselling in the management of myofascial pain dysfunction. J Oral Rehabil 2009;36(2):79-85.

Carlson 2001

Carlson CR, Bertrand PM, Ehrlich AD, Maxwell AW, Burton RG. Physical self-regulation training for the management of temporomandibular disorders. J Orofac Pain 2001;15(1):47-55.

Conti 2012

Published and unpublished data

Conti PCR, Alencar ENde, Da Mota Correa A S, Lauris JRP, Porporatti AL, Costa YM. Behavioural changes and occlusal splints are effective in the management of masticatory myofascial pain: a short-term evaluation. J Oral Rehabil 2012;39(10):754-60.

Crockett 1986

Crockett DJ, Foreman ME, Alden L, Blasberg B. A comparison of treatment modes in the management of myofascial pain dysfunction syndrome. Biofeedback Self Regul 1986;11(4):279-91.

Dworkin 1994

Dworkin SF, Turner JA, Wilson L, Massoth D, Whitney C, Huggins KH, Burgess J, Sommers E, Truelove EL. Brief group cognitive-behavioral intervention for temporo- mandibular disorders. Pain 1994;59:175-87.

Dworkin 2002a

Dworkin SF, Turner JA, Mancl L, Wilson L, Massoth D, Huggins KH, LeResche L, Truelove E. A randomized clinical trial of a tailored comprehensive care treatment program for temporomandibular disorders. J Orofac Pain 2002;16(4):259-76.

Dworkin 2002b

Dworkin SF, Huggins KH, Wilson L, Mancl L, Turner J, Massoth D, LeResche L, Truelove E. A randomized clinical trial using research diagnostic criteria for temporomandibular disorders-axis II to target clinic cases for a tailored self-care TMD treatment program. J Orofac Pain 2002;16(1):48-63.

Ferrando 2012

Ferrando M, Galdón MJ, Durá E, Andreu Y, Jiménez Y, Poveda R. Enhancing the efficacy of treatment for temporomandibular patients with muscular diagnosis through cognitive-behavioral intervention, including hypnosis: a randomized study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2012;113(1):81-9.

Litt 2010

Litt MD, Shafer DM, Kreutzer DL. Brief cognitive-behavioral treatment for TMD pain: Long-term outcomes and moderators of treatment. Pain 2010;151(1):110-6.

Niemela 2012

Niemela K, Korpela M, Raustia A, Ylostalo P, Sipila K. Efficacy of stabilisation splint treatment on temporomandibular disorders. J Oral Rehabil 2012;39(11):799-804.

Truelove 2006

Truelove E, Huggins KH, Mancl L, Dworkin SF. The efficacy of traditional, low-cost and nonsplint therapies for temporomandibular disorder: a randomized controlled trial. J Am Dent Assoc 2006;137(8):1099-107.

Turner 2006

Turner JA, Mancl L, Aaron LA. Short- and long-term efficacy of brief cognitive-behavioral therapy for patients with chronic temporomandibular disorder pain: A randomized, controlled trial. Pain 2006;121(3):181-194.

Excluded studies

Cunha 2012

Cunha CO, Correa AS, Pinto LM, Alencar EN, Bonjardim LR, Conti PC. Repositioning occlusal splints and NTI-tss in Temporomandibular Joint arthralgia. IADR Abstracts General Session 2012 2012;Abstract #2222.

Gatchel 2006

Gatchel RJ, Stowell AW, Wildenstein L, Riggs R, Ellis E. Efficacy of an early intervention for patients with acute temporomandibular disorder-related pain: a one-year outcome study. J Am Dent Assoc 2006;137(3):339-47.

Glaros 2007

Glaros AG, Kim-Weroha N, Lausten LF, Kelly L. Comparison of Habit Reversal and a Behaviorally-Modified Dental Treatment for Temporomandibular Disorders: A Pilot Investigation. Appl Psychophysiol Biofeedback 2007;32(3-4):149-54.

Michelotti 2012

Michelotti A, Iodice G, Vollaro S, Steenks MH, Farella M. Evaluation of the short-term effectiveness of education versus an occlusal splint for the treatment of myofascial pain of the jaw muscles. J Am Dent Assoc 2012;143(1):47-53.

Minakuchi 2004

Minakuchi H, Kuboki T, Maekawa K, Matsuka Y, Yatani H. Self-reported remission, difficulty, and satisfaction with nonsurgical therapy used to treat anterior disc displacement without reduction. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics 2004;98(4):435-40.

Schiffman 2007

Schiffman EL,Look JO, Hodges JS, Swift JQ, Decker KL, Hathaway KM, Templeton RB, Fricton JR. Randomized Effectiveness Study of Four Therapeutic Strategies for TMJ Closed Lock. J Dent Res 2007;86(1):58-63.

Shedden Mora 2012

Shedden Mora M, Weber D, Borkowski S, Rief W. Nocturnal masseter muscle activity is related to symptoms and somatization in temporomandibular disorders. J Psychosom Res 2012;73:307-312.

Stowell 2007

Stowell AW, Gatchel RJ, Wildenstein L. Cost-effectiveness of treatments for temporomandibular disorders: biopsychosocial intervention versus treatment as usual. J Am Dent Assoc 2007;138(2):202-8.

Turk 1996

Turk DC, Rudy TE, Kubinski JA, Zaki HS, Greco CM. Dysfunctional patients with temporomandibular disorders: evaluating the efficacy of a tailored treatment protocol. J Consult Clin Psychol 1996;64(1):139-46.

Winocur 2002

Winocur E, Gavish A, Emodi-Perlman A, Halachmi M, Eli I. Hypnorelaxation as treatment for myofascial pain disorder: a comparative study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;93(4):429-34.

Wright 1995

Wright E, Anderson G, Schulte J. A randomized clinical trial of intraoral soft splints and palliative treatment for masticatory muscle pain. J Orofac Pain 1995;9(2):192-9.

Studies awaiting classification

Huggins2004-Truelove 2004a

* Huggins KH, Truelove E, Mancl L, LeResche L, Dworkin SF. RCT for TMD Utilizing Case Manager: Long Term Clinical Findings. IADR Abstracts 82nd General Session 2004 2004;Abstract #0133.

Shedden Mora 2010

Shedden Mora MC, Bleichhardt G, Weber D, Neff A, Rief W. Biofeedback-based cognitive-behavioral treatment for chronic temporomandibular disorders. Preliminary data from a randomized controlled trial [Biofeedback bei kraniomandibulären Dysfunktionen. Vorläufige Wirksamkeit und Akzeptanz eines Biofeedback-gestützten kognitivverhaltenstherapeutischenTherapiekonzepts]. Psychotherapeut 2010;55(3):217-224.

Ongoing studies

Other references

Additional references

Other published versions of this review

Data and analyses

1 "Usual treatment" vs. Psychosocial intervention

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Self-reported pain short-term	7	418	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.18, 0.33]
1.1.1 "Usual treatment" vs. psychosocial intervention	6	329	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.26, 0.36]
1.1.2 "Usual treatment" vs. psychosocial intervention + "usual treatment"	1	89	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.20, 0.64]

1.2 Self-reported pain long-term	3	238	Std. Mean Difference (IV, Random, 95% CI)	0.23 [-0.25, 0.71]
1.2.1 "Usual treatment" vs. psychosocial intervention	2	164	Std. Mean Difference (IV, Random, 95% CI)	0.11 [-0.53, 0.75]
1.2.2 "Usual treatment" vs. psychosocial intervention + "usual treatment"	1	74	Std. Mean Difference (IV, Random, 95% CI)	0.47 [0.01, 0.93]
1.3 Pain interference short-term	2	133	Mean Difference (IV, Random, 95% CI)	0.37 [-0.29, 1.02]
1.3.1 "Usual treatment" vs. psychosocial intervention	1	44	Mean Difference (IV, Random, 95% CI)	0.50 [-0.35, 1.35]
1.3.2 "Usual treatment" vs. psychosocial intervention + "usual treatment"	1	89	Mean Difference (IV, Random, 95% CI)	0.17 [-0.86, 1.20]
1.4 Pain interference long-terr	2	106	Mean Difference (IV, Random, 95% CI)	0.20 [-0.55, 0.95]
1.4.1 "Usual treatment" vs. psychosocial intervention	1	32	Mean Difference (IV, Random, 95% CI)	0.20 [-0.80, 1.20]
1.4.2 "Usual treatment" vs psychosocial intervention + "usual treatment"	1	74	Mean Difference (IV, Random, 95% CI)	0.20 [-0.92, 1.32]
1.5 Muscle Pain short-term	4	280	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.03, 0.44]
1.5.1 "Usual treatment" vs. psychosocial intervention	4	280	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.03, 0.44]
1.6 Muscle Pain long-term	2	164	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.51, 0.39]
1.6.1 "Usual treatment" vs. psychosocial intervention	2	164	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.51, 0.39]
1.7 Unassisted jaw opening without pain short-term	4	266	Mean Difference (IV, Random, 95% CI)	-1.66 [-5.60, 2.28]
1.7.1 "Usual treatment" vs. psychosocial intervention	4	266	Mean Difference (IV, Random, 95% CI)	-1.66 [-5.60, 2.28]
1.8 Unassisted jaw opening without pain long-term	2	164	Mean Difference (IV, Random, 95% CI)	-2.50 [-8.45, 3.45]
1.8.1 "Usual treatment" vs. psychosocial intervention	2	164	Mean Difference (IV, Random, 95% CI)	-2.50 [-8.45, 3.45]
1.9 Somatization short-term	1	44	Mean Difference (IV, Random, 95% CI)	0.23 [-0.03, 0.49]
1.9.1 "Usual treatment" vs. psychosocial intervention	1	44	Mean Difference (IV, Random, 95% CI)	0.23 [-0.03, 0.49]

1.10 Somatization long-term	1	32	Mean Difference (IV, Random, 95% CI)	0.30 [-0.07, 0.67]
1.10.1 "Usual treatment" vs. psychosocial intervention	1	32	Mean Difference (IV, Random, 95% CI)	0.30 [-0.07, 0.67]
1.11 Depression short-term	1	163	Std. Mean Difference (IV, Random, 95% CI)	0.44 [-0.22, 1.09]
1.11.1 "Usual treatment" vs. psychosocial intervention	1	74	Std. Mean Difference (IV, Random, 95% CI)	0.78 [0.31, 1.26]
1.11.2 "Usual treatment" vs psychosocial intervention + "usual treatment"	1	89	Std. Mean Difference (IV, Random, 95% CI)	0.11 [-0.30, 0.53]
1.12 Depression long-term	2	106	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.32, 0.45]
1.12.1 "Usual treatment" vs. psychosocial intervention	1	32	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.59, 0.82]
1.12.2 "Usual treatment" vs psychosocial intervention + "usual treatment"	1	74	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.42, 0.50]

2 Tailored "usual treatment" vs psychosocial intervention

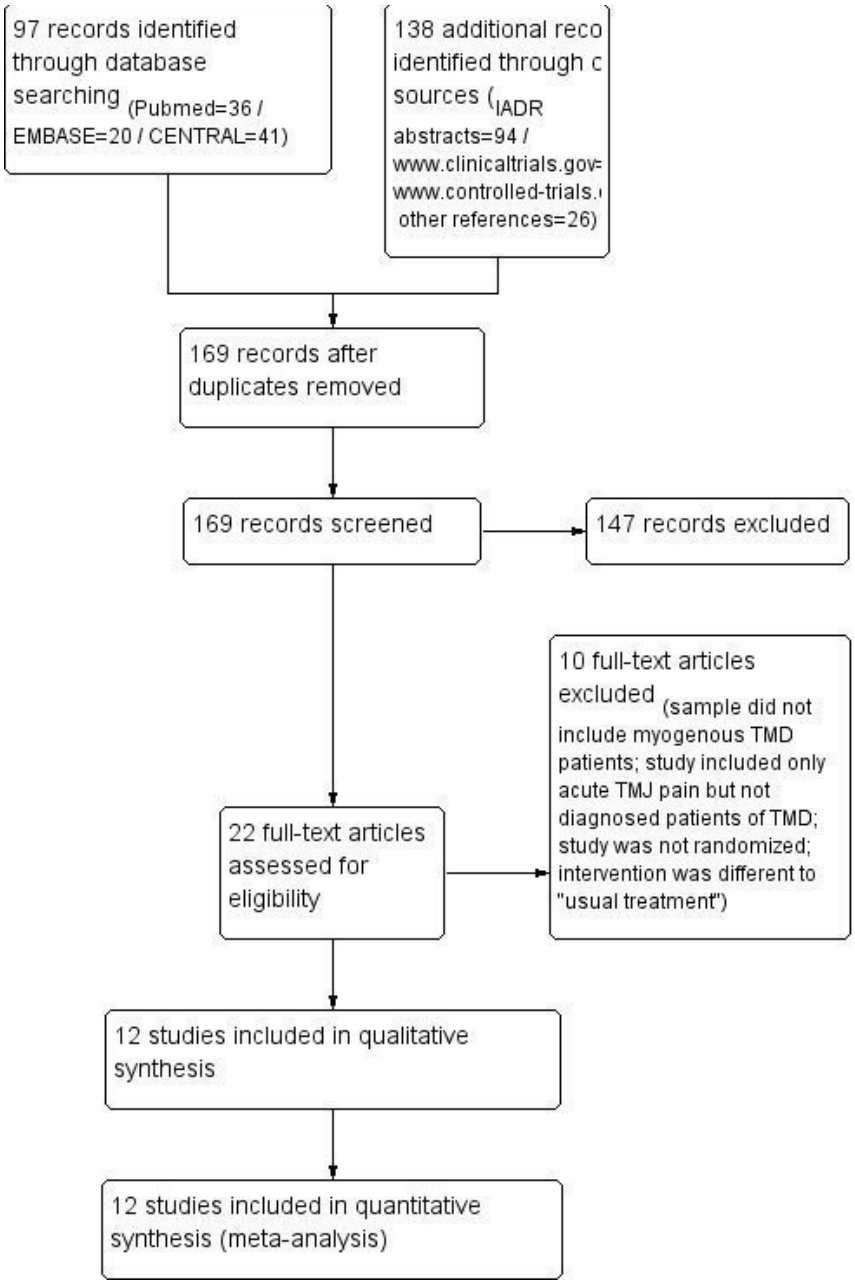
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 Self-reported pain short-term	5	571	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.22, 0.37]
2.1.3 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"	4	447	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.34, 0.50]
2.1.4 Tailored "usual treatment" vs psychosocial intervention	1	124	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.25, 0.46]
2.2 Self-reported pain long-term	4	510	Mean Difference (IV, Random, 95% CI)	0.66 [0.23, 1.09]
2.2.3 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"	3	394	Mean Difference (IV, Random, 95% CI)	0.55 [-0.02, 1.12]
2.2.4 Tailored "usual treatment" vs. psychosocial intervention	1	116	Mean Difference (IV, Random, 95% CI)	0.80 [0.14, 1.46]
2.3 Pain interference short-term	4	423	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.26, 0.30]
2.3.3 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"	3	299	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.26, 0.30]

2.3.4 Tailored "usual treatment" vs. psychosocial intervention	1	124	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
2.4 Pain Interference long-term	3	356	Mean Difference (IV, Random, 95% CI)	0.66 [-0.09, 1.41]
2.4.1 Tailored "usual treatment" vs. psychosocial intervention	1	116	Mean Difference (IV, Random, 95% CI)	Not estimable
2.4.2 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"	2	240	Mean Difference (IV, Random, 95% CI)	0.66 [-0.09, 1.41]
2.5 Muscle Pain upon palpation at long-term	1	107	Mean Difference (IV, Random, 95% CI)	0.30 [-1.66, 2.26]
2.5.1 Tailored "usual treatment" vs psychosocial intervention + "usual treatment"	1	107	Mean Difference (IV, Random, 95% CI)	0.30 [-1.66, 2.26]
2.6 Unassisted jaw opening without pain short-term	2	263	Mean Difference (IV, Random, 95% CI)	Not estimable
2.6.1 Tailored "usual treatment" vs psychosocial intervention + "usual treatment"	1	139	Mean Difference (IV, Random, 95% CI)	Not estimable
2.6.2 Tailored "usual treatment" vs psychosocial intervention	1	124	Mean Difference (IV, Random, 95% CI)	Not estimable
2.7 Unassisted jaw opening without pain long-term	3	362	Mean Difference (IV, Random, 95% CI)	Not estimable
2.7.1 Tailored "usual treatment" vs psychosocial intervention + "usual treatment"	2	246	Mean Difference (IV, Random, 95% CI)	Not estimable
2.7.2 Tailored "usual treatment" vs psychosocial intervention	1	116	Mean Difference (IV, Random, 95% CI)	Not estimable
2.8 Somatization short-term	2	240	Mean Difference (IV, Random, 95% CI)	0.30 [-0.24, 0.84]
2.8.1 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"	2	240	Mean Difference (IV, Random, 95% CI)	0.30 [-0.24, 0.84]
2.9 Somatization long-term	3	362	Mean Difference (IV, Random, 95% CI)	0.13 [-0.46, 0.71]

2.9.2 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"	2	246	Mean Difference (IV, Random, 95% CI)	-0.20 [-0.77, 0.37]
2.9.3 Tailored "usual treatment" vs. psychosocial intervention	1	116	Mean Difference (IV, Random, 95% CI)	0.40 [-0.06, 0.86]
2.10 Depression short-term	3	388	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.03, 0.47]
2.10.1 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"	3	388	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.03, 0.47]
2.11 Depression long-term	4	510	Std. Mean Difference (IV, Random, 95% CI)	0.21 [0.00, 0.41]
2.11.2 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"	3	394	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.05, 0.46]
2.11.3 Tailored "usual treatment" vs. psychosocial intervention	1	116	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.15, 0.58]

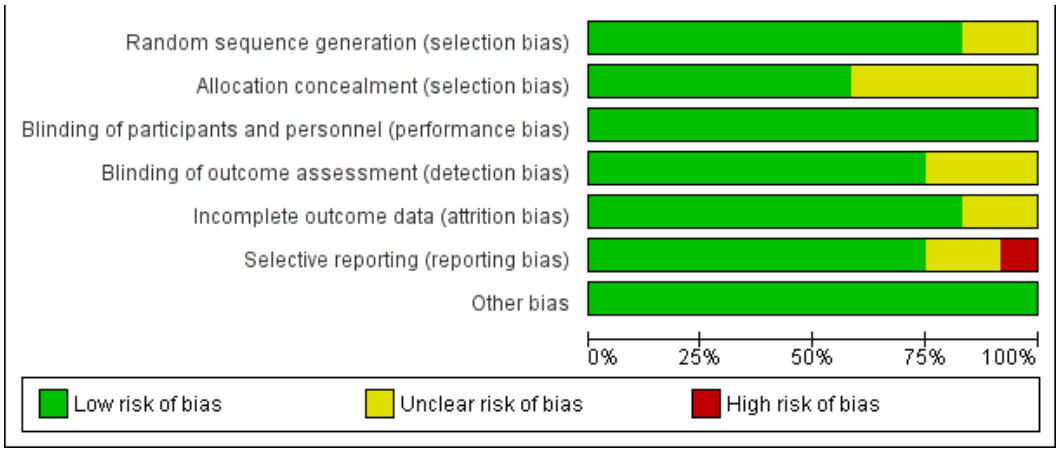
Figures

Figure 1



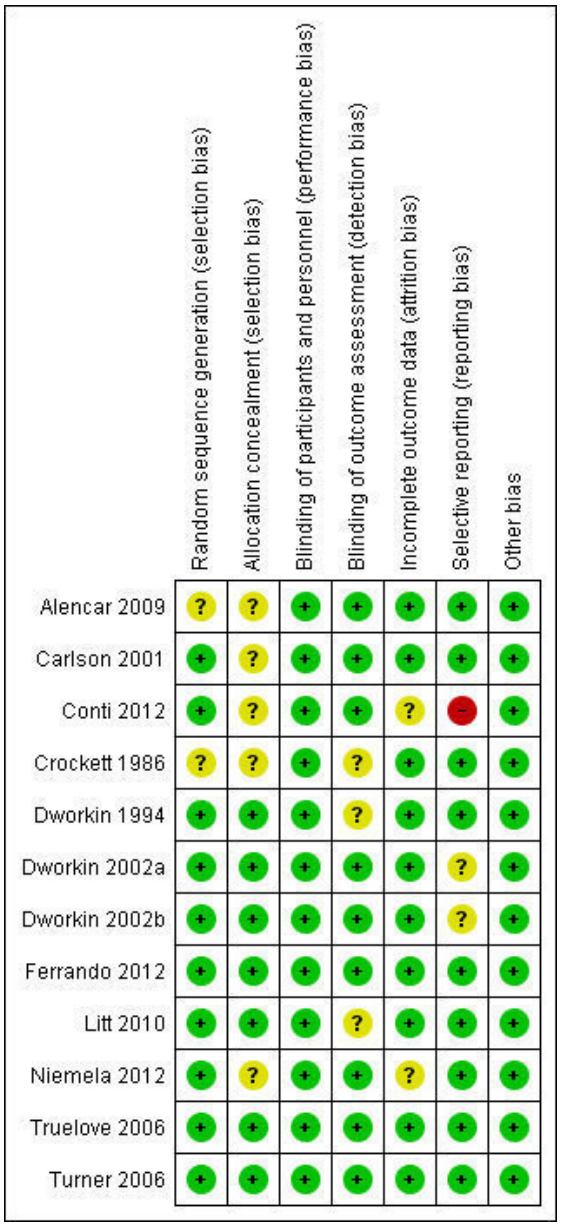
Study flow diagram.

Figure 2



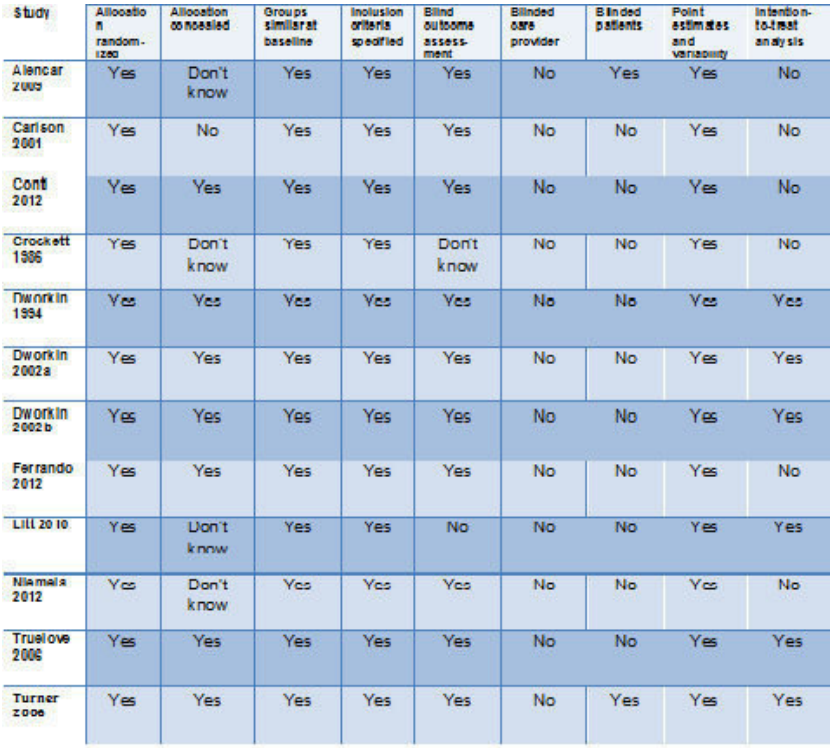
Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3



Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 4



Study	Allocation random-ized	Allocation concealed	Groups similar at baseline	Inclusion criteria specified	Blind outcome assess-ment	Blinded care provider	Blinded patients	Point estimates and variability	Intention-to-treat analysis
Alencar 2009	Yes	Don't know	Yes	Yes	Yes	No	Yes	Yes	No
Carlson 2001	Yes	No	Yes	Yes	Yes	No	No	Yes	No
Conti 2012	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
Crockett 1986	Yes	Don't know	Yes	Yes	Don't know	No	No	Yes	No
Dworkin 1994	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Dworkin 2002a	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Dworkin 2002b	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Ferrando 2012	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
Litt 2010	Yes	Don't know	Yes	Yes	No	No	No	Yes	Yes
Niemala 2012	Yes	Don't know	Yes	Yes	Yes	No	No	Yes	No
Truelove 2006	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Turner 2006	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes

Delphi List: "Usual treatment" vs. Psychosocial Interventions

Appendices

1 MEDLINE via Pubmed search strategy

The search strategy was conducted following the next steps in MEDLINE via PubMed:

Condition:

#1 Myofascial Pain Syndromes [MeSH]

#2 Craniomandibular Disorders [MeSH]

#3 Temporomandibular Joint Dysfunction Syndrome [MeSH]

#4 Temporomandibular Joint Disorders [MeSH]

#5 myofascial [tiab] AND pain [tiab] AND syndrom* [tiab]

#6 myofascial [tiab] AND trigger point [tiab] AND pain [tiab]

#7 craniomandibular [tiab] AND disorder* [tiab]

#8 craniomandibular disease* [tiab]

#9 temporomandibular joint dysfunction syndrome [tiab] OR myofascial pain dysfunction syndrome, temporomandibular joint [tiab]

#10 TMJ [tiab] AND syndrome [tiab]

#11 Costen* [tiab] AND syndrome [tiab]

#12 temporomandibular [tiab] AND joint [tiab] AND syndrome [tiab]

#13 temporomandibular [tiab] AND joint [tiab] AND disorder* [tiab]

#14 TMJ [tiab] AND disorder* [tiab]

#15 temporomandibular [tiab] AND disorder* [tiab]

#16 temporomandibular [tiab] AND joint [tiab] AND disease* [tiab]

#17 TMJ [tiab] AND disease* [tiab]

#18 craniofacial pain [tiab]OR masticatory muscle disorder [tiab] OR masticatory muscle pain [tiab] OR orofacial muscle pain [tiab] OR chronic muscle pain [tiab] OR myofacial pain [tiab]OR myogenous facial pain [tiab]OR myofunctional pain [tiab] OR orofacial myofunctional disorder* [tiab] OR myofunctional disorder [tiab]OR myoarthropat*[tiab]

#19 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18

Intervention A:

#20 occlusal splints [MeSH]

#21 occlusal [tiab] AND splint* [tiab]

#22 oral splint* [tiab] OR oral appliance* [tiab] OR occlusal appliance* [tiab] OR bite splint* [tiab] OR bite plate* [tiab]

#23 stabilization splint* [tiab] OR stabilization splint* [tiab]

#24 standard treatment [tiab] OR usual treatment [tiab] OR standard care [tiab] OR usual care [tiab]

#25 #20 OR #21 OR #22 OR #23 OR #24

Intervention B:

#26 cognitive therapy [MeSH]

#27 hypnosis, dental [MeSH]

#28 self care [MeSH]

#29 counseling [MeSH]

#30 cogniti* [tiab] AND therap* [tiab]

#31 cogniti* [tiab] AND psychotherap* [tiab]

#32 cogniti* [tiab] AND behavio* [tiab] AND therap* [tiab]

#33 dental [tiab] AND hypnos* [tiab]

#34 self [tiab] AND care [tiab]

#35 self-care [tiab] OR self-management [tiab] OR self management [tiab]

#36 CBT [tiab] OR cogniti* biobehavio* therap* [tiab]OR cogniti* behavio* [tiab]

#37 oral habit reversal [tiab] OR hypnos* [tiab]

#38 self-care treatment* [tiab] OR self care treatment* [tiab] OR self-care strateg* [tiab] OR self care strateg* [tiab]

#39 counsel* [tiab]

#40 relaxation training [tiab] OR self-efficacy enhancement [tiab] OR fear-avoidance technique* [tiab] OR hypnorelaxation [tiab]

#41 #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40

#42 #19 AND #25 AND #41

Database entry date

06.11.2012

Limits:

Filters: Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized trials in MEDLINE: sensitivity- maximizing version (2008 revision); PubMed format as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of *The Cochrane Handbook for Systematic Reviews of Interventions,* Version 5.0.2 [updated March 2011].

2 EMBASE Search Strategy

Search details:

Condition:

#1 'myofascial pain'/exp

#2 'temporomandibular joint disorder'/exp

#3 myofascial :ab,ti AND pain :ab,ti AND syndrom*:ab,ti

#4 myofascial :ab,ti AND trigger point :ab,ti AND pain :ab,ti

#5 craniomandibular :ab,ti AND disorder*:ab,ti

#6 craniomandibular disease*:ab,ti

#7 temporomandibular joint dysfunction syndrome :ab,ti OR myofascial pain dysfunction syndrome, temporomandibular joint :ab,ti

#8 TMJ :ab,ti AND syndrome :ab,ti

#9 Costen* :ab,ti AND syndrome :ab,ti

#10 temporomandibular :ab,ti AND joint :ab,ti AND syndrome :ab,ti

#11 temporomandibular :ab,ti AND joint :ab,ti AND disorder* :ab,ti

#12 TMJ :ab,ti AND disorder* :ab,ti

#13 temporomandibular :ab,ti AND disorder* :ab,ti

#14 temporomandibular :ab,ti AND joint :ab,ti AND disease* :ab,ti

#15 TMJ :ab,ti AND disease* :ab,ti

#16 craniofacial pain :ab,tiOR masticatory muscle disorder :ab,ti OR masticatory muscle pain :ab,ti OR orofacial muscle pain :ab,ti OR chronic muscle pain :ab,ti OR myofacial pain :ab,tiOR myogenous facial pain :ab,tiOR myofunctional pain :ab,ti OR orofacial myofunctional disorder* :ab,ti OR myofunctional disorder :ab,tiOR myoarthropat*:ab,ti

#17 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17

Intervention A:

#18 occlusal splint[MeSH]

#19 occlusal:ab,ti AND splint*:ab,ti

#20(oral splint*):ab,ti OR (oral appliance*):ab,ti OR (occlusal appliance*):ab,ti

#21(bite splint*):ab,ti OR (bite plate*):ab,ti

#22(stabilization splint*):ab,ti OR (stabilization splint*):ab,ti

#23(standard treatment):ab,ti OR (usual treatment):ab,ti OR (standard care):ab,ti OR (usual care):ab,ti

#24 #18 OR #19 OR #20 OR #21 OR #22 OR #23

Intervention B:

#26 'cognitive therapy'/exp

#27 'hypnosis'/exp

#28 'self care'/exp

#29 'counseling'/exp

#30 cogniti*:ab,ti AND therap*:ab,ti

#31 cogniti*:ab,ti AND psychotherap*:ab,ti

#32 cogniti*:ab,ti AND behavio*:ab,ti AND therap*:ab,ti

#33 dental:ab,ti AND hypnos*:ab,ti

#34 self:ab,ti AND care:ab,ti

#35 self-care:ab,ti OR self-management:ab,ti OR self managemen:ab,ti

#36 CBT :ab,ti OR cogniti* biobehavio* therap* :ab,tiOR cogniti* behavio* :ab,ti

#37 oral habit reversal :ab,ti OR hypnos* :ab,ti

#38 (self-care treatment*):ab,ti OR (self care treatment*):ab,ti OR (self-care strateg*):ab,ti OR (self care strateg*):ab,ti#39 counsel* :ab,ti

#40 (relaxation training):ab,ti OR (self-efficacy enhancement):ab,ti OR (fear-avoidance technique*):ab,ti OR (hypnorelaxation):ab,ti

#41 #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40

#42 #17 AND 24# AND 41

#43 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'randomized controlled trial'/exp OR 'single blind procedure'/exp

#44 random$ OR factorial$ OR crossover$ OR cross AND over$ OR 'cross over$' OR placebo$ OR doubl$ AND adj AND blind$ OR singl$ AND adj AND blind$ OR assign$ OR allocat$ OR volunteer$

#45 #44 OR #44

#46 #42 AND #45

Database entry date:

07.11.2012

3 CENTRAL search strategy

IDSearchHits
#1MeSH descriptor: [Myofascial Pain Syndromes] explode all trees

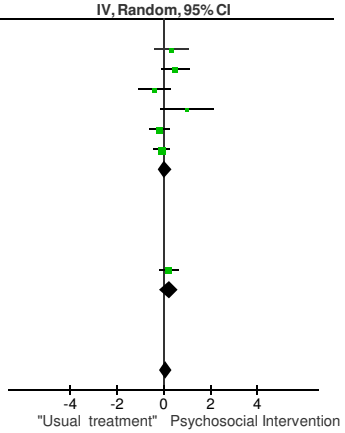
#2MeSH descriptor: [Craniomandibular Disorders] explode all trees
#3MeSH descriptor: [Temporomandibular Joint Dysfunction Syndrome] explode all trees
#4MeSH descriptor: [Temporomandibular Joint Disorders] explode all trees
#5myofascial:ti,ab and pain:ti,ab and syndrom*:ti,ab
#6myofascial:ti,ab and trigger point:ti,ab and pain:ti,ab
#7craniomandibular:ti,ab and disorder*:ti,ab
#8craniomandibular disease*:ti,ab
#9temporomandibular joint dysfunction syndrome:ti,ab or myofascial pain dysfunction syndrome, temporomandibular joint:ti,ab
#10TMJ:ti,ab and syndrome:ti,ab
#11Costen*:ti,ab and syndrome:ti,ab
#12temporomandibular:ti,ab and joint:ti,ab and syndrome:ti,ab
#13temporomandibular:ti,ab and joint:ti,ab and disorder*:ti,ab
#14TMJ:ti,ab and disorder*:ti,ab
#15temporomandibular:ti,ab and disorder*:ti,ab
#16temporomandibular:ti,ab and joint:ti,ab and disease*:ti,ab
#17TMJ:ti,ab and disease*:ti,ab
#18craniofacial pain:ti,ab or masticatory muscle disorder:ti,ab or masticatory muscle pain:ti,ab or orofacial muscle pain:ti,ab or chronic muscle pain:ti,ab or myofacial pain:ti,ab or myogenous facial pain:ti,ab or myofunctional pain:ti,ab or orofacial myofunctional disorder*:ti,ab or myofunctional disorder:ti,ab or myoarthropat*:ti,ab
#19#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18
#20MeSH descriptor: [Occlusal Splints] explode all trees
#21occlusal:ti,ab and splint*:ti,ab
#22oral splint*:ti,ab or oral appliance*:ti,ab or occlusal appliance*:ti,ab or bite splint*:ti,ab or bite plate*:ti,ab
#23stabilization splint*:ti,ab or stabilization splint*:ti,ab
#24standard treatment:ti,ab or usual treatment:ti,ab or standard care:ti,ab or usual care:ti,ab
#25#20 or #21 or #22 or #23 or #24
#26MeSH descriptor: [Cognitive Therapy] explode all trees
#27MeSH descriptor: [Hypnosis, Dental] explode all trees
#28MeSH descriptor: [Self Care] explode all trees
#29MeSH descriptor: [Counseling] explode all trees
#30cogniti*:ti,ab and therap*:ti,ab
#31cogniti*:ti,ab and psychotherap*:ti,ab
#32cogniti*:ti,ab and behavio*:ti,ab and therap*:ti,ab
#33dental:ti,ab and hypnos*:ti,ab
#34self:ti,ab and care:ti,ab
#35self-care:ti,ab or self-management:ti,ab or self management:ti,ab
#36CBT:ti,ab or cogniti* biobehavio* therap*:ti,ab or cogniti* behavio*:ti,ab
#37oral habit reversal:ti,ab or hypnos*:ti,ab
#38self-care treatment*:ti,ab or self care treatment*:ti,ab or self-care strateg*:ti,ab or self care strateg*:ti,ab
#39counsel*:ti,ab
#40relaxation training:ti,ab or self-efficacy enhancement:ti,ab or fear-avoidance technique*:ti,ab or hypnorelaxation:ti,ab
#41#26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40
#42#19 and #25 and #41

Database entry: 06.12.2012

1 "Usual treatment" vs. Psychosocial intervention

1.1 Self-reported pain short-term

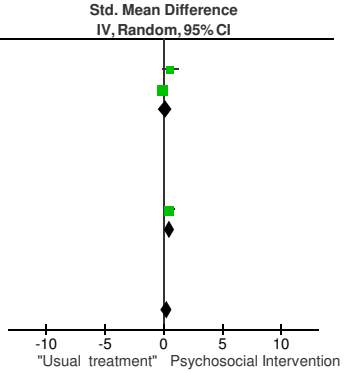
Study or Subgroup	"Usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.1 "Usual treatment" vs. psychosocial intervention								
Alencar 2009 (1)	0.31	0.2	14	0.24	0.24	14	9.3%	0.31 [-0.44, 1.05]
Carlson 2001 (2)	2.4	1.9	21	1.6	1.3	23	12.8%	0.49 [-0.11, 1.09]
Conti 2012 (3)	13.9	22.9	21	24.5	29.2	14	10.7%	-0.41 [-1.09, 0.28]
Crockett 1986 (4)	29	8.9	7	18.6	10.6	7	4.6%	0.99 [-0.14, 2.13]
Niemela 2012 (5)	34	32	39	40	26	37	18.4%	-0.20 [-0.65, 0.25]
Truelove 2006 (6)	4.4	2	68	4.6	2	64	24.2%	-0.10 [-0.44, 0.24]
Subtotal (95% CI)			**170**			**159**	**80.1%**	**0.05 [-0.26, 0.36]**
Heterogeneity: Tau² = 0.06; Chi² = 8.58, df = 5 (P = 0.13); I² = 42%								
Test for overall effect: Z = 0.33 (P = 0.74)								
1.1.2 "Usual treatment" vs. psychosocial intervention + "usual treatment"								
Litt 2010 (7)	2.04	3.06	40	1.38	2.99	49	19.9%	0.22 [-0.20, 0.64]
Subtotal (95% CI)			**40**			**49**	**19.9%**	**0.22 [-0.20, 0.64]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.01 (P = 0.31)								
Total (95% CI)			**210**			**208**	**100.0%**	**0.08 [-0.18, 0.33]**
Heterogeneity: Tau² = 0.04; Chi² = 9.40, df = 6 (P = 0.15); I² = 36%								
Test for overall effect: Z = 0.57 (P = 0.57)								
Test for subgroup differences: Chi² = 0.38, df = 1 (P = 0.54), I² = 0%								



(1) Mod-SSI
(2) MPI Pain severity
(3) VAS
(4) Average over 3 weeks of weekly reports of pain intensity (0-4)
(5) VAS
(6) CPI
(7) MPI Pain severity

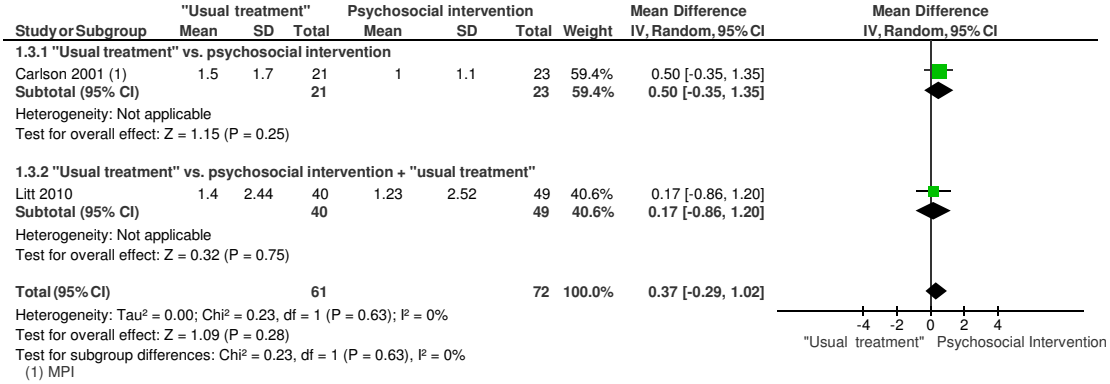
1.2 Self-reported pain long-term

Study or Subgroup	"Usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.2.1 "Usual treatment" vs. psychosocial intervention								
Carlson 2001 (1)	2	1.5	13	1.2	1.5	19	23.9%	0.52 [-0.20, 1.24]
Truelove 2006 (2)	3	2	68	3.3	2	64	41.1%	-0.15 [-0.49, 0.19]
Subtotal (95% CI)			**81**			**83**	**65.0%**	**0.11 [-0.53, 0.75]**
Heterogeneity: Tau² = 0.14; Chi² = 2.72, df = 1 (P = 0.10); I² = 63%								
Test for overall effect: Z = 0.33 (P = 0.74)								
1.2.2 "Usual treatment" vs. psychosocial intervention + "usual treatment"								
Litt 2010 (3)	2.64	2.97	36	1.23	2.95	38	35.0%	0.47 [0.01, 0.93]
Subtotal (95% CI)			**36**			**38**	**35.0%**	**0.47 [0.01, 0.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.00 (P = 0.05)								
Total (95% CI)			**117**			**121**	**100.0%**	**0.23 [-0.25, 0.71]**
Heterogeneity: Tau² = 0.11; Chi² = 5.79, df = 2 (P = 0.06); I² = 65%								
Test for overall effect: Z = 0.94 (P = 0.35)								
Test for subgroup differences: Chi² = 0.82, df = 1 (P = 0.37), I² = 0%								



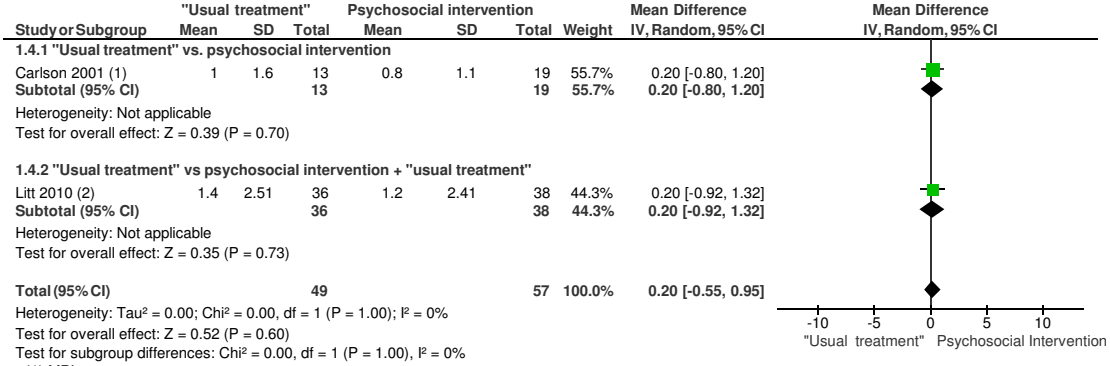
(1) MPI Pain severity
(2) CPI
(3) MPI Pain severity (0-6)

1.3 Pain interference short-term



(1) MPI

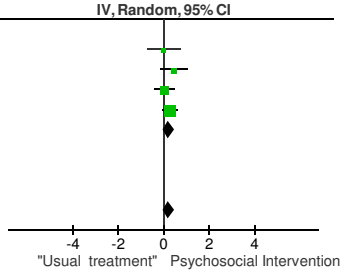
1.4 Pain interference long-term



(1) MPI
(2) MPI (0-6)

1.5 Muscle Pain short-term

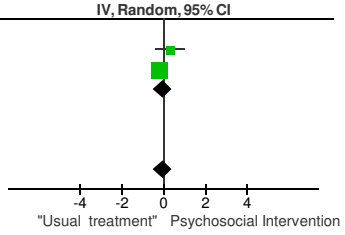
Study or Subgroup	"Usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.5.1 "Usual treatment" vs. psychosocial intervention								
Alencar 2009 (1)	0.3	0.5	14	0.3	0.7	14	10.1%	0.00 [-0.74, 0.74]
Carlson 2001 (2)	19.3	22.4	21	11.2	12.1	23	15.4%	0.45 [-0.15, 1.05]
Niemela 2012 (3)	9.5	4.6	39	9.3	5.3	37	27.4%	0.04 [-0.41, 0.49]
Truelove 2006 (4)	5.6	5.4	68	4.3	4	64	47.1%	0.27 [-0.07, 0.61]
Subtotal (95% CI)			**142**			**138**	**100.0%**	**0.21 [-0.03, 0.44]**
Heterogeneity: Tau² = 0.00; Chi² = 1.58, df = 3 (P = 0.66); I² = 0%								
Test for overall effect: Z = 1.73 (P = 0.08)								
Total (95% CI)			**142**			**138**	**100.0%**	**0.21 [-0.03, 0.44]**
Heterogeneity: Tau² = 0.00; Chi² = 1.58, df = 3 (P = 0.66); I² = 0%								
Test for overall effect: Z = 1.73 (P = 0.08)								
Test for subgroup differences: Not applicable								



(1) 6 muscle sites (0-3)
(2) 17 muscle sites scored 0-3
(3) according to RDC/TMD
(4) mean extraoral muscle sites tender to palpation (out of 16)

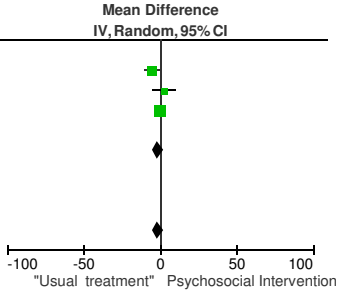
1.6 Muscle Pain long-term

Study or Subgroup	"Usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.6.1 "Usual treatment" vs. psychosocial intervention								
Carlson 2001	12.8	13.2	13	9.3	10.5	19	30.0%	0.29 [-0.42, 1.00]
Truelove 2006	3.6	4.1	68	4.5	4.5	64	70.0%	-0.21 [-0.55, 0.13]
Subtotal (95% CI)			**81**			**83**	**100.0%**	**-0.06 [-0.51, 0.39]**
Heterogeneity: Tau² = 0.04; Chi² = 1.55, df = 1 (P = 0.21); I² = 36%								
Test for overall effect: Z = 0.25 (P = 0.80)								
Total (95% CI)			**81**			**83**	**100.0%**	**-0.06 [-0.51, 0.39]**
Heterogeneity: Tau² = 0.04; Chi² = 1.55, df = 1 (P = 0.21); I² = 36%								
Test for overall effect: Z = 0.25 (P = 0.80)								
Test for subgroup differences: Not applicable								



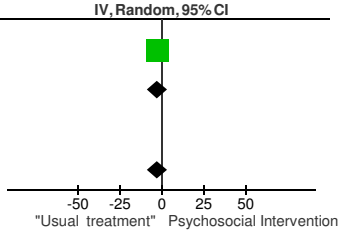
1.7 Unassisted jaw opening without pain short-term

Study or Subgroup	"Usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.7.1 "Usual treatment" vs. psychosocial intervention								
Carlson 2001	36.2	8.6	21	41.6	8.3	23	34.2%	-5.40 [-10.40, -0.40]
Crockett 1986	43	7.23	7	40.7	7.11	7	20.2%	2.30 [-5.21, 9.81]
Niemela 2012	45.9	8.7	39	46.5	7.8	37	45.5%	-0.60 [-4.31, 3.11]
Truelove 2006	40	0	68	40.8	0	64		Not estimable
Subtotal (95% CI)			**135**			**131**	**100.0%**	**-1.66 [-5.60, 2.28]**
Heterogeneity: Tau² = 5.29; Chi² = 3.53, df = 2 (P = 0.17); I² = 43%								
Test for overall effect: Z = 0.82 (P = 0.41)								
Total (95% CI)			**135**			**131**	**100.0%**	**-1.66 [-5.60, 2.28]**
Heterogeneity: Tau² = 5.29; Chi² = 3.53, df = 2 (P = 0.17); I² = 43%								
Test for overall effect: Z = 0.82 (P = 0.41)								
Test for subgroup differences: Not applicable								



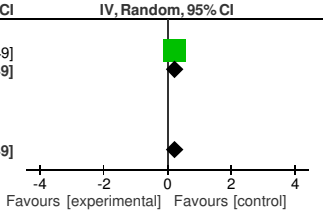
1.8 Unassisted jaw opening without pain long-term

Study or Subgroup	"Usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.8.1 "Usual treatment" vs. psychosocial intervention								
Carlson 2001	39.3	8.4	13	41.8	8.5	19	100.0%	-2.50 [-8.45, 3.45]
Truelove 2006	44	0	68	44	0	64		Not estimable
Subtotal (95% CI)			**81**			**83**	**100.0%**	**-2.50 [-8.45, 3.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.82 (P = 0.41)								
Total (95% CI)			**81**			**83**	**100.0%**	**-2.50 [-8.45, 3.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.82 (P = 0.41)								
Test for subgroup differences: Not applicable								



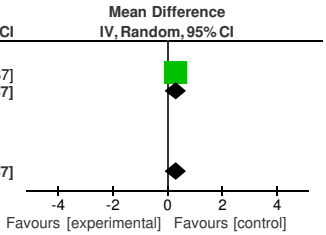
1.9 Somatization short-term

Study or Subgroup	"Usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.9.1 "Usual treatment" vs. psychosocial intervention								
Carlson 2001	0.58	0.51	21	0.35	0.36	23	100.0%	0.23 [-0.03, 0.49]
Subtotal (95% CI)			**21**			**23**	**100.0%**	**0.23 [-0.03, 0.49]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.71 (P = 0.09)								
Total (95% CI)			**21**			**23**	**100.0%**	**0.23 [-0.03, 0.49]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.71 (P = 0.09)								
Test for subgroup differences: Not applicable								



1.10 Somatization long-term

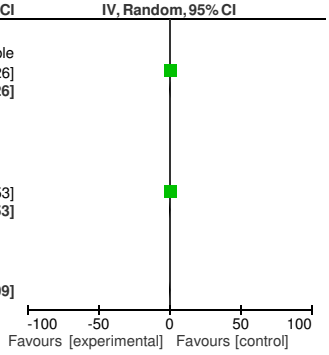
Study or Subgroup	"Usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.10.1 "Usual treatment" vs. psychosocial intervention								
Carlson 2001	0.6	0.64	13	0.3	0.28	19	100.0%	0.30 [-0.07, 0.67]
Subtotal (95% CI)			**13**			**19**	**100.0%**	**0.30 [-0.07, 0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.59 (P = 0.11)								
Total (95% CI)			**13**			**19**	**100.0%**	**0.30 [-0.07, 0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.59 (P = 0.11)								
Test for subgroup differences: Not applicable								



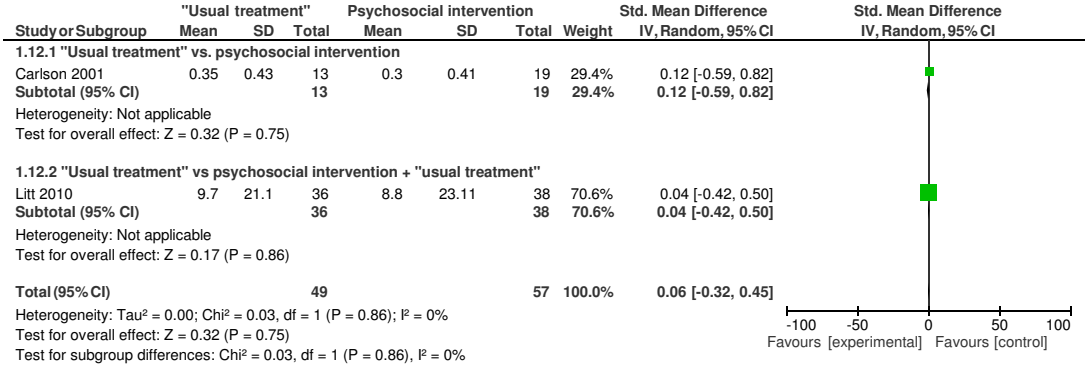
1.11 Depression short-term

Study or Subgroup	"Usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.11.1 "Usual treatment" vs. psychosocial intervention								
Carlson 2001 (1)	0.4	0.36	21	0.28	0.31	23		Not estimable
Litt 2010	1.42	0.55	36	1.02	0.46	38	48.5%	0.78 [0.31, 1.26]
Subtotal (95% CI)			**36**			**38**	**48.5%**	**0.78 [0.31, 1.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.24 (P = 0.001)								
1.11.2 "Usual treatment" vs psychosocial intervention + "usual treatment"								
Litt 2010 (2)	14.82	35	40	11.2	27.95	49	51.5%	0.11 [-0.30, 0.53]
Subtotal (95% CI)			**40**			**49**	**51.5%**	**0.11 [-0.30, 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.54 (P = 0.59)								
Total (95% CI)			**76**			**87**	**100.0%**	**0.44 [-0.22, 1.09]**
Heterogeneity: Tau² = 0.17; Chi² = 4.29, df = 1 (P = 0.04); I² = 77%								
Test for overall effect: Z = 1.31 (P = 0.19)								
Test for subgroup differences: Chi² = 4.29, df = 1 (P = 0.04), I² = 76.7%								

(1) SCL90-R
(2) CESD Depression Score (0-60)

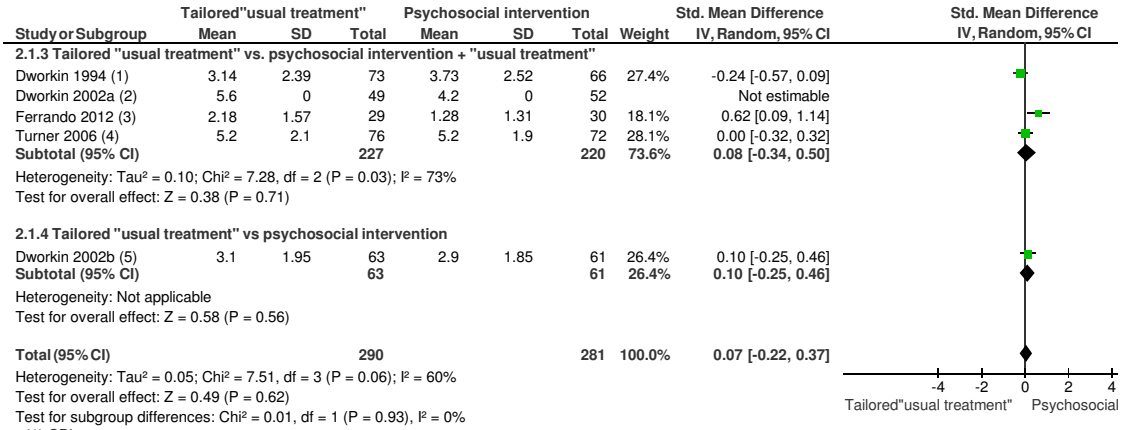


1.12 Depression long-term



2 Tailored "usual treatment" vs psychosocial intervention

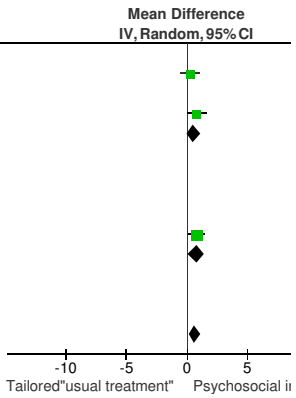
2.1 Self-reported pain short-term



2.2 Self-reported pain long-term

Study or Subgroup	Tailored "usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.2.3 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"								
Dworkin 1994 (1)	3.03	2.31	73	2.74	2.6	66	27.5%	0.29 [-0.53, 1.11]
Dworkin 2002a (2)	4.5	0	51	4.1	0	56		Not estimable
Turner 2006 (3)	4.7	2.3	76	3.9	2.6	72	29.5%	0.80 [0.01, 1.59]
Subtotal (95% CI)			**200**			**194**	**57.0%**	**0.55 [-0.02, 1.12]**
Heterogeneity: Tau² = 0.00; Chi² = 0.77, df = 1 (P = 0.38); I² = 0%								
Test for overall effect: Z = 1.90 (P = 0.06)								
2.2.4 Tailored "usual treatment" vs. psychosocial intervention								
Dworkin 2002b (4)	3	2.34	61	2.2	1.11	55	43.0%	0.80 [0.14, 1.46]
Subtotal (95% CI)			**61**			**55**	**43.0%**	**0.80 [0.14, 1.46]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.39 (P = 0.02)								
Total (95% CI)			**261**			**249**	**100.0%**	**0.66 [0.23, 1.09]**
Heterogeneity: Tau² = 0.00; Chi² = 1.07, df = 2 (P = 0.58); I² = 0%								
Test for overall effect: Z = 3.00 (P = 0.003)								
Test for subgroup differences: Chi² = 0.31, df = 1 (P = 0.58), I² = 0%								

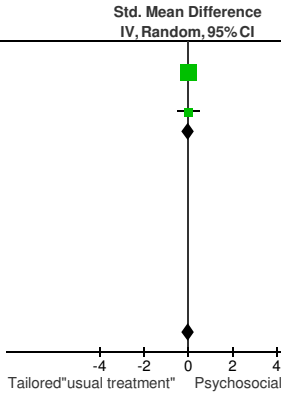
(1) CPI
(2) CPI
(3) CPI
(4) CPI



2.3 Pain interference short-term

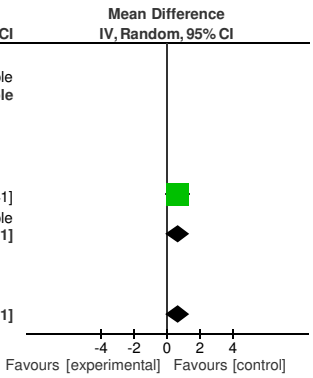
Study or Subgroup	Tailored "usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.3.3 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"								
Dworkin 1994	2.16	2.48	73	2.11	2.52	66	70.2%	0.02 [-0.31, 0.35]
Dworkin 2002a	3.9	0	49	2.7	0	52		Not estimable
Ferrando 2012 (1)	0.99	1.21	29	0.98	1.09	30	29.8%	0.01 [-0.50, 0.52]
Subtotal (95% CI)			**151**			**148**	**100.0%**	**0.02 [-0.26, 0.30]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%								
Test for overall effect: Z = 0.12 (P = 0.91)								
2.3.4 Tailored "usual treatment" vs. psychosocial intervention								
Dworkin 2002b	0.8	0.39	63	0.6	0	61		Not estimable
Subtotal (95% CI)			**63**			**61**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**214**			**209**	**100.0%**	**0.02 [-0.26, 0.30]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%								
Test for overall effect: Z = 0.12 (P = 0.91)								
Test for subgroup differences: Not applicable								

(1) MPI



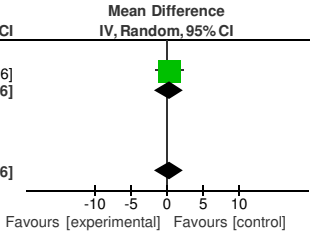
2.4 Pain Interference long-term

Study or Subgroup	Tailored"usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.4.1 Tailored "usual treatment" vs. psychosocial intervention								
Dworkin 2002b	1	0.78	61	0.3	0	55		Not estimable
Subtotal (95% CI)			**61**			**55**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
2.4.2 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"								
Dworkin 1994	1.75	2.65	73	1.09	1.79	66	100.0%	0.66 [-0.09, 1.41]
Dworkin 2002a	2.6	0	49	2.3	0	52		Not estimable
Subtotal (95% CI)			**122**			**118**	**100.0%**	**0.66 [-0.09, 1.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.73 (P = 0.08)								
Total (95% CI)			**183**			**173**	**100.0%**	**0.66 [-0.09, 1.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.73 (P = 0.08)								
Test for subgroup differences: Not applicable								



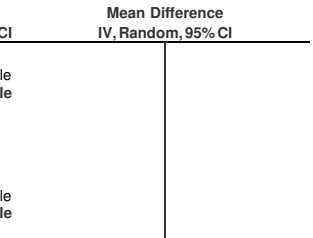
2.5 Muscle Pain upon palpation at long-term

Study or Subgroup	Tailored"usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.5.1 Tailored "usual treatment" vs psychosocial intervention + "usual treatment"								
Dworkin 2002a	7.5	5.71	51	7.2	4.49	56	100.0%	0.30 [-1.66, 2.26]
Subtotal (95% CI)			**51**			**56**	**100.0%**	**0.30 [-1.66, 2.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.30 (P = 0.76)								
Total (95% CI)			**51**			**56**	**100.0%**	**0.30 [-1.66, 2.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.30 (P = 0.76)								
Test for subgroup differences: Not applicable								



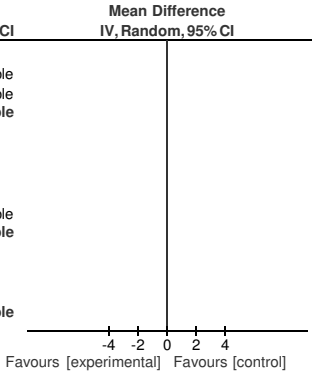
2.6 Unassisted jaw opening without pain short-term

Study or Subgroup	Tailored"usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.6.1 Tailored "usual treatment" vs psychosocial intervention + "usual treatment"								
Dworkin 1994	38.9	0	73	38.1	0	66		Not estimable
Subtotal (95% CI)			**73**			**66**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
2.6.2 Tailored "usual treatment" vs psychosocial intervention								
Dworkin 2002b	43	0	63	46	0	61		Not estimable
Subtotal (95% CI)			**63**			**61**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**136**			**127**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



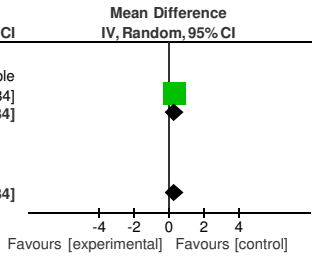
2.7 Unassisted jaw opening without pain long-term

Study or Subgroup	Tailored"usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.7.1 Tailored "usual treatment" vs psychosocial intervention + "usual treatment"								
Dworkin 1994	38.5	0	73	39.2	0	66		Not estimable
Dworkin 2002a	39.2	0	51	36	0	56		Not estimable
Subtotal (95% CI)			**124**			**122**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
2.7.2 Tailored "usual treatment" vs psychosocial intervention								
Dworkin 2002b	44	0	61	45	0	55		Not estimable
Subtotal (95% CI)			**61**			**55**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**185**			**177**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



2.8 Somatization short-term

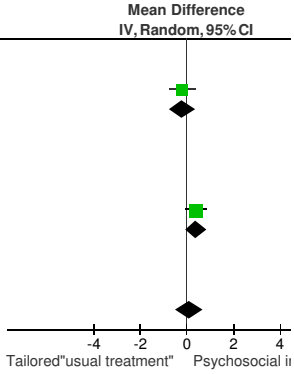
Study or Subgroup	Tailored"usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.8.1 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"								
Dworkin 1994	0.54	0	73	0.59	0	66		Not estimable
Dworkin 2002a	1.4	1.6	49	1.1	1.1	52	100.0%	0.30 [-0.24, 0.84]
Subtotal (95% CI)			**122**			**118**	**100.0%**	**0.30 [-0.24, 0.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.09 (P = 0.27)								
Total (95% CI)			**122**			**118**	**100.0%**	**0.30 [-0.24, 0.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.09 (P = 0.27)								
Test for subgroup differences: Not applicable								



2.9 Somatization long-term

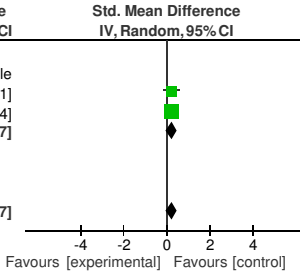
Study or Subgroup	Tailored"usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.9.2 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"								
Dworkin 1994 (1)	0.44	0	73	0.44	0	66		Not estimable
Dworkin 2002a (2)	1.3	1.5	51	1.5	1.5	56	45.8%	-0.20 [-0.77, 0.37]
Subtotal (95% CI)			**124**			**122**	**45.8%**	**-0.20 [-0.77, 0.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.69 (P = 0.49)								
2.9.3 Tailored "usual treatment" vs. psychosocial intervention								
Dworkin 2002b	0.5	1.4	61	0.1	1.1	55	54.2%	0.40 [-0.06, 0.86]
Subtotal (95% CI)			**61**			**55**	**54.2%**	**0.40 [-0.06, 0.86]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.72 (P = 0.09)								
Total (95% CI)			**185**			**177**	**100.0%**	**0.13 [-0.46, 0.71]**
Heterogeneity: Tau² = 0.11; Chi² = 2.60, df = 1 (P = 0.11); I² = 62%								
Test for overall effect: Z = 0.42 (P = 0.68)								
Test for subgroup differences: Chi² = 2.60, df = 1 (P = 0.11), I² = 61.5%								

(1) SCL-90-R
(2) SCL-90-R



2.10 Depression short-term

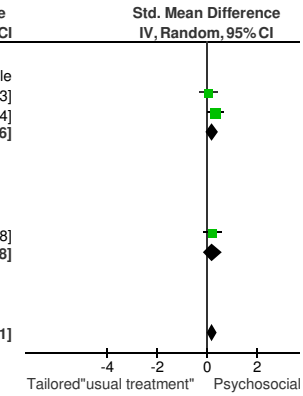
Study or Subgroup	Tailored"usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.10.1 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"								
Dworkin 1994	-0.06	0	73	0.04	0	66		Not estimable
Dworkin 2002a	1.6	2	49	1.2	1.7	52	40.6%	0.21 [-0.18, 0.61]
Turner 2006 (1)	11	10.6	76	8.8	9.3	72	59.4%	0.22 [-0.10, 0.54]
Subtotal (95% CI)			**198**			**190**	**100.0%**	**0.22 [-0.03, 0.47]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.99); I² = 0%								
Test for overall effect: Z = 1.71 (P = 0.09)								
Total (95% CI)			**198**			**190**	**100.0%**	**0.22 [-0.03, 0.47]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.99); I² = 0%								
Test for overall effect: Z = 1.71 (P = 0.09)								
Test for subgroup differences: Not applicable								



(1) BDI

2.11 Depression long-term

Study or Subgroup	Tailored"usual treatment" Mean	SD	Total	Psychosocial intervention Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.11.2 Tailored "usual treatment" vs. psychosocial intervention + "usual treatment"								
Dworkin 1994 (1)	-0.2	0	73	-0.06	0	66		Not estimable
Dworkin 2002a (2)	1.2	2	51	1.1	1.7	56	29.0%	0.05 [-0.33, 0.43]
Turner 2006 (3)	11.4	10.1	76	8.3	9.1	72	39.7%	0.32 [-0.00, 0.64]
Subtotal (95% CI)			**200**			**194**	**68.7%**	**0.21 [-0.05, 0.46]**
Heterogeneity: Tau² = 0.00; Chi² = 1.10, df = 1 (P = 0.30); I² = 9%								
Test for overall effect: Z = 1.56 (P = 0.12)								
2.11.3 Tailored "usual treatment" vs. psychosocial intervention								
Dworkin 2002b (4)	0.5	1.4	61	0.2	1.4	55	31.3%	0.21 [-0.15, 0.58]
Subtotal (95% CI)			**61**			**55**	**31.3%**	**0.21 [-0.15, 0.58]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.14 (P = 0.25)								
Total (95% CI)			**261**			**249**	**100.0%**	**0.21 [0.00, 0.41]**
Heterogeneity: Tau² = 0.00; Chi² = 1.10, df = 2 (P = 0.58); I² = 0%								
Test for overall effect: Z = 2.01 (P = 0.04)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.98), I² = 0%								



(1) SCL-90-R
(2) SCL-90-R
(3) BDI
(4) SCL-90-R

PART 5

GENERAL DISCUSION AND CONCLUSION

The number of published systematic reviews has dramatically increased during the last two decades. However, the methods for evaluating quality of the evidence are still in discussion. Up to now the Cochrane Collaboration recommendations are seen as the most comprehensive to conduct a systematic review [132].

When evaluating systematic reviews which compare surgical and non-surgical treatments for TMD (1966-2007), the results were reduced to only two systematic reviews. These reviews compiled only a scarce percentage of high quality evidence (1.6%-7.7% of the patient's data). The reported reviews by *Kropmans* and *Reston* were evaluated with methodological quality criteria giving a mean of 23.5±0.6% and 77.5±12.8% respectively using three different quality lists (AMSTAR, OQAQ, and CASP). The authors draw attention to the limited quality of the included studies. After decades of study in TMD, this lack of quality should foster an ethical discussion [71].

Two systematic reviews of acupuncture for TMD treatment were published by the same authors. In one review using the Jadad scale [316], and in the other using the Delphi list [313], they set approximately the same studies for analysis although the data of publication defined according to the search strategy was different. For both reviews the included RCTs were almost the same, except for the inclusion of one extra study in the latter review due to the extended data of publication. Despite of the wide use of the Jadad scale, the author is inclined to believe that the Delphi list gathers more critical issues related to the quality of the trials, and do not weigh blinding excessively. The blinding was found not applicable in our review to many of the included studies that compared different modalities of treatment, for example, splint therapy versus psychosocial interventions.

Although the value of this kind of scales is controversial, the author decided to confront the criteria for evaluating the quality of the studies, in order to elucidate if there was a difference with the "gold standard" Cochrane´s risk of bias tool.

Thus, the author complementary added a Delphi list [595] to each systematic review and then compared them with the risk of bias obtained by using the Cochrane´s risk of bias tool. Not surprisingly, both tools were always in agreement. The evaluated issues were very similar, except for the items of intention-to-treat analysis and balance at baseline included in the Delphi list; and from the Cochrane's tool the items of reporting bias and attrition bias that partially overlapped with the ITT analysis. The author considers the use of the tool more user-friendly, especially due to the more precise definition of the dimensions for evaluation.

In our series of systematic reviews, the author recognizes several limitations. The author defined language and publication data as filters, fact that reduce the extension of our findings. Most importantly, we did not use two parallel independent reviewers to screen the potential articles. The extraction and evaluation of the studies was supervised by a second author who had access to the entire articles. As observed by the Cochrane Collaboration, this method may result in some errors during the extraction of the data [247]. However, we did not need any referral to a third author, due to the fact that we fully agreed on the evaluation process after discussion.

On the contrary, the meta-analysis of "Usual treatment" vs. Psychosocial Interventions (Part IV) was supported by an external research team, ensuring a multidisciplinary approach of the reviewers. It was conducted following the recommendations of the Cochrane Collaboration without using any filters more than the one specified in the document (s. Part IV: Meta-analysis of "Usual treatment" vs. Psychosocial Interventions).

In an attempt to integrate and interpret the qualitative evidence of the systematic reviews, and the quantitative evidence of our meta-analysis, the author stresses two fundamental points: current therapies in the context of the etiological theories for myofacial pain, and the need of applying core outcomes for the study of TMD.

During the last past decade a consensual view of the etiological factors of TMD highlight a multifactorial etiology. The history of the proposed treatments accumulates some unfortunate tries during the 30s and 40s. Currently, non-invasive therapies are preferred over the invasive ones, and multimodal interventions prevail over single therapies.

Despite the multiple different therapies available in the literature, there is no evidence that one single therapeutical option is more effective than the others. This situation probably confirms the multifactorial etiology of the TMD. Alternatively, this fact may indicate a psychological necessity of the chronic patient to be treated by any form of intervention; therefore a placebo action cannot be discarded.

The associated etiological principles of the current non-invasive therapies are identifiable when remitted to the treatment of myofacial pain. Two principal theories for chronic muscle pain are the vicious cycle and the pain adaptation model.

Acupuncture, Low level laser therapy and analgesics are linked to the vicious cycle theory when they state that relief of painful symptoms may stop the chronicity process of TMD. Those therapies pursue immediate or short-term results in terms of pain relief. Due to the chronicity of myofacial pain, these alternatives are not efficient enough to improve jaw functionality, and do not influence any psychological aspect of this condition. No data of possible long-term effects are available.

Other pharmacological interventions and physiotherapies based on jaw exercises tackle the muscular disability using relaxing effects. These therapies are also based on the vicious cycle theory, when expecting to cease the muscular hyperactivity allowing the recovery of the tissues. The author did not find any advantage of these therapies over other alternatives.

Although the mechanism of action of the occlusal appliances is debatable, many experts attribute them a reminder effect linked to habit modification. Likewise, some psychosocial interventions focused on replace harmful habits and promote a functional re-education. Due to the behavioral character involved in such habits the author considers these treatments in agreement with the pain adaptation model.

In the same way, the rationales of other psychological interventions are associated to the pain adaptation model. These psychosocial interventions highlight the self management of the TMD patients improving the ability of cope changing the personal interpretation of pain.

The therapies based on the pain adaptation model showed weak to moderate clinical improvements at long-term. Nonetheless, those reports were almost

always directed exclusively to functional (splint therapy) or psychological effects (psychosocial interventions).

Taken together, treatments based on a single modality are sufficient to generate clinical improvements on myofacial pain patients at short-term –without making any difference which therapy was applied. In general, RCTs reporting results at short-term did not control psychological outcomes.

The multimodal therapies have shown better probabilities to allow medical progress at long-term in patients with major psychological disturbances [340]. "Usual treatment", tailored psychosocial interventions including self-strategies with physiotherapeutical components, and Chinese Traditional Medicine reported important improvements at long-term in myofacial pain patients.

At this point raise the question how to harmonize the chronic pain theories with the specific etiology of TMD, but more precisely of myofacial pain. We already know that none of the muscle pain theories can totally explain this phenomenon. Thus the definition of the components of an ideal multimodal therapy depends on our future ability to distinguish the improvers and predictors of the promising treatments.

The chronicity of musculoskeletal pain conditions are probably related with sensitization phenomena [47]. Suggestions of peripheral and central sensitization in TMD patients are often reported during the last decade. This mechanism may also explain the close relationship between TMD and headache [42]. Observations of central nervous system substrate revealed a different pattern for patients of myofacial pain in comparison with healthy volunteers, suggesting a dysregulation of the limbic and trigeminal system [632]. Brain morphological changes have been also reported for other chronic pain conditions. Those modifications are probably related to the chronicity process, i.e. neuronal plasticity [618].

Epidemiological studies have failed to define predictors for TMD, probably due to the dramatic anatomical changes from childhood to adulthood which reduce the predictive value of the results [93]. On the other hand, the follow-up of chronic pain patients has many challenges related to the condition itself and the associated psychological profile of the patients. Some studies showed the effect of therapies, for instance splint therapy, however with serious diminution of the sample. It is remarkable that patients not willing to participate in a study can modify the validity of the outcomes.

Regarding the influence of parafunctional activities as bruxism and occlusion, they may be better considered as risk factors. There is no evidence pointing out a direct relationship with those factors and the development of myofacial pain. Alternatively, they can be considered as modifying or perpetuating agents of this condition. The localist point of view of the etiological factors for myofacial pain can be applied neither for diagnosis nor for therapy. Nonetheless, this not implies those factors have no role in other diagnostic forms of TMD.

As mentioned before, to determine mediators, predictors and moderators inherent to the treatments will allow the experts to clarify the targets of the therapy. With the current evidence, The author is not able to conclude these parameters. According to *Turner* [577] "mediator is a variable that is responsible for all or part of the effects of a treatment on an outcome"…"moderators are baseline characteristics (that may or may not be theoretically identified) that interact with treatment to affect outcomes… Non-specific predictors are patient baseline characteristics that predict response in both treatment and control groups". Interestingly, two RCTs reported on mediators, predictors and moderators of CBT with different results. In the study by *Turner* [577], belief in one's ability to control pain was mediator of jaw limitations; while changes in control, disability, and harm beliefs; catastrophizing; and TMD self-efficacy mediated effects in one-year pain intensity. Among the factors evaluated as moderator, only high scores of masticatory disability at baseline showed significant effects. No predictors were found. In contrast, in the study by *Litt* [344], readiness, somatization, and self-efficacy were moderators for CBT in the treatment of TMD patients.

A critical analysis of the study designs in TMD teaches us the necessity of unifying the search for clinical targets. Elements of the study design are essential to weigh the results of a clinical study. Ideally patients who reject to participate in the clinical trial have to be analyzed in order to evaluate the validity of the current study [634]. Only few RCTs included such analysis within the trial.

Furthermore, the chosen outcomes are an important factor to discriminate the clinical effects of one therapy for TMD. It means that reports of therapeutical success are limited to the evaluated variables. For example, if one study design consider only psychological outcomes, this study cannot be compared with

other trials focused on jaw functioning. Therefore, the reported clinical successes are relative and restricted to the selected outcomes.

As commented in the discussion of our meta-analysis, it became important to reach a consensus about a core of outcomes for myofacial pain and TMD in order to permit comparisons between clinical studies. The clinical examination is mandatory over monitoring tests (EMG, sonography, jaw tracking, etc.). Some of these monitoring and diagnostic are influenced by the vicious cycle theory, and have not proven clinical application, or do not offer theoretical fundaments [350].

Accordingly to the recommendation by *Turk* [574], a group of experts defined a core for chronic pain trials which are summarized in the next table [157]:

Recommended core outcome measures for clinical trials of chronic pain treatment efficacy and effectiveness
Pain
11-point (0–10) numerical rating scale of pain intensity
Usage of rescue analgesics
Categorical rating of pain intensity (none, mild, moderate, severe) in circumstances in which numerical ratings may be problematic
Physical functioning (either one of two measures)
Multidimensional Pain Inventory Interference Scale
Brief Pain Inventory interference items
Emotional functioning (at least one of two measures)
Beck Depression Inventory
Profile of Mood States
Participant ratings of global improvement and satisfaction with treatment
Patient Global Impression of Change
Symptoms and adverse events
Passive capture of spontaneously reported adverse events and symptoms and use of open-ended prompts
Participant disposition
Detailed information regarding participant recruitment and progress through the trial, including all information specified in the CONSORT guidelines

***Table 10**. Recommended core outcome for chronic pain* [157]

The author coincides with these authors in emphasizing pain intensity, activity interference, depression scales, but we also consider relevant for TMD patients the inclusion of unassisted jaw opening, muscle pain upon palpation, somatization, and ideally also anxiety.

Regarding the measurement of self-reported pain, the use of numeral rating scales or the visual analog scale gives important references on the actual situation of the patient. Considering that pain is the principal reason for

consulting, the monitoring of pain in myofacial pain patients is highly relevant for the clinical success of the treatment. Moreover, pain intensity was strongly related to pain activity interference and jaw use limitations in one sample of TMD patients [2].

The pain related-activity interference gives indirect information of the impact of quality of life of the patients. Simple scales of measurement are already available in the RDC/TMD.

In relation to the clinical outcomes, limited jaw opening can be regarded as a diagnostic criterion according to the RDC/TMD. The simple measurement of the interincisal distance with a ruler helps the clinician to comprehend the functional disability of the patient.

Considering the psychological variables which play a role in the myofacial pain condition, the author cannot identify undoubtedly the most relevant. It was observed, for example, that psychological distress and pain severity predict sleep disturbances in TMD patients [626]

Other findings underline the complexity of the myofacial pain condition. Depression and somatization were correlated with higher scores of muscle pain in a sample of Chinese TMD patients. In the same study, somatization was also linked to jaw disability [624]. Moreover, in other study among TMD patients (90% with myofacial pain diagnosis) catastrophizing was found related to pain severity and pain interference. In addition, catastrophizing explained the extraoral muscle palpation outcomes when the data were adjusted to characteristic pain [576].

Furthermore, patients with myofacial pain reacted with higher levels of anxiety and increased neuroendocrine activity (elevated concentrations of cortisol, adrenaline and noradrenaline) after been given a task involving a stressful situation [630]. Additionally, persons subjected to post-traumatic stress disorders (due to war trauma and torture) exhibited greater incidence of TMD [25].

In a sample of university students (n=492), women reporting stress were at double higher risk than female bruxers to present TMJ sounds (OR= 10.56, and OR=5.0 respectively) than women not reporting stress or bruxism [27].

The psychological instruments have to be validated for specific populations. Nonetheless, the author observed in our series of systematic reviews and meta-analysis a preference for the use of the Symptom Check List-90 Revisited (SCL-90R) and the Beck Depression Inventory (BDI).

Optionally, the Brief Symptoms Inventory 18 (BSI-18) embraces three dimensions, namely, somatization, depression, and anxiety, summed up in a psychological distress score. This test has been recently validated for TMD patients [153].

If not included as outcomes, the psychological profile of the patients may act as an essential resource to distinguish types of patients more receptive than others to different multimodal approaches for TMD. For instance, relaxation is apparently more effective when it is associated with concrete activities, like jaw muscle exercises [2]. This observation may be related with a particular profile of patients. Persons with low scores of catastrophizing prefer therapies based on concrete activities. On the contrary, those patients with higher scores of catastrophizing tend to respond better when the therapy includes some self-management component.

As stated by some authors, TMD can be enclosed into a group of idiopathic facial pain conditions. Specifically, myofacial pain patients exhibited high levels of psychological disturbances. Nevertheless, the sole treatment of psychological outcomes does not guarantee clinical improvement. After many years of research, our next challenge is to define a profile for TMD or definitely treat this condition as a psychosomatic condition.

The author highly encourages the researchers on this topic to define core outcomes and to analyze the moderators and predictors of the treatment.

References

1. Aaron LA, Burke MM, Buchwald D: Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder. Arch Intern Med 2000;160:221-227

2. Aaron LA, Turner JA, Mancl LA, Sawchuk CN, Huggins KH, Truelove EL: Daily pain coping among patients with chronic temporomandibular disorder pain: an electronic diary study. J Orofac Pain 2006;20:125-137

3. Abe S, Yamaguchi T, Rompré PH, Grandmont P de, Chen Y, Lavigne GJ: Tooth wear in young subjects: a discriminator between sleep bruxers and controls? Int J Prosthodont 2009;22:342-350

4. Abekura H, Yokomura M, Sadamori S, Hamada T: The initial effects of occlusal splint vertical thickness on the nocturnal EMG activities of masticatory muscles in subjects with a bruxism habit. Int J Prosthodont 2008;21:116-120

5. Abrahamsen R, Zachariae R, Svensson P: Effect of hypnosis on oral function and psychological factors in temporomandibular disorders patients. J Oral Rehabil 2009;36:556-570

6. Abrahamsen, Randi; Baad-Hansen, Lene; Zachariae, Robert; Svensson, Peter Effect of hypnosis on pain and blink reflexes in patients with painful temporomandibular disorders. Clin J Pain 2011;27:344-351

7. Abramowicz S, Dolwick MF: 20-Year Follow-Up Study of Disc Repositioning Surgery for Temporomandibular Joint Internal Derangement. J Oral Maxillofac Surg 2010;68:239-242

8. Abramowicz S, Dolwick M, Lewis S, Dolce C: Temporomandibular joint reconstruction after failed teflon-proplast implant: case report and literature review. International J Oral Maxillofac Surg 2008;37:763-767

9. Abrams K, Jones D: Meta-analysis and the synthesis of evidence. Journal of Mathematics Applied in Medicine and Biology 1995;12:297-313

10. Adachi N, Matsumoto S, Tokuhisa M, Kobayashi K, Yamada T: Antibodies against mycobacterial antigens in the synovial fluid of patients with TMD. J Dent Res 2000;79:1752-1757

11. Afari N, Wen Y, Buchwald D, Goldberg J, Plesh O: Are post-traumatic stress disorder symptoms and temporomandibular pain associated? Findings from a community-based twin registry. J Orofac Pain 2008;22:41-49

12. Affaitati G, Fabrizio A, Savini A, Lerza R, Tafuri E, Constantini R, Lapenna D, Giamberardino MA: A randomized, controlled study comparing a lidocaine patch, a placebo patch, and anesthetic injection for treatment of trigger points in patients with myofascial pain syndrome: evaluation of pain and somatic pain thresholds. Clin Ther 2009;31:705-720

13. Agarwal P, Keleuskar V, Bagewadi AS, Shetti A: Capsaicin-fighting fire with fire. J Indian Acad Oral Med Radiol 2009;21:51-54

14. Aggarwal VR, Lovell K, Peters S, Javidi H, Joughin A, Goldthorpe J: Psychosocial interventions for the management of chronic orofacial pain. Cochrane Database Syst Rev 2011;11, CD008456

15. Aggarwal VR, McBeth J, Zakrzewska JM, Lunt M, Macfarlane GJ: Are reports of mechanical dysfunction in chronic oro-facial pain related to somatisation? A population based study. Eur J Pain 2008;12:501-507

16. Ahlberg K, Ahlberg J, Könönen M, Partinen M, Hublin C, Savolainen A: Reported bruxism and restless legs syndrome in media personnel with or without irregular shift work. Acta Odontol Scand 2005;63:94-98

17. Ahlberg J, Rantala M, Savolainen A, Suvinen T, Nissinen M, Sarna S, Lindholm H, Könonen M: Reported bruxism and stress experience. Community Dent Oral Epidemiol 2002;30:405-408

18. Ahlers MO, Freesmeyer WB, Fussnegger M, Göz G, Jakstat H, Koeck B, Neff A, Ottl P, Reiber T: Zur Therapie der funktionellen Erkrankungen des kraniomandibulären Systems. DZZ 2005;60

19. Ahmad M, Hollender L, Anderson Q, Kartha K, Ohrbach R, Truelove E, John MT, Schiffman EL: Research diagnostic criteria for temporomandibular disorders (RDC/TMD): development of image analysis criteria and examiner reliability for image analysis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;107:844-860

20. Ahn S, Baek S, Kim T, Nahm D: Discrimination of internal derangement of temporomandibular joint by lateral cephalometric analysis. Am J Orthod Dentofacial Orthoped 2006;130:331-339

21. Ahn DK, Choi HS, Yeo SP, Woo YW, Lee MK, Yang GY, Jeon HJ, Park JS, Mokha SS: Blockade of central cyclooxygenase (COX) pathways enhances the cannabinoid-induced antinociceptive effects on inflammatory temporomandibular joint (TMJ) nociception. Pain 2007;132:23-32

22. Ahrari, Farzaneh; Madani, Azam S.; Ghafouri, Zahra S.; Tunér, Jan The efficacy of low-level laser therapy for the treatment of myogenous temporomandibular joint disorder Lasers Med Sci 2013;Jan 15 [Epub ahead of print]

23. Aigner N, Fialka C, Radda C, Vecsei V: Adjuvant laser acupuncture in the treatment of whiplash injuries: a prospective, randomized placebo-controlled trial. Wien Klin Wochenschr 2006;118:95-99

24. Aizawa S, Tsukiyama Y, Koyano K, Clark GT: Reperfusion response changes induced by repeated, sustained contractions in normal human masseter muscle. Arch Oral Biol 2002;47:537-543

25. Ajanović M, Lončarević AŠ, Kazazić LD, Bejtović B, Strujić S, Smajkić N: The Prevalence of Symptoms and Signs of Temporomandibular Dysfunctions in Patients with the Posttraumatic Stress Disorder. Acta Stomatol Croat 2009;43:202-214

26. Akhter R, Hassan NM, Aida J, Kanehira T, Zaman KU, Morita M: Association between experience of stressful life events and muscle-related temporomandibular disorders in patients seeking free treatment in a dental hospital. Eur J Med Res 2007;12:535-540

27. Akhter R, Morita M, Esaki M, Nakamura K, Kanehira T: Development of temporomandibular disorder symptoms: a 3-year cohort study of university students. J Oral Rehabil 2011;38:395-403

28. Alabas O, Tashani O, Tabasam G, Johnson M: Gender role affects experimental pain responses: A systematic review with meta-analysis. EJP 2012;16:1211-1223

29. Al-Ani Z, Davies SJ, Gray RJM, Sloan P, Glenny AM: Stabilisation splint therapy for temporomandibular pain dysfunction syndrome. Cochrane Database Syst Rev 2004; CD002778

30. Al-Badawi EA, Mehta N, Forgione AG, Lobo SL, Zawawi KH: Efficacy of pulsed radio frequency energy therapy in temporomandibular joint pain and dysfunction. Cranio 2004;22:10-20

31. Alexiou K, Stamatakis H, Tsiklakis K: Evaluation of the severity of temporomandibular joint osteoarthritic changes related to age using cone beam computed tomography. Dentomaxillofacial Radiology 2009;38:141-147

32. Al-Jabrah OA, Al-Shumailan YR: Prevalence of temporomandibular disorder signs in patients with complete versus partial dentures. Clin Oral Invest 2006;10:167-173

33. Al-Jundi MA: Treatment need for temporomandibular disorders in the general population - a meta-analysis. Doktorgrade, Martin-Luther-Universität Halle-Wittenberg, Wittenberg 2006

34. Al-Jundi MA, John MT, Setz JM, Szentpétery A, Kuss O: Meta-analysis of treatment need for temporomandibular disorders in adult nonpatients. J Orofac Pain 2008;22:97-107

35. Alkan A, Kilic E: A new approach to arthrocentesis of the temporomandibular joint. Int J Oral Maxillofac Surg 2009;38:85-86

36. Allen KD, Athanasiou KA: Tissue Engineering of the TMJ disc: a review. Tissue Eng 2006;12:1183-1196

37. Alonso A, Kaimal S, Look J, Swift J, Fricton J, Myers S, Kehl L: A Quantitative Evaluation of Inflammatory Cells in Human Temporomandibular Joint Tissues From Patients With and Without Implants. J Oral Maxillofac Surg 2009;67:788-796

38. Alvarez-Arenal A, Junquera Lm, Fernandez Jp, Gonzalez I, Olay S: Effect of occlusal splint and transcutaneous electric nerve stimulation on the signs and symptoms of temporomandibular disorders in patients with bruxism. J Oral Rehabil 2002;29:858-863

39. (American Academy of Sleep Medicine) No authors listed: The international classification of sleep disorders, revised. Diagnostic and coding manual; (ICSD). American Academy of Sleep Medicine, Rochester Minn 2001. http://www.esst.org/adds/ICSD.pdf

40. Anastassaki A, Magnusson T: Patients referred to a specialist clinic because of suspected temporomandibular disorders: a survey of 3194 patients in respect of diagnoses, treatments, and treatment outcome. Acta Odontol Scand 2004;62:183-192

41. Anderson KO, Green CR, Payne R: Racial and Ethnic Disparities in Pain: Causes and Consequences of Unequal Care. J Pain 2009;10:1187-1204

42. Anderson GC, John MT, Ohrbach R, Nixdorf DR, Schiffman EL, Truelove ES, List T: Influence of headache frequency on clinical signs and symptoms of TMD in subjects with temple headache and TMD pain. Pain 2010; doi:10.1016/j.pain.2010.11.007

43. Aoki KR: Evidence for antinociceptive activity of Botulinum Toxin Type A in pain management. Headache 2003;43:9-15

44. Arat ZM, Akçam MO, Gökalp H: Long-term effects of chin-cap therapy on the temporomandibular joints. Eur J Orthod 2003;25:471-475

45. Arayasantiparb R, Tsuchimochi M: Quantification of disc displacement in internal derangement of the temporomandibular joint using magnetic resonance imaging. Odontology 2010;98:73-81

46. Ardizone I, Celemin A, Aneiros F, Del Rio J, Sanchez T, Moreno I: Electromyographic study of activity of the masseter and anterior temporalis muscles in patients with temporomandibular joint (TMJ) dysfuction: Comparison with the clinical dysfunction index. Med Oral 2009: e14-e19

47. Arendt-Nielsen L, Fernández-de-las-Peñas C, Graven-Nielsen T: Basic aspects of musculoskeletal pain: from acute to chronic pain. J Man Manip Ther 2011;19:186-193

48. Argoff CE: A review of the use of topical analgesics for myofascial pain. Curr Pain Headache Rep 2002;6:375-378

49. Ariji Y, Sakuma S, Izumi M et al.: Ultrasonographic features of the masseter muscle in female patients with temporomandibular disorder associated with myofascial pain. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;98:337-341

50. Arima T, Svensson P, Arendt-Nielsen L: Experimental grinding in healthy subjects: a model for postexercise jaw muscle soreness? J Orofac Pain 1999;13:104-114

51. Ash MM: Schienentherapie. Evidenzbasierte Diagnostik und Behandlung bei TMD und CMD. Urban and Fischer, München Jena 2006

52. Astin JA: Mind-body therapies for the management of pain. Clin J Pain 2004;20:27-32

53. Auerbach SM, Laskin DM, Frantsve LM, Orr T: Depression, pain, exposure to stressful life events, and long-term outcomes in temporomandibular disorder patients. J Oral Maxillofac Surg 2001;59:628-33; discussion 634

54. Ay S, Evcik D, Tur BS: Comparison of injection methods in myofascial pain syndrome: a randomized controlled trial. Clin Rheumatol 2010;29:19-23

55. Azrin NH, Nunn RG, Frantz-Renshaw SE: Habit reversal vs negative practice treatment of self-destructive oral habits (biting, chewing or licking of the lips, cheeks, tongue or palate). J Behav Ther Exp Psychiatry 1982;13:49-54

56. Baad-Hansen L, Leijon G, Svensson P, List T: Comparison of clinical findings and psychosocial factors in patients with atypical odontalgia and temporomandibular disorders. J Orofac Pain 2008;22:7-14

57. Baba K, Yugami K, Yaka T, Ai M: Impact of balancing-side tooth contact on clenching induced mandibular displacements in humans J Oral Rehabil 2001;28:721-727

58. Bader G, Kampe T, Tagdae T: Body movement during sleep in subjects with long-standing bruxing behavior. Int J Prosthodont 2000;13:327-333

59. Baker P, Haywood V, Plummer K: Method for immediate fabrication of an occlusal device. J Prosthet Dent 2007;98:411-415

60. Bakke M, Moller E, Werdelin L, Dalager T, Kitai N, Kreiborg S: Treatment of severe temporomandibular joint clicking with botulinum toxin in the lateral pterygoid muscle in two cases of anterior disc displacement. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;100:693-700

61. Baltali E, Zhao K, Koff M, Durmus E, An K, Keller E: A Method for Quantifying Condylar Motion in Patients With Osteoarthritis Using an Electromagnetic Tracking Device and Computed Tomography Imaging. J Oral Maxillofac Surg 2008;66:848-857

62. Bangasser DA, Valentino RJ: Sex differences in molecular and cellular substrates of stress. Cell Mol Neurobiol 2012;32:709-723

63. Barclay P, Hollender L, Maravilla K, Truelove EL: Comparison of clinical and magnetic resonance imaging diagnoses in patients with disk displacement in the temporomandibular joint. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1999;88:37-43

64. Bayar GR, Tutuncu R, Acikel C: Psychopathological profile of patients with different forms of bruxism. Clin Oral Invest 2012;16:305-311

65. Bendtsen L, Jensen R: Amitriptyline reduces myofascial tenderness in patients with chronic tension-type headache. Cephalalgia 2000;20:603-610

66. Bennett R: Myofascial pain syndromes and their evaluation. Best Pract Res Clin Rheumatol 2007;21:427-445

67. Benoliel R, Sharav Y: Masticatory myofascial pain, and tension-type and chronic daily headache. In: Sharav Y, Benoliel R (Hrsg): Orofacial pain and headache. Mosby, Edinburgh 2008, 109-148

68. Benyamin RM, Vallejo R, Kramer J, Rafeyan R: Corticosteroid induced psychosis in the pain management setting. Pain Physician 2008;11:917-920

69. Bergström I, List T, Magnusson T: A follow-up study of subjective symptoms of temporomandibular disorders in patients who received acupuncture and/or interocclusal appliance therapy 18-20 years earlier. SODE 2008;66:88-92

70. Bertram S, Rudisch A, Innerhofer K, Pümpel E, Grubwieser G, Emshoff R: Diagnosing TMJ internal derangement and osteoarthritis with magnetic resonance imaging. J Am Dent Assoc 2001;132:753-761

71. Bessa-Nogueira RV, Vasconcelos BC, Niederman R: The methodological quality of systematic reviews comparing temporomandibular joint disorder surgical and non-surgical treatment. BMC Oral Health 2008;8:27

72. Bevacqua B, Fattouh M: Pulsed radiofrequency for treatment of painful trigger points. Pain Pract 2008;8:149-150

73. Bevilaqua-Grosso D, Chaves, TC, Oliveira AS, Monteiro-Pedro Vde: Anamnestic index severity and signs and symptoms of TMD. Cranio 2006;24:112-118

74. Bjordal JM, Couppé C, Chow RT, Tunér J, Ljunggren EA: A systematic review of low level laser therapy with location-specific doses for pain from chronic joint disorders. Aust J Physiother 2003;49:107-116

75. Bjordal JM, Johnson MI, Iversen V, Aimbire F, Lopes-Martins RAB: Low-Level Laser Therapy in Acute Pain: A Systematic Review of Possible Mechanisms of Action and Clinical Effects in Randomized Placebo-Controlled Trials. Photomed and Laser Surg 2006;24:158-168

76. Blasberg B: Atypical facial pain.pdf. In: Silverman S, Eversole LR, Truelove EL (Hrsg): Essentials of oral medicine. BC Decker Inc, Hamilton ON 2001, 348-353

77. Blasberg B, Greenberg M: Temporomandibular Disorders. In: Burket LW, Greenberg MS, Glick M, Ship JA (Hrsg): Burket's oral medicine. BC Decker, Hamilton Ont 2008, 223-255

78. Bodéré C, Téa SH, Giroux-Metges MA, Woda A: Activity of masticatory muscles in subjects with different orofacial pain conditions. Pain 2005;116:33-41

79. Boever JA de, Nilner M, Orthlieb J, Steenks MH: Recommendations by the EACD for examination, diagnosis, and management of patients with temporomandibular disorders and orofacial pain by the general dental practitioner. J Orofac Pain 2008;22:268-278

80. Boever JA de, van Den Berghe L, Boever AL de, Keersmaekers K: Comparison of clinical profiles and treatment outcomes of an elderly and a younger temporomandibular patient group. J Prosthet Dent 1999;81:312-317

81. Bonjardim LR, Gavião MB, Pereira LJ, Castelo PM: Anxiety and depression in adolescents and their relationship with signs and symptoms of TMD. Int J Prosthodont 2005;18:347-352

82. Bont L, van der Kuijl B, Stegenga B, Vencken L, Boering G: Computed tomography in differential diagnosis of temporomandibular joint disorders. Int J Oral and Maxillofac Surg 1993;22:200-209

83. Borodic G: The use of botulinum toxin for the treatment of chronic facial pain. J Pain 2002;3:21-27

84. Brennan P, Ilankovan V: Arthrocentesis for Temporomandibular Joint Pain Dysfunction Syndrome. J Oral Maxillofac Surg 2006;64:949-951

85. Brusati R, Pedrazzoli M, Colletti G: Functional results after condylectomy in active laterognathia. Journal of Cranio-Maxillofacial Surgery 2010;38:179-184

86. Bumann A. Lotzmann U, Mah J: TMJ Disorders and Orofacial Pain: The Role of Dentistry in a Multidisciplinary Diagnostic Approach (Color Atlas of Dental Medicine). Georg Thieme, Stuttgart 2002

87. Cai H, Luo J, Long X, Li X, Cheng Y: Free-radical oxidation and superoxide dismutase activity in synovial fluid of patients with temporomandibular disorders. J Orofac Pain 2006;20:53-58

88. Cairns BE, Sessle BJ, Hu JW: Evidence that excitatory amino acid receptors within the temporomandibular joint region are involved in the reflex activation of the jaw muscles. J Neurosci 1998;18:8056-8064

89. Cairns BE, Wang K, Hu JW, Sessle BJ: Arendt-Nielsen, Lars; Svensson, Peter The effect of glutamate-evoked masseter muscle pain on the human jaw-stretch reflex differs in men and women. J Orofac Pain 2003;17:317-325

90. Campbell LC, Riley JL, Kashikar-Zuck S, Gremillion H, Robinson ME: Somatic, affective, and pain characteristics of chronic TMD patients with sexual versus physical abuse histories. J Orofac Pain 2000;14:112-119

91. Cao Y, Xie Q, Li K, Light AR, Fu K: Experimental occlusal interference induces long-term masticatory muscle hyperalgesia in rats. Pain 2009;144:287-293

92. Carlsson GE: Epidemiology and treatment need for temporomandibular disorders. J Orofac Pain 1999;13:232-237

93. Carlsson GE, Egermark I, Magnusson T: Predictors of signs and symptoms of temporomandibular disorders: a 20-year follow-up study from childhood to adulthood. Acta Odontol Scand 2002;60:180-185

94. Carlsson GE, Magnusson T: Behandlung temporomandibulärer Funktionsstörungen in der Praxis. Quintessence Publ, Chicago 2000

95. Carr JE, Chong I: Habit Reversal Treatment of Tic Disorders: A Methodological Critique of the Literature. Behav Modif 2005;29:858-875

96. Carroll D, Moore RA, McQuay HJ, Fairman F, Tramèr M, Leijon G: Transcutaneous electrical nerve stimulation (TENS) for chronic pain. Cochrane Database Syst Rev 2001 CD003222

97. Carvalho ALA de, Cury AADB, Garcia RCMR: Prevalence of bruxism and emotional stress and the association between them in Brazilian police officers. Braz Oral Res 2008;22:31-35

98. Casanova-Rosado JF, Medina-Solís CE, Vallejos-Sánchez AA, Casanova-Rosado AJ, Hernández-Prado B, Ávila-Burgos L: Prevalence and associated factors for temporomandibular disorders in a group of Mexican adolescents and youth adults. Clin Oral Invest 2006;10:42-49

99. Castroflorio T, Titolo C, Deregibus A, Debernardi C, Bracco P: The orthodontic treatment of TMD patients: EMG effects of a functional appliance. Cranio 2007;25:206-212

100. Célic R, Jerolimov V, Panduric J: A study of the influence of occlusal factors and parafunctional habits on the prevalence of signs and symptoms of TMD. Int J Prosthodont 2002;15:43-48

101. Celić R, Pandurić J, Dulcić N: Psychologic status in patients with temporomandibular disorders. Int J Prosthodont 2006;19:28-29

102. Ceneviz C, Maloney G, Mehta N: Myofascial pain may mimic trigeminal neuralgia. Cephalalgia 2006;26:899-901

103. Chang H, Israel H: Analysis of Inflammatory Mediators in Temporomandibular Joint Synovial Fluid Lavage Samples of Symptomatic Patients and Asymptomatic Controls. J Oral Maxillofac Surg 2005;63:761-765

104. Chang W, Wu J, Yang W, Jiang J: Therapeutic effects of low-level laser on lateral epicondylitis from differential interventions of Chinese-Western medicine: systematic review. Photomed Laser Surg 2010;28:327-336

105. Charlett SD, Coatesworth AP: Referred otalgia: a structured approach to diagnosis and treatment. Int J of Clin Pract 2007;61:1015-1021

106. Chiappe G, Fantoni F, Landi N, Biondi K, Bosco M: Clinical value of 12 occlusal features for the prediction of disc displacement with reduction (RDC/TMD Axis I group IIa). J Oral Rehabil 2009;36:322-329

107. Chirani, R.A.; Jacq, J.J.; Roux, C.; Meriot, P. 3-D reconstruction and functional analysis of the temporomandibular joint. In: MICCAI 2001, LNCS 2208 Edited by W. Niessen, W; Viergever, M. Springer-Verlag 2001: 1265-66

108. Chuang S: Incidence of temporomandibular disorders (TMDs) in senior dental students in Taiwan. J Oral Rehabil 2002;29:1206-1211

109. Ciancaglini R, Gherlone EF, Radaelli G: Association between loss of occlusal support and symptoms of functional disturbances of the masticatory system. J Oral Rehabil 1999:26:248-253

110. Ciancaglini R, Gherlone EF, Radaelli G: The relationship of bruxism with craniofacial pain and symptoms from the masticatory system in the adult population. J Oral Rehabil 2001;28:842-848

111. Clark GT, Tsukiyama Y, Baba K, Watanabe T: Sixty-eight years of experimental occlusal interference studies: what have we learned? J Prosthet Dent 1999;82:704-713

112. Colhado OCG, Boeing M, Ortega LB: Botulinum toxin in pain treatment. Rev Bras Anestesiol 2009;59:366-381

113. Cooper BC, Kleinberg I: Examination of a large patient population for the presence of symptoms and signs of temporomandibular disorders. Cranio 2007;25:114-126

114. Cosme DC, Baldisserotto SM, Canabarro SAde, Shinkai RS: Bruxism and voluntary maximal bite force in young dentate adults Int J Prosthodont 2005;18:328-332

115. Costen J: A syndrome of ear and sinus symptoms dependent upon disturbed function of the temporomandibular joint. Ann Otol Rhinol Laryngol 1934;43:1-15

116. Coster PJ de, van den Berghe LI, Martens LC: Generalized joint hypermobility and temporomandibular disorders: inherited connective tissue disease as a model with maximum expression. J Orofac Pain 2005;19:47-57

117. Coté T, Mohan A, Polder J, Walton M, Braun M: Botulinum toxin type A injections: Adverse events reported to the US Food and Drug Administration in therapeutic and cosmetic cases. J Am Acad Dermatol 2005;53:407-415

118. Craddock HL: Occlusal Changes Following Posterior Tooth Loss in Adults. Part 3. A Study of Clinical Parameters Associated with the Presence of Occlusal Interferences Following Posterior Tooth Loss. J Prosthodontics 2007;0, 071010080758003

119. Crawford SD: Condylar axis position, as determined by the occlusion and measured by the CPI instrument, and signs and symptoms of temporomandibular dysfunction. Angle Orthod 1999;69:103-15; discussion 115-6

120. Crider AB, Glaros AG: A meta-analysis of EMG biofeedback treatment of TMD. J Orofac Pain 1999;13:29-37

121. Crider A, Glaros AG, Gevirtz RN: Efficacy of Biofeedback-Based Treatments for Temporomandibular Disorders. Appl Psychophysiol Biofeedback 2005;30:333-345

122. Crockett DJ, Foreman ME, Alden L, Blasberg B: A comparison of treatment modes in the management of myofascial pain dysfunction syndrome. Biofeedback Self Regul 1986;11:279-291

123. Cui M, Khanijou S, Rubino J, Aoki KR: Subcutaneous administration of botulinum toxin A reduces formalin-induced pain. Pain 2004;107:125-133

124. Cummings TM, White AR: Needling therapies in the management of myofascial trigger point pain: a systematic review. Arch Phys Med Rehabil 2001;82:986-992

125. da Cunha LA, Firoozmand LM, da Silva AP, Camargo SEA, Esteves SA, Oliveira W: Efficacy of low-level laser therapy in the treatment of temporomandibular disorder. Int Dent J 2008;58:213-217

126. Dahiwale SS, Dange SP, Khalikar A: A device for diagnosing role of occlusion in myofascial pain dysfunction syndrome. Journal of Indian Prosthodontic Society 2007;7:32-34

127. Dao TT, LeResche L: Gender differences in pain. J Orofac Pain 2000;14:169-84; discussion 184-95

128. Davis PJ, Reeves JL, Hastie BA, Graff-Radford SB, Naliboff BD: Depression determines illness conviction and pain impact: a structural equation modeling analysis. Pain Med 2000;1:238-246

129. Dawson PE. Evaluation, diagnosis and treatment of occlusal problems. Mosby 2nd Edition. St. Louis 1989

130. De Laat A, Macaluso GM: Sleep bruxism as a motor disorder. Mov Disord 2002;17:S67

131. DeBar LL, Vuckovic N, Schneider J, Ritenbaugh C: Use of complementary and alternative medicine for temporomandibular disorders. J Orofac Pain 2003;17:224-236

132. Dechartres A, Charles P, Hopewell S, Ravaud P, Altman DG: Reviews assessing the quality or the reporting of randomized controlled trials are increasing over time but raised questions about how quality is assessed. J Clin Epidemiol 2011;64:136-144

133. Decuadro Sáenz G, Doassans I, Sorrenti N et al.: Anatomía del músculo pterigoideo lateral. Su rol en la disfunción miofascial TM. Estudio en cadáveres humanos. Med Oral 2007;9:93-99

134. Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

135. Delaney A, Bagshaw SM, Ferland A, Manns B, Laupland KB, Doig CJ: A systematic evaluation of the quality of meta-analyses in the critical care literature. Crit Care 2005;9: R575-82

136. Delaney A, Bagshaw SM, Ferland A, Laupland K, Manns B, Doig C: The quality of reports of critical care meta-analyses in the Cochrane Database of Systematic Reviews: an independent appraisal. Crit Care Med 2007;35:589-594

137. Deng YM, Fu MK, Hägg U: Prevalence of temporomandibular joint dysfunction (TMJD) in Chinese children and adolescents. A cross-sectional epidemiological study. Eur J Orthod 1995;17:305-309

138. Deodato F, Cristiano S, Trusendi R, Giorgetti R: A functional approach to the TMJ disorders. Progr Orthod 2003;4:20-37

139. Deodato F, Trusendi R, Giorgetti R, Scalese MU: Predisposition for temporomandibular joint disorders: loose ligaments. Cranio 2006;24:179-183

140. Dersh J: Chronic Pain and Psychopathology: Research Findings and Theoretical Considerations. Psychosomatic Medicine 2002;64:773-786

141. Detamore MS, Athanasiou KA, Mao J: A Call to Action for Bioengineers and Dental Professionals: Directives for the Future of TMJ Bioengineering. Ann Biomed Eng 2007;35:1301-1311

142. Diedrichs G, Bockholt R: [Function damage of masticatory organ. Retrospective study of 1,778 patients in a West German clinic]. Funktionsstorungen des Kauorgans. Eine retrospektive Studie an 1778 Patienten der Westdeutschen Kieferklinik. ZWR 1990:99:96-101

143. Dijkgraaf LC, Zardeneta G, Cordewener FW, Liem RS, Schmitz JP, Bont LG de, Milam SB: Crosslinking of fibrinogen and fibronectin by free radicals: A possible initial step in adhesion formation in osteoarthritis of the temporomandibular joint. J Oral Maxillofac Surg 2003;61:101-111

144. Dijkstra P, Kropmans T, Stegenga B: The Association between Generalized Joint Hypermobility and Temporomandibular Joint Disorders: A Systematic Review. J Dent Res 2002;81:158-163

145. Dimitroulis G: A review of 56 cases of chronic closed lock treated with temporomandibular joint arthroscopy. J Oral Maxillofac Surg 2002;60:519-24; discussion 525

146. Diraçoğlu D, Saral IB, Keklik B, Kurt H, Emekli U, Ozçakar L, Karan A, Aksoy C: Arthrocentesis versus nonsurgical methods in the treatment of temporomandibular disc displacement without reduction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:3-8

147. Doepel M, Söderling E, Ekberg EL, Nilner M, Le Bell Y: Salivary cortisol and IgA levels in patients with myofascial pain treated with occlusal appliances in the short term. J Oral Rehabil 2009;36:210-216

148. Dohrenwend BP, Raphael KG, Marbach JJ, Gallagher RM: Why is depression comorbid with chronic myofascial face pain? A family study test of alternative hypotheses. Pain 1999;83:183-192

149. Dooland K, Townsend G, Kaidonis J: Prevalence and side preference for tooth grinding in twins. Aust Dent J 2006;51:219-224

150. Dorsher PT: Can classical acupuncture points and trigger points be compared in the treatment of pain disorders? Birch's analysis revisited. J Altern Complement Med 2008;14:353-359

151. Duan X, Wu J, Mao Y, Wang H, Wang M: A retrospective study on the relationship between aging and tomographic findings in 174 patients with TMD. Oral Radiol 1999;15:9-17

152. Dundar U, Evcik D, Samli F, Pusak H, Kavuncu V: The effect of gallium arsenide aluminum laser therapy in the management of cervical myofascial pain syndrome: a double blind, placebo-controlled study. Clin Rheumatol 2007;26:930-934

153. Durá E, Andreu Y, Galdón M, Ferrando M, Murgui S, Poveda R, Jimenez Y: Psychological assessment of patients with temporomandibular disorders: confirmatory analysis of the dimensional structure of the Brief Symptoms Inventory 18. J Psychosom Res 2006;60:365-370

154. Dworkin BR, Turner JA, Wilson L, Massoth D, Whitney C, Huggins KH, Burgess J, Sommers E, Truelove EL: Brief group cognitive-behavioral intervention for temporo- mandibular disorders. Pain 1994;59:175-187

155. Dworkin SF, Huggins KH, Wilson L, Mancl L, Turner J, Massoth D, LeResche L, Truelove E: A randomized clinical trial using research diagnostic criteria for temporomandibular disorders-axis II to target clinic cases for a tailored self-care TMD treatment program. J Orofac Pain 2002;16:48-63

156. Dworkin SF, Sherman J, Mancl L, Ohrbach R, LeResche L, Truelove E: Reliability, validity, and clinical utility of the research diagnostic criteria for Temporomandibular Disorders Axis II Scales: depression, non-specific physical symptoms, and graded chronic pain. J Orofac Pain 2002;16:207-220

157. Dworkin R, Turk D, Farrar J et al.: Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 2005;113:9-19

158. Dworkin R, LeResche L.: Research Diagnostic Criteria for Temporomandibular Disorders: review, criteria, examinations, and specifications, critique. J Craniomandib Disord 1992;6:301-355

159. Dworkin SF, Turner JA, Mancl L et al.: A randomized clinical trial of a tailored comprehensive care treatment program for temporomandibular disorders. J Orofac Pain 2002;16:259-276

160. Dylina TJ, Calif M: A common-sense approach to splint therapy.pdf. J Prosthet Dent 2001;86:539-545

161. Edwards D, Gatchel R, Adams L, Stowell AW: Emotional Distress and Medication Use in Two Acute Pain Populations: Jaw and Low Back. Pain Pract 2006;6:242-253

162. Egermark I, Carlsson GE, Magnusson T: A 20-year longitudinal study of subjective symptoms of TMD from childhood to adulthood. Acta Odontol Scand 2001;59:40-48

163. Egger M, Smith GD, Schneider M, Minder C: Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629-634

164. Eitner S, Stingl K, Schlegel AK, Wichmann M, Nickenig A: Biopsychosocial correlations in patients with chronic oro-facial pain. Part II. Experiences of pain and dramatic events before the 16th year of life. J Oral Rehab 2009;36:408-414

165. Ekberg E, Nilner M: The influence of stabilisation appliance therapy and other factors on the treatment outcome in patients with temporomandibular disorders of arthrogeneous origin. Swed Dent J 1999;23:39-47

166. Ekberg E, Nilner M: A 6- and 12-month follow-up of appliance therapy in TMD patients: a follow-up of a controlled trial. Int J Prosthodont 2002;15:564-570

167. Ekberg E, Vallon D, Nilner M: The efficacy of appliance therapy in patients with temporomandibular disorders of mainly myogenous origin. A randomized, controlled, short-term trial. J Orofac Pain 2003;17:133-139

168. el-Islam MF, Moussa MA, Malasi TH, Suleiman MA, Mirza IA: Assessment of depression in Kuwait by principal component analysis. J Affect Disord 1988;14:109-114

169. Elder C, Ritenbaugh C, Aickin M, Hammerschlag R, Dworkin S, Mist S, Harris RE: Reductions in pain medication use associated with traditional Chinese medicine for chronic pain. Perm J 2012;16:18-23

170. Emodi-Perlman A, Eli I, Friedman-Rubin P, Goldsmith C, Reiter S, Winocur E: Bruxism, oral parafunctions, anamnestic and clinical findings of temporomandibular disorders in children. J Oral Rehabil 2012;39:126-135

171. Emshoff R, Brandlmaier I, Bertram S, Rudisch A: Magnetic resonance imaging findings of osteoarthrosis and effusion in patients with unilateral temporomandibular joint pain. Int J Oral Maxillofac Surg 2002;31:598-602

172. Engel E: The need for e new medical model: a challenge for biomedicine. Science 1977;4286:129-136

173. Epker J, Gatchel RJ: Coping profile differences in the biopsychosocial functioning of patients with temporomandibular disorder. Psychosom Med 2000;62:69-75

174. Eriksson P, Haggmanhenrikson B, Zafar H: Jaw–neck dysfunction in whiplash-associated disorders. Arch Oral Biol 2007;52:404-408

175. Ernberg M, Lundeberg T, Kopp S: Effect of propranolol and granisetron on experimentally induced pain and allodynia/hyperalgesia by intramuscular injection of serotonin into the human masseter muscle. Pain 2000;84:339-346

176. Ernst E, White AR: Acupuncture as a treatment for temporomandibular joint dysfunction: a systematic review of randomized trials. Arch Otolaryngol Head Neck Surg 1999;125:269-272

177. Ettlin DA, Mang H, Colombo V, Palla S, Gallo LM: Stereometric assessment of TMJ space variation by occlusal splints. J Dent Res 2008;87:877-881

178. Farella M, Michelotti A, Gargano A, Cimino R, Ramaglia L: Myofascial pain syndrome misdiagnosed as odontogenic pain: a case report. Cranio 2002;20:307-311

179. Farella M, Soneda K, Vilmann A, Thomsen CE, Bakke M: Jaw Muscle Soreness after Tooth-clenching Depends on Force Level. J Dent Res 2010;89:717-721

180. Fargas-Babjak A: Acupuncture, transcutaneous electrical nerve stimulation, and laser therapy in chronic pain. Clin J Pain 2001;17:S105-13

181. Fernandes G, Franco AL, Siqueira JTT, Gonçalves DAG, Camparis CM: Sleep bruxism increases the risk for painful temporomandibular disorder, depression and non-specific physical symptoms. J Oral Rehabil 2012;39:538-544

182. Fernández-de-las-Peñas C, Cuadrado ML, Pareja JA: Myofascial trigger points, neck mobility and forward head posture in unilateral migraine. Cephalalgia 2006;26:1061-1070

183. Ferrari R, Schrader H, Obelieniene D: Prevalence of temporomandibular disorders associated with whiplash injury in Lithuania. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1999;87:653-657

184. Ferrario VF, Sforza C, Tartaglia GM, Dellavia C: Immediate effect of a stabilization splint on masticatory muscle activity in temporomandibular disorder patients. J Oral Rehabil 2002;29:810-815

185. Ferreira J, Ko C, Myers S, Swift J, Fricton J: Evaluation of Surgically Retrieved Temporomandibular Joint Alloplastic Implants: Pilot Study. J Oral Maxillofac Surg 2008;66:1112-1124

186. Fietzek UM, Kossmehl P, Barthels A, Ebersbach G, Zynda B, Wissel J: Botulinum toxin B increases mouth opening in patients with spastic trismus. Eur J Neurol 2009;16:1299-1304

187. Fillingim RB, Edwards RR, Powell T: The relationship of sex and clinical pain to experimental pain responses. Pain 1999;83:419-425

188. Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL: Sex, gender, and pain: a review of recent clinical and experimental findings. J Pain 2009;10:447-485

189. Fink M, Rosted P, Bernateck M, Stiesch-Scholz M, Karst M: Acupuncture in the Treatment of Painful Dysfunction of the Temporomandibular Joint – a Review of the Literature. Forsch Komplementärmed 2006;13:109-115

190. Fishbain, D. A.; Cutler, R.; Rosomoff, H. L.; Rosomoff, R. S. Chronic pain-associated depression: antecedent or consequence of chronic pain? A review. Clin J Pain 1997;13:116-137

191. Fletcher MC, Piecuch JF, Lieblich SE: Anatomy and pathophysiology of the temporomandibular joint. Chapter 47. In: Miloro M, Ghali GE, Larsen PE, Waite P (Hrsg): Peterson's principles of Oral and Maxillofacial Surgery. Band 2. BC Decker, India 2004, 933-947

192. Forssell H, Kalso E: Application of principles of evidence-based medicine to occlusal treatment for temporomandibular disorders: are there lessons to be learned? J Orofac Pain 2004;18:9-22; discussion 23-32

193. Forssell H, Kalso E, Koskela P, Vehmanen R, Puukka P, Alanen P: Occlusal treatments in temporomandibular disorders: a qualitative systematic review of randomized controlled trials. Pain 1999;83:549-560

194. Forst R, Ingenhorst A: Das myofasziale Syndrom. Internist 2005;46:1207-1217

195. Fredriksson L, Alstergren P, Kopp S: Absolute and relative facial pressure-pain thresholds in healthy individuals J Orofac Pain 2000;14:98-104

196. Freesmeyer WB, Fussnegger, Ahlers MO: Wiederherstellende Verfahren bei gestörter Kaufunktion. Laryngo-Rhino-Otol 2005;84:248-260

197. Freund B, Schwartz M, Symington J: Botulinum toxin: new treatment for temporomandibular disorders. Br J Oral Maxillofac Surg 2000;38:466-471

198. Frick E, Seidl O: Assessing psychosomatic aspects of chronic orofacial pain syndrome. Psychother Psychosom Med Psychol 2005;55:191-199

199. Fricton J: Current evidence providing clarity in management of temporomandibular disorders: summary of a systematic review of randomized clinical trials for intra-oral appliances and occlusal therapies. J Evid Based Dent Pract 2006;6:48-52

200. Fricton J, Schiffman E: Reliability of a Craniomandibular Index. J Dent Res 1986;65:1359-1364

201. Fujii, T. The relationship between the occlusal interference side and the symptomatic side in temporomandibular disorders J Oral Rehabil 2003;30:295-300

202. Galal N, El Beialy W, Deyama Y, Yoshimura Y, Yoshikawa T, Suzuki K, Totsuka Y: Effect of estrogen on bone resorption and inflammation in the temporomandibular joint cellular elements. Int J Mol Med 2008;21:785-790

203. Gam AN Thorsen H, Lønnberg F: The effect of low-level laser therapy on musculoskeletal pain: a meta-analysis. Pain 1993;52:63-66

204. Gameiro GH, Silva Andrade A, Nouer DF, Ferraz de Arruda Veiga MC: How may stressful experiences contribute to the development of temporomandibular disorders? Clin Oral Invest 2006;10:261-268

205. Gatchel RJ, Stowell AW, Buschang P: The relationships among depression, pain, and masticatory functioning in temporomandibular disorder patients. J Orofac Pain 2006;20:288-296

206. Gavish A, Winocur E, Ventura YS, Halachmi M, Gazit E: Effect of stabilization splint therapy on pain during chewing in patients suffering from myofascial pain. J Oral Rehabil 2002;29:1181-1186

207. Gavish A, Winocur E, Menashe S, Halachmi M, Eli I, Gazit E: Experimental chewing in myofascial pain patients. J Orofac Pain 2002;16:22-28

208. Gesch D, Bernhardt O, Kirbschus A: Association of maloclussion and functional occlusion with TMD in adults. A systematic review of population-based studies. Quintessence Int 2004;35:211-221

209. Gesch D, Bernhardt O, Alte D, Schwahn C, Kocher T, John U, Hensel E: Prevalence of signs and symptoms of temporomandibular disorders in an urban and rural German population: results of a population-based Study of Health in Pomerania. Quintessence Int 2004;35:143-150

210. Gesch D, Bernhardt O, Mack F, John U, Kocher T, Alte D: Association of malocclusion and functional occlusion with subjective symptoms of TMD in adults. Results of the study of Health in Pomerania (SHIP). Angle Orthod 2005;75:183-190

211. Girardot A: Value of CPI, MPI. Angle Orthod 1999;69:392-395

212. Glaros AG: Temporomandibular disorders and facial pain: a psychophysiological perspective. Appl Psychophysiol Biofeedback 2008;33:161-171

213. Glaros AG, Forbes M, Shanker J, Glass EG: Effect of parafunctional clenching on temporomandibular disorder pain and proprioceptive awareness. Cranio 2000;18:198-204

214. Glaros AG, Kim-Weroha N, Lausten L, Franklin KL: Comparison of habit reversal and a behaviorally-modified dental treatment for temporomandibular disorders: a pilot investigation. Appl Psychophysiol Biofeedback 2007;32:149-154

215. Glaros AG, Owais Z, Lausten L: Reduction in parafunctional activity: a potential mechanism for the effectiveness of splint therapy. J Oral Rehabil 2007;34:97-104

216. Glaros AG, Urban D, Locke J: Headache and temporomandibular disorders: evidence for diagnostic and behavioural overlap. Cephalalgia 2007;27:542-549

217. Gleditsch J: The "very point" technique: a needle based point detection method. Acupuncture in Medicine 1995;13:20-21

218. Gleditsch JM: MAPS: Mikro-Aku-Punkt-Systeme. Grundlagen und Praxis der somatotopischen Therapie. Hippokrates, Stuttgart 2002

219. Goddard G, Karibe H, McNeill C, Villafuerte E: Acupuncture and sham acupuncture reduce muscle pain in myofascial pain patients. J Orofac Pain 2002;16:71-76

220. Goldenberg DL: Diagnosis and Differential Diagnosis of Fibromyalgia. Am J Med 2009; 122:S14-S21

221. Gonçalves DA, Bigal ME, Jales LC, Camparis CM, Speciali JG: Headache and Symptoms of Temporomandibular Disorder: An Epidemiological Study. Headache 2010;50:231-241

222. Gonçalves J, Cassano D, Wolford L, Santospinto A, Marquez I: Postsurgical Stability of Counterclockwise Maxillomandibular Advancement Surgery: Affect of Articular Disc Repositioning. J Oral Maxillofac Surg 2008;66:724-738

223. González-García R, Rodríguez-Campo FJ, Monje F, Sastre-Pérez J, Gil-Díez Usandizaga JL: Operative versus simple arthroscopic surgery for chronic closed lock of the temporomandibular joint: a clinical study of 344 arthroscopic procedures. Int J Oral Maxillofac Surg 2008;37:790-796

224. Goulet JP, Lavigne GJ, Lund JP: Jaw pain prevalence among French-speaking Canadians in Quebec and related symptoms of temporomandibular disorders. J Dent Res 1995;74:1738-1744

225. Gramling SE, Neblett J, Grayson R, Townsend D: Temporomandibular disorder: efficacy of an oral habit reversal treatment program. J Behav Ther Exp Psychiatry 1996;27:245-255

226. Green CA, Pope CR: Gender, psychosocial factors and the use of medical services: a longitudinal analysis. Soc Sci Med 1999;48:1363-1372

227. Greene CS: Clinical research. Studying relationships between occlusion and TM disorders. Angle Orthod.1999;69:391-2; author reply 394-5

228. Greenspan JD, Craft RM, LeResche L et al.: Studying sex and gender differences in pain and analgesia: a consensus report. Pain 2007;132 Suppl 1:S26-45

229. Guardanardini L, Manfredini D, Ferronato G: Arthrocentesis of the temporomandibular joint: a proposal for a single-needle technique. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106:483-486

230. Gündel H, Ladwig KH, Wolowski A et al.: Psychische und somatische Befunde bei ätiologisch nicht eindeutigen Kiefer- bzw. Gesichtsschmerzen. Schmerz 2002;16:285-293

231. Gungormus Z, Erciyas K: Evaluation of the relationship between anxiety and depression and bruxism. J Int Med Res 2009;37:547-550

232. Gür A, Karakoç M, Nas K, Cevik R, Saraç J, Demir E: Efficacy of low power laser therapy in fibromyalgia: a single-blind, placebo-controlled trial. Lasers Med Sci 2002;17:57-61

233. Gur A, Sarac AJ, Cevik R, Altindag O, Sarac S: Efficacy of 904 nm gallium arsenide low level laser therapy in the management of chronic myofascial pain in the neck: a double-blind and randomize-controlled trial. Lasers Surg Med 2004;35:229-235

234. Gutiérrez MF, Miralles R, Fuentes A, Cavada G, Valenzuela S, Santander H, Fresno MJ: The effect of tooth clenching and grinding on anterior temporalis electromyographic activity in healthy subjects. Cranio 2010;28:43-49

235. Hachmann A, Martins EA, Araujo FB, Nunes R: Efficacy of the nocturnal bite plate in the control of bruxism for 3 to 5 year old children. J Clin Pediatr Dent 1999;24:9-15

236. Hakgüder A, Birtane M, Gürcan S, Kokino S, Turan FN: Efficacy of low level laser therapy in myofascial pain syndrome: an algometric and thermographic evaluation. Lasers Surg Med 2003;33:339-343

237. Harada T, Ichiki R, Tsukiyama Y, Koyano K: The effect of oral splint devices on sleep bruxism: a 6-week observation with an ambulatory electromyographic recording device. J Oral Rehabil 2006;33:482-488

238. Hasegawa K, Okamoto M, Nishigawa G, Oki K, Minagi S: The design of non-occlusal intraoral appliances on hard palate and their effect on masseter muscle activity during sleep. Cranio 2007;25:8-15

239. Hatch JP, Rugh JD, Sakai S, Prihoda TJ: Reliability of the craniomandibular index. J Orofac Pain 2002;16:284-295

240. Hecker HU, Peuker ET, Steveling A, Bijak M: Practice of acupuncture. The complete guide: ear-scalp-mouth-hand. Thieme Stuttgart 2006

241. Heffez LB: Surgery for internal derangements of the temporomandibular joint. 989-1014 *In*: Michael Miloro: Peterson's principles of Oral and MaxillofacialSurgery, India BC Decker 2004

242. Helkimo M: Studies on function and dysfunction of the masticatory system. II. Index for anamnestic and clinical dysfunction and occlusal state. Sven Tandlak Tidskr 1974;67:101-121

243. Henningsen P, Löwe B: Depression, pain, and somatoform disorders. Curr Opin Psychiatry 2006;19:19-24

244. Henry C, Tull G, Whittumhudson J, Wolford L: Analysis of estrogen binding sites of the posterior ligament of the human TMJ. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:698-701

245. Hentschel K, Capobianco DJ, Dodick DW: Facial Pain. Neurologist 11, 244-249 (2005)

246. Herb K, Cho S, Stiles MA: Temporomandibular joint pain and dysfunction. Current Science Inc 2006;10:408-414

247. Higgins JPT, Green S: Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0. http://www.cochrane-handbook.org/ 2011

248. Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration 2011. Available from www.cochrane-handbook.org.

249. Hiltunen K, Peltola JS, Vehkalahti MM, Närhi T, Ainamo A: A 5-year follow-up of signs and symptoms of TMD and radiographic findings in the elderly. Int J Prosthodont 2003;16:631-634

250. Hintze H, Wiese M, Wenzel A: Cone beam CT and conventional tomography for the detection of morphological temporomandibular joint changes. Dentomaxillofacial Radiology 2007;36:192-197

251. Hintze, H; Wiese, M; Wenzel, A Comparison of three radiographic methods for detection of morphological temporomandibular joint changes: panoramic, scanographic and tomographic examination Dentomaxillofacial Radiology 2009;38:134-140

252. Hirsch C, John MT, Zwijnenburg A, Reiber T: Zum Vorkommen nichtdentogener orofazialer Schmerzen in der Bevölkerung. In: Lipp MDW (Hrsg): Kiefer- und Gesichtsschmerz. Diagnose und Therapie in der zahnärztlichen Praxis ; Referate der 7. Jahrestagung des Interdisziplinären Arbeitskreises Zahnärztliche Anästhesie. Schlüter, Hannover 2002, 17-19

253. Hirsch C, John MT, Stang A: Association between generalized joint hypermobility and signs and diagnoses of temporomandibular disorders. Eur J Oral Sci 2008;116:525-30

254. Hirsch C, John MT, Drangsholt MT, Mancl LA: Relationship between overbite/overjet and clicking or crepitus of the temporomandibular joint. J Orofac Pain 2005;19:218-225

255. Huddleston SJ, Lobbezoo F, Chen YJ, Naeije M: A comparative study between clinical and instrumental methods for the recognition of internal derangements with a clicking sound on condylar movement. J Orofac Pain 2004;18:138-147

256. Hülse M, Losert-Bruggner B, Schöttl R, Zawadzki W. Neuromuskulär ausgerichtete Bisslagebestimmung mit Hilfe niedrigfrequenter transkutaner elektrischer Nervenstimulation. Manuel Med 2003;41:120-128

257. Hutchins B, Patel H, Spears R: Attenuation of pro-inflammatory neuropeptide levels produced by a cyclooxygenase-2 inhibitor in an animal model of chronic TMJ inflammation. J Orofac Pain 2002;16:312-316

258. Ikebe K, Hazeyama T, Iwase K, Sajima H, Gonda T, Maeda Y, Nokubi T: Association of symptomless TMJ sounds with occlusal force and masticatory performance in older adults. J Oral Rehabil 2008;35:317-323

259. Imai H, Sakamoto I, Yoda T, Yamashita Y: A model for internal derangement and osteoarthritis of the temporomandibular joint with experimental traction of the mandibular ramus in rabbit. Oral Dis 2001;7:185-191

260. International RDC-TMD Consortium Network: Translations. http://www.rdc-tmdinternational.org/TMDAssessmentDiagnosis/RDCTMD/Translations.aspx, 27.09.2012

261. Ioi H, Matsumoto R, Nishioka M, Goto Tk, Nakata S, Nakasima A, Counts AL: Relationship of TMJ osteoarthritis / osteoarthrosis to head posture and dentofacial morphology. Orthod Craniofac Res 2008;11:8-16

262. Isong U, Gansky SA, Plesh O: Temporomandibular joint and muscle disorder-type pain in U.S. adults: the National Health Interview Survey. J Orofac Pain 2008;22:317-322

263. Itoh K, Kitakoji H: Acupuncture for Chronic Pain in Japan: A Review. Evid Base Compl Alternative Med 2007;4:431-438

264. Iwama H, Ohmori S, Kaneko T, Watanabe K: Water-diluted local anesthetic for trigger-point injection in chronic myofascial pain syndrome: evaluation of types of local anesthetic and concentrations in water. Reg Anesth Pain Med 2001;26:333-336

265. Janal MN, Raphael KG, Nayak S, Klausner J: Prevalence of myofascial temporomandibular disorder in US community women. J Oral Rehabil 2008;35:801-809

266. Jaquiéry C, Kunz C, Rohner D, Bornstein M, Geissmann A, Hammer B: Langzeitkontrolle von 37 Patienten mit Diskusretrofixation im Zeitraum von 1986-1995. Mund-, Kiefer- und Gesichtschirurgie 2001;5:126-129

267. Jegindø EE, Vase L, Skewes JC, AJ Terkelsen, J Hansen, AW Geertz, A Roepstorff, TS Jensen: Expectations contribute to reduced pain levels during prayer in highly religious participants. J Behav Med 2012 doi: 10.1007/s10865-012-9438-9

268. Jinha AE: Article 50 million: an estimate of the number of scholarly articles in existence. Learn Pub 2010;23:258-263

269. Johansson A, Unell L, Carlsson GE, Söderfeldt B, Halling A: Gender difference in symptoms related to temporomandibular disorders in a population of 50-year-old subjects. J Orofac Pain 2003;17:29-35

270. Johansson A, Unell L, Carlsson GE, Söderfeldt B, Halling A, Widar F: Associations between social and general health factors and symptoms related to TMD and bruxism in a population of 50-year-old subjects. Acta Odontol Scand 2004;62:231-237

271. Johansson A, Unell L, Carlsson GE, Söderfeldt B, Halling A: Risk factors associated with symptoms of temporomandibular disorders in a population of 50- and 60-year-old subjects. J Oral Rehabil 2006;33:473-481

272. John MT: Research Diagnostic Criteria for temporomandibular disorder - German version (RDC/TMD-G), 1-21. http://www.rdc-tmdinternational.org/LinkClick.aspx?fileticket=JLVnaTE8xfk%3Dandtabid=145andmid=953

273. John MT: Improving TMD classification using the Delphi technique. J Oral Rehabil 2010;37:766-770

274. John MT, Hirsch C, Reiber T, Dworkin SF: Translating the research diagnostic criteria for temporomandibular disorders into German: evaluation of content and process. J Orofac Pain 2006;20:43-52

275. Jokstad A, Mo A, Krogstad BS: Clinical comparison between two different splint designs for temporomandibular disorder therapy. SODE 2005;63:218-226

276. Jüni P: Systematic reviews in health care: Assessing the quality of controlled clinical trials. BMJ 2001;323:42-46

277. Kader Alomari F, Khalef Alsakarna B: Clinical features of TMD among Jordanian children. Pakistan Oral and Dental Journal 2009;29

278. Kafas P, Kalfas S, Leeson R: Chronic TMJ dysfunction. A condition for a multidisciplinary approach. J Med Sci 2007;7:492-502

279. Kalamir, Allan; Pollard, Henry; Vitiello, Andrew; Bonello, Rodney Intra-oral myofascial therapy for chronic myogenous temporomandibular disorders: a randomized, controlled pilot study J Man Manip Ther 2010;18:139-146

280. Kamanli A, Kaya A, Ardicoglu O, Ozgocmen S, Zengin FO, Bayik Y: Comparison of lidocaine injection, botulinum toxin injection, and dry needling to trigger points in myofascial pain syndrome. Rheumatol Int 2005;25:604-611

281. Kang S, Lee D, Choi J, Kim S, Kim Y, Ahn H: Association between estrogen receptor polymorphism and pain susceptibility in female temporomandibular joint osteoarthritis patients. International J Oral Maxillofac Surg 2007;36:391-394

282. Kanter RJ de, Truin GJ, Burgersdijk RC, van 't Hof MA, Battistuzzi PG, Kalsbeek H, Käyser AF: Prevalence in the Dutch adult population and a meta-analysis of signs and symptoms of temporomandibular disorder. J Dent Res 1993;72:1509-1518

283. Kao M, Hsieh Y, Kuo F, Hong C: Electrophysiological assessment of acupuncture points. Am J Phys Med Rehabil 2006;85:443-448

284. Kares H, Schindler H, Schöttl R: Der etwas andere Kopf- und Gesichtsschmerz. Craniomandibuläre Dysfunktionen CMD. Schlüter, Hannover 2008

285. Karlis V, Glickman R: Nonsurgical management of temporomandibular disorders. Chapter 48. In: Miloro M, Ghali GE, Larsen PE, Waite P (Hrsg): Peterson's principles of Oral and Maxillofacial Surgery. Band 2. BC Decker, India 2004, 949-962

286. Karst M. Begleitende Schmerztherapie (131-143) In: Ernst A, Freesmeyer WB. Funktionstörungen im Kopf-Hals-Bereich für Mediziner und Zahnmediziner. Georg Thieme Verlag 2008

287. Kasch H, Hjorth T, Svensson P, Nyhuus L, Jensen TS: Temporomandibular disorders after whiplash injury: a controlled, prospective study. J Orofac Pain 2002;16:118-128

288. Kato T, Masuda Y, Kanayama H, Nakamura N, Yoshida A, Morimoto T: Heterogeneous activity level of jaw-closing and -opening muscles and its association with arousal levels during sleep in the guinea pig. Am J Physiol Regul Integr Comp Physiol 2009;298:R34

289. Kato T, Montplaisir J, Guitard F, Sessle B, Lund J, Lavigne G: Evidence that Experimentally Induced Sleep Bruxism is a Consequence of Transient Arousal. J Dent Res 2003;82:284-288

290. Kato T, Rompré P, Montplaisir JY, Sessle BJ, Lavigne GJ: Sleep bruxism: an oromotor activity secondary to micro-arousal. J Dent Res 2001;80:1940-1944

291. Kato T, Thie NM, Huynh N, Miyawaki S, Lavigne GJ: Topical review: sleep bruxism and the role of peripheral sensory influences. J Orofac Pain 2003;17:191-213

292. Kavuncu V, Sahin S, Kamanli A, Karan A, Aksoy C: The role of systemic hypermobility and condylar hypermobility in temporomandibular joint dysfunction syndrome. Rheumatol Int 2006;26:257-260

293. Kessler RC, McGonagle KA, Swartz M, Blazer DG, Nelson CB: Sex and depression in the National Comorbidity Survey. I: Lifetime prevalence, chronicity and recurrence. J Affect Disord 1993;29:85-96

294. Kim M: Orthodontics and temporomandibular disorder: A meta-analysis. Am J Orthod Dentofacial Orthoped 2002;121:438-446

295. Kim S: The presence of bacteria in the synovial fluid of the temporomandibular joint and clinical significance: preliminary study. J Oral Maxillofac Surg 2003;61:1156-1161

296. Kim ST: Myofascial pain and toothaches. Aust Endod J 2005;31:106-110

297. Kimos P, Biggs C, Mah J, Heo G, Rashiq S, Thie N, Major P: Analgesic action of gabapentin on chronic pain in the masticatory muscles: A randomized controlled trial. Pain 2007;127:151-160

298. Kirveskari P, Jamsa T: Health risk from occlusal interferences in females. Eur J Orthod 2009;31:490-495

299. Klobas L, Gambardella U, Hansson TL: A 5-year follow-up of temporomandibular disorder treatment emphasizing condylar asymmetry. Cranio 2006;24:265-273

300. Klobas L, Tegelberg A, Axelsson S: Symptoms and signs of temporomandibular disorders in individuals with chronic whiplash-associated disorders. Swed Dent J 2004;28:29-36

301. Koh H, Robinson P: Occlusal adjustment for treating and preventing temporomandibular joint disorders. Cochrane Database Syst Rev 2003/ published 2009 CD003812 doi: 10.1002/14651858.

302. Komiyama O, Kawara M, Arai M, Asano T, Kobayashi K: Posture correction as part of behavioural therapy in treatment of myofascial pain with limited opening. J Oral Rehabil 1999;26:428-435

303. Korff M von, Dworkin SF, Le Resche L, Kruger A: An epidemiologic comparison of pain complaints. Pain 1988;32:173-183

304. Korff M von, Ormel J, Keefe FJ, Dworkin SF: Grading the severity of chronic pain. Pain 1992;50:133-149

305. Korn H: Biofeedback und zahnmedizinische Behandlungsansätze bei temporomandibulären Störungen und Bruxismus. Verhaltenstherapie 2005;15:94-102

306. Korszun A, Young EA, Singer K, Carlson NE, Brown MB, Crofford L: Basal circadian cortisol secretion in women with temporomandibular disorders. J Dent Res 2002;81:279-283

307. Koyano K, Tsukiyama Y, Ichiki R, Kuwata T: Assessment of bruxism in the clinic. J Oral Rehabil 2008;35:495-508

308. Kreiner M, Betancor E, Clark GT: Occlusal stabilization appliances. Evidence of their efficacy. J Am Dent Assoc 2001;132:770-777

309. Kuboki T, Takenami Y, Orsini MG, Maekawa K, Yamashita A, Azuma Y, Clark GT: Effect of occlusal appliances and clenching on the internally deranged TMJ space. J Orofac Pain 1999;13:38-48

310. Kurita H, Kurashina K, Ohtsuka A: Efficacy of a mandibular manipulation technique in reducing the permanently displaced temporomandibular joint disc. J Oral Maxillofac Surg 1999;57:784-787

311. Kurita H, Ikeda K, Kurashina K: Evaluation of the effect of a stabilization splint on occlusal force in patients with masticatory muscle disorders. J Oral Rehabil 2000;27:79-82

312. Kurita H, Ohtsuka A, Kobayashi H, Kurashina K: Alteration of the horizontal mandibular condyle size associated with temporomandibular joint internal derangement in adult females. Dentomaxillofac Radiol 2002;31:373-378

313. La Touche R, Angulo-Díaz-Parreño S, de-la-Hoz JL et al.: Effectiveness of acupuncture in the treatment of temporomandibular disorders of muscular origin: a systematic review of the last decade. J Altern Complement Med 2010;16:107-112

314. La Touche R, Fernández-De-Las-Peñas C, Fernández-Carnero J, Escalante K, Angulo-Díaz-Parreño S, Paris-Alemany A, Cleland Ja: The effects of manual therapy and exercise directed at the cervical spine on pain and pressure pain sensitivity in patients with myofascial temporomandibular disorders. J Oral Rehabil 2009;36:644-652

315. La Touche R, Paris-Alemany A, Piekartz H von, Mannheimer JS, Fernandez-Carnero J, Rocabado M: The influence of cranio-cervical posture on maximal mouth opening and pressure pain threshold in patients with myofascial temporomandibular pain disorders. Clin J Pain 2011;27:48-55

316. La Touche R, Goddard G, De-la-Hoz JL et al.: Acupuncture in the treatment of pain in temporomandibular disorders: a systematic review and meta-analysis of randomized controlled trials. Clin J Pain 2010;26:541-550

317. Landulpho AB, E Silva WAB, E Silva FA, Vitti M: Electromyographic evaluation of masseter and anterior temporalis muscles in patients with temporomandibular disorders following interocclusal appliance treatment. J Oral Rehabil 2004;31:95-98

318. Lao L, Huang Y, Feng C, Berman BM, Tan MT: Evaluating traditional Chinese medicine using modern clinical trial design and statistical methodology: application to a randomized controlled acupuncture trial. Stat Med 2012;31:619-627

319. Lariviere WR, Melzack R: The role of corticotropin-releasing factor in pain and analgesia. Pain 2000;84:1-12

320. Lavigne G, Huynh N, Kato T, Okura K, Adachi K, Yao D, Sessle B: Genesis of sleep bruxism: Motor and autonomic-cardiac interactions. Arch Oral Biol 2007;52:381-384

321. Lavigne GJ, Kato T, Kolta A, Sessle BJ: Neurobiological mechanisms involved in sleep bruxism. Crit Rev Oral Biol Med 2003;14:30-46

322. Lavigne Gj, Khoury S, Abe S, Yamaguchi T, Raphael K: Bruxism physiology and pathology: an overview for clinicians. J Oral Rehabil 2008;35:476-494

323. Lavigne G, Rompre P, Montplaisir J: Sleep Bruxism: Validity of Clinical Research Diagnostic Criteria in a Controlled Polysomnographic Study. J Dent Res 1996;75:546-552

324. Lavigne G, Rompre P, Poirier G, Huard H, Kato T, Montplaisir J: Rhythmic Masticatory Muscle Activity during Sleep in Humans. J Dent Res 2001;80:443-448

325. Le Bell Y, Jämsä T, Korri S, Niemi PM, Alanen P: Effect of artificial occlusal interferences depends on previous experience of temporomandibular disorders. Acta Odontol Scand 2002;60:219-222

326. Le Bell Y, Niemi P, Jämsä T, Kylmälä M, Alanen P: Subjective reactions to intervention with artificial interferences in subjects with and without a history of temporomandibular disorders. Acta Odontol Scand 2006;64:59-63

327. Learreta JA, Matos JLF, Matos MF. Durst AC: Current diagnosis of temporomandibular pathologies. Cranio 2009;27:125-133

328. Lee MS, Kang JW, Ernst E: Does moxibustion work? An overview of systematic reviews. BMC Res Notes 2010;3:284-288

329. Lee Y, Kim H, Wu T, Wang X, Dionne RA: Genetically mediated interindividual variation in analgesic responses to cyclooxygenase inhibitory drugs. Clin Pharmacol Ther 2006;79:407-418

330. Lee LTK, Yeung RWK, Wong MCM, McMillan AS: Diagnostic sub-types, psychological distress and psychosocial dysfunction in southern Chinese people with temporomandibular disorders. J Oral Rehabil 2008;35:184-190

331. Lee J, Yun K, Kim C, Park J: Articular disc position in association with mandibular setback surgery. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:e19

332. Leever DL: The expanded critique concept for enlarging the reviewer's influence regarding original research articles. Angle Orthod 1999;69:389-91; author reply 394-5

333. Leite FMG, Atallah AN, El Dib R, Grossmann E, Januzzi E, Andriolo RB, da Silva EMK: Cyclobenzaprine for the treatment of myofascial pain in adults. Cochrane Database Syst Rev 2009 CD006830

334. LeResche L: Epidemiology of Temporomandibular Disorders: Implications for the Investigation of Etiologic Factors. Crit Rev Oral Biol Med 1997;8:291-305

335. LeResche L, Mancl L, Sherman JJ, Gandara B, Dworkin SF: Changes in temporomandibular pain and other symptoms across the menstrual cycle. Pain 2003;106:253-261

336. Lewis J, Tehan P: A blinded pilot study investigating the use of diagnostic ultrasound for detecting active myofascial trigger points. Pain 1999;79:39-44

337. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, Clarke M, Devereaux PJ, Kleijnen J, Moher D: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Ann Intern Med 2009;151:W65-94

338. Lindern JJ von: Type A botulinum toxin in the treatment of chronic facial pain associated with temporo-mandibular dysfunction. Acta Neurol Belg 2001;101:39-41

339. Lindern JJ von, Niederhagen B, Berge S, Appel T: Type A botulinum toxin in the treatment of chronic facial pain associated with masticatory hyperactivity. J Oral Maxillofac Surg 2003;61:774-778

340. List T, Axelsson S: Management of TMD: evidence from systematic reviews and meta-analyses. J Oral Rehabil 2010;37:430-451

341. List T, Axelsson S, Leijon G: Pharmacologic interventions in the treatment of temporomandibular disorders, atypical facial pain, and burning mouth syndrome. A qualitative systematic review. J Orofac Pain 2003;17:301-310

342. List T, Leijon G, Helkimo M, Oster A, Dworkin SF, Svensson P: Clinical findings and psychosocial factors in patients with atypical odontalgia: a case-control study. J Orofac Pain 2007;21:89-98

343. Litt MD, Shafer DM, Ibanez CR, Kreutzer DL, Tawfik-Yonkers Z: Momentary pain and coping in temporomandibular disorder pain: Exploring mechanisms of cognitive behavioral treatment for chronic pain. Pain 2009;145:160-168

344. Litt MD, Shafer DM, Kreutzer DL: Brief cognitive-behavioral treatment for TMD pain: Long-term outcomes and moderators of treatment. Pain 2010;151:110-116

345. Liu HX, Liang QJ, Xiao P, Jiao HX, Gao Y, Ahmetjiang A: The effectiveness of cognitive-behavioural therapy for temporomandibular disorders: a systematic review. J Oral Rehabil 2012;39:55-62

346. Lobbezoo F, Ahlberg J, Glaros AG, Kato T, Koyano K, Lavigne GJ, Leeuw R.de, Manfredini D, Svensson P, Winocur E: Bruxism defined and graded: an international consensus. J Oral Rehabil 2013;40:2-4

347. Lobbezoo F, Naeije M: Bruxism is mainly regulated centrally, not peripherally. J Oral Rehabil 2001;28:1085-1091

348. Locker D, Grushka M: Prevalence of oral and facial pain and discomfort: preliminary results of a mail survey. Community Dent Oral Epidemiol 1987;15:169-172

349. Lund JP, Donga R, Widmer CG, Stohler CS: The pain-adaptation model: a discussion of the relationship between chronic musculoskeletal pain and motor activity. Can J Physiol Pharmacol 1991;69:683-694

350. Lund JP, Widmer CG, Feine JS: Validity of diagnostic and monitoring tests used for temporomandibular disorders. J Dent Res 1995;74:1133-1143

351. Luther F, Layton S, McDonald F: Orthodontics for treating temporomandibular joint (TMJ) disorders (1996-2010), doi: 10.1002/14651858

352. Macedo CR, Silva AB, Machado MA, Saconato H, Prado GF: Occlusal splints for treating sleep bruxism (tooth grinding). Cochrane Database Syst Rev 2007 CD005514

353. Macfarlane TV, Blinkhorn AS, Davies RM, Kincey J, Worthington HV: Oro-facial pain in the community: prevalence and associated impact. Community Dent Oral Epidemiol 2002;30:52-60

354. Magnusson T, Egermark I, Carlsson GE: A prospective investigation over two decades on signs and symptoms of TMD and associated variables. A final summary. Acta Odontol Scand 2005;63:99-109

355. Magnusson T, Egermark I, Carlsson GE: A longitudinal epidemiologic study of signs and symptoms of TMD from 15 to 35 years of age. J Orofac Pain 2000;14:310-319

356. Magnusson T, List T, Helkimo H: Self-assessment of pain and discomfort in patients with temporomandibular disorders: a comparison of five different scales with respect to their precision and sensitivity as well as their capacity to register memory of pain and discomfort. J Oral Rehabil 1995;22:549-556

357. Magnusson T, Syren M: Therapeutic jaw exercises and interocclusal appliance therapy. A comparison between two common treatments of temporomandibular disorders. Swed Dent J 1999;23:27-37

358. Maixner W, Fillingim R, Sigurdsson A, Kincaid S, Silva S: Sensitivity of patients with painful temporomandibular disorders to experimentally evoked pain: evidence for altered temporal summation of pain. Pain 1998;76:71-81

359. Majid O: Clinical use of botulinum toxins in oral and maxillofacial surgery. International J Oral Maxillofac Surg 2010;39:197-207

360. Major M, Rompré PH, Guitard F, Tenbokum L, O'Connor KO, Nielsen T, Lavigne GJ: A controlled daytime challenge of motor performance and vigilance in sleep bruxers. J Dent Res 1999;78:1754-1762

361. Major AS: Schienentherapie. Evidenzbasierte Diagnostik und Behandlung bei TMD und CMD. Urban and Fischer, München, Jena 2006

362. Manfredini D, Chiappe G, Bosco M: Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) axis I diagnoses in an Italian patient population. J Oral Rehabil 33, 551-558 (2006)

363. Manfredini D, Ciapparelli A, Dell'Osso L, Bosco M: Mood disorders in subjects with bruxing behavior. J Dent 2005;33:485-490

364. Manfredini D, Guarda-Nardini L: Agreement between Research Diagnostic Criteria for Temporomandibular Disorders and Magnetic Resonance Diagnoses of Temporomandibular disc displacement in a patient population. Int J Oral and Maxillofac Surg 2008;37:612-616

365. Manfredini D, Landi N, Tognini F, Orlando B, Bosco M: Muscle relaxants in the treatment of myofascial face pain. A literature review. Minerva Stomatol 2004;53:305-313

366. Marbach JJ, Raphael KG, Janal MN, Hirschkorn-Roth R: Reliability of clinician judgements of bruxism. J Oral Rehabil 2003;30:113-118

367. Marklund S, Wänman A: A century of controversy regarding the benefit or detriment of occlusal contacts on the mediotrusive side. J Oral Rehabil 2000;27:553-562

368. Marklund S, Wänman A: Risk factors associated with incidence and persistence of signs and symptoms of temporomandibular disorders. Acta Odontol Scand 2010;68:289-299

369. Martin WJJM, Forouzanfar T: The efficacy of anticonvulsants on orofacial pain: a systematic review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:627-633

370. Mason L: Systematic review of topical capsaicin for the treatment of chronic pain. BMJ 2004;328:991-1000

371. Matheus RA, Ramos-Perez FMM de, Menezes AV, Ambrosano GMB, Haiter-Neto F, Bóscolo FN, Almeida SM de: The relationship between temporomandibular dysfunction and head and cervical posture. J Appl Oral Sci 2009;17:204-208

372. Mazza D, Marini M, Impara L, Cassetta M, Scarpato P, Barchetti F, Di Paolo C: Anatomic examination of the upper head of the Lateral Pterygoid Muscle using Magnetic Resonance Imaging and clinical data. J Craniofac Surg 2009;20:1508-1511

373. McCarty WL, Farrar WB: Surgery for internal derangements of the temporomandibular joint. J Prosthet Dent 1979;42:191

374. McMillan AS, Wong MCM, Zheng J, Lam CLK: Prevalence of orofacial pain and treatment seeking in Hong Kong Chinese. J Orofac Pain 2006;20:218-225

375. McNeely ML, Armijo Olivo S, Magee DJ: A systematic review of the effectiveness of physical therapy interventions for TMD. Phys Ther 2006;86:710-725

376. Medeiros JS de, Vieira GF, Nishimura PY: Laser application effects on the bite strength of the masseter muscle, as an orofacial pain treatment. Photomed Laser Surg 2005;23:373-376

377. Medlicott MS, Harris S.R.: A systematic review of the effectiveness of exercise, manual therapy, electrotherapy, relaxation training, and biofeedback in the management of TMD. Phys Ther 2006;86:955-973

378. Mejersjö C, Wenneberg B: Diclofenac sodium and occlusal splint therapy in TMJ osteoarthritis: a randomized controlled trial. J Oral Rehabil 2008;35:729-738

379. Melchers L, Van Weert E, Beurskens C, Reintsema H, Slagter A, Roodenburg J, Dijkstra P: Exercise adherence in patients with trismus due to head and neck oncology: a qualitative study into the use of the Therabite®. Int J Oral Maxillofac Surg 2009;38:947-954

380. Melis M, Abou-Atme YS: Prevalence of bruxism awareness in a Sardinian population. Cranio 2003;21:144-151

381. Melzack R., Wall P.: Pain mechanisms: a new theory. Science 1965;3699:971-979

382. Melzack R: Evolution of the neuromatrix theory of pain. The Prithvi Raj Lecture: presented at the third World Congress of World Institute of Pain, Barcelona 2004. Pain Pract 2004;5:85-94

383. Mense, S Neurobiologische Grundlagen von Muskelschmerz. Schmerz 1999;13:3-17

384. Micheelis W, Heinrich R: Dritte Deutsche Mundgesundheitsstudie (DMS III). Ergebnisse, Trends und Problemanalysen auf der Grundlage bevölkerungsrepräsentativer Stichproben in Deutschland 1997. Zusammenfassung. Dt. Ärzte-Verl, Köln 1999

385. Michelotti A, Farella M, Gallo L, Veltri A, Palla S, Martina R: Effect of Occlusal Interference on Habitual Activity of Human Masseter. J Dent Res 2005;84:644-648

386. Michelotti A, Parisini F, Farella M, Cimino R, Martina R: Fisioterapia muscolare in pazienti con disordini temporomandibolari. Studio clinico controllato. Minerva Stomatol 2000;49:541-548

387. Milam SB: Pathogenesis of degenerative temporomandibular joint arthritides. Odontology 2005;93:7-15

388. Milano V, Desiate A, Bellino R, Garofalo T: Magnetic resonance imaging of temporomandibular disorders: classification, prevalence and interpretation of disc displacement and deformation. Dentomaxillofac Radiol 2000;29:352-361

389. Miles TS: Control of human mandibular posture during locomotion. J Physiol 2004;554:216-226

390. Miller VJ, Bookhan V, Brummer D, Singh JC: A mouth opening index for patients with TMD. J Oral Rehabil 1999;26:534-537

391. Miller VJ, Karic VV, Myers SL: Differences in initial symptom scores between myogenous TMD patients with high and low temporomandibular opening index. Cranio 2006;24:25-28

392. Miller VJ, Yoeli Z, Barnea E, Zeltser C: The effect of parafunction on condylar asymmetry in patients with temporomandibular disorders. J Oral Rehabil 1998;25:721-724

393. Min H, Lee M, Kim J et al.: Alteration of BMP-4 andRunx2expression patterns in mouse temporomandibular joint after ovariectomy. Oral Dis 2007;13:220-227

394. Minagi S, Natsuaki N, Sato T, Akamatsu Y, Shimamura M: Maintenance of condylar position using an occlusal splint after mechanical vibrating-traction of the TMJ. J Oral Rehabil 2001;28:1129-1132

395. Mishra KD, Gatchel RJ, Gardea MA: The relative efficacy of three cognitive-behavioral treatment approaches to temporomandibular disorders. J Behav Med 2000;23:293-309

396. Miyake R, Ohkubo R, Takehara J, Morita M: Oral parafunctions and association with symptoms of temporomandibular disorders in Japanese university students. J Oral Rehabil 2004;31:518-523

397. Moayedi M, Davis KD: Theories of pain: from Specificity to Gate Control. J Neurophysiol 2012, doi: 10.1152/jn.00457.2012

398. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535

399. Moher D, Liberati A, Tetzlaff J, Altman DG, the PRISMA Group: Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6:e1000097. www.prisma-statement.org

400. Moipolai P, Karic VV, Miller VJ: The effect of the gonial angle, ramus length, age and gender on the temporomandibular opening index. J Oral Rehabil 2003;30:1195-1199

401. Morey-Mas M-A, Caubet-Biayna J, Varela-Sende L, Iriarte-Ortabe J-I: Sodium Hyaluronate Improves Outcomes After Arthroscopic Lysis and Lavage in Patients With Wilkes Stage III and IV Disease. J Oral Maxillofac Surg 2010;68:1069-1074

402. Morley S, Eccleston C, Williams A: Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache. Pain 1999;80:1-13

403. Mujakperuo HR, Watson M, Morrison R, Macfarlane TV: Pharmacological interventions for pain in patients with temporomandibular disorders. Cochrane Database Syst Rev 2010, CD004715

404. Mulet M, Decker KL, Look JO, Lenton PA, Schiffman EL: A randomized clinical trial assessing the efficacy of adding 6 x 6 exercises to self-care for the treatment of masticatory myofascial pain. J Orofac Pain 2007;21:318-328

405. Munhoz WC, Marques AP: Body posture evaluations in subjects with internal temporomandibular joint derangement. Cranio 2009;27:231-242

406. Munhoz WC, Marques AP, Siqueira JTT de: Evaluation of body posture in individuals with internal temporomandibular joint derangement. Cranio 2005;23:269-277

407. Naeije M: Local kinematic and anthropometric factors related to the maximum mouth opening in healthy individuals. J Oral Rehabil 2002;29:534-539

408. Nagamatsu-Sakaguchi C, Minakuchi H, Clark GT, Kuboki T: Relationship between the frequency of sleep bruxism and the prevalence of signs and symptoms of temporomandibular disorders in an adolescent population. Int J Prosthodont 2008;21:292-298

409. Naikmasur V, Bhargava P, Guttal K, Burde K: Soft occlusal splint therapy in the management of myofascial pain dysfunction syndrome: a follow-up study. Indian J Dent Res 2008;19:196-203

410. Nakata A, Takahashi M, Ikeda T, Hojou M, Araki S: Perceived psychosocial job stress and sleep bruxism among male and female workers. Commun Dent Oral Epidemiol 2008;36:201-209

411. Narita N, Funato M, Ishii T, Kamiya K, Matsumoto T: Effects of jaw clenching while wearing an occlusal splint on awareness of tiredness, bite force, and EEG power spectrum. J Prosthodont Res 2009;53:120-125

412. Neff A, Gündel H: Anhaltender idiopatischer Gesichtsschmerz bzw. kraniomandibuläre Dysfunktion. In: Henningsen P, Gündel H, Ceballos-Baumann AO (Hrsg): Neuro-Psychosomatik. Grundlagen und Klinik neurologischer Psychosomatik : mit 34 Tabellen. Schattauer, Stuttgart 2006, 211-220

413. Nekora-Azak A, Evlioglu G, Ordulu M, Işsever H: Prevalence of symptoms associated with temporomandibular disorders in a Turkish population. J Oral Rehabil 2006;33:81-84

414. Nelson DA, Landau WM: Jaws: diversities of gnathological history and temporomandibular joint enterprise. J Neurol Neurosurg Psychiatr 1999;67:141-147

415. Nilner M, Ekberg E, Doepel M, Andersson J, Selovuo K, Le Bell Y: Short-term effectiveness of a prefabricated occlusal appliance in patients with myofascial pain. J Orofac Pain 2008;22:209-218

416. Nilsson H, Ekberg E: Do psychological factors and general health influence the short-term efficacy of resilient appliance therapy in patients with temporomandibular disorder pain? Acta Odontol Scand 2010;68:141-147

417. Nilsson H, Limchaichana N, Nilner M, Ekberg E: Short-term treatment of a resilient appliance in TMD pain patients: a randomized controlled trial. J Oral Rehabil 2009;36:547-555

418. Nilsson I, List T, Drangsholt M: Prevalence of temporomandibular pain and subsequent dental treatment in Swedish adolescents. J Orofac Pain 2005;19:144-150

419. Nilsson H: Resilient appliance therapy of temporomandibular disorders. Subdiagnoses, sense of coherence and treatment outcomes. Swed Dent J Suppl 2010;206:9-88

420. Nishimura M, Segami N, Kaneyama K, Sato J, Fujimura K: Comparison of cytokine level in synovial fluid between successful and unsuccessful cases in arthrocentesis of the temporomandibular joint. J Oral Maxillofac Surg 2004;62:284-287

421. Nishioka GJ, Montgomery MT: Masticatory muscle hyperactivity in temporomandibular disorders: is it an extrapyramidally expressed disorder? J Am Dent Assoc 1988;116:514-520

422. Nitzan DW, Etsion I: Adhesive force: the underlying cause of the disc anchorage to the fossa and/or eminence in the temporomandibular joint--a new concept. Int J Oral Maxillofac Surg 2002;31:94-99

423. Nozawa-Inoue K, Amizuka N, Ikeda N, Suzuki A, Kawano Y, Maeda T: Synovial membrane in the temporomandibular joint--its morphology, function and development. Arch Histol Cytol 2003;66:289-306

424. Nunes Rossetti LM, Orlato Rossetti PH, Rodrigues Conti PC, Pereira Araujo CR de: Association between sleep bruxism and TMD. A polysomnographic pilot study. Cranio 2008;26:16-24

425. Núñez SC, Garcez AS, Suzuki SS, Ribeiro MS: Management of mouth opening in patients with temporomandibular disorders through low-level laser therapy and transcutaneous electrical neural stimulation. Photomed Laser Surg 2006;24:45-49

426. Oakley M, Vieira AR: The many faces of the genetics contribution to temporomandibular joint disorder. Orthod Craniofac Res 2008;11:125-135

427. Ogi N, Nagao T, Toyama M: Chronic Dental Infections Mimicking Temporomandibular Disorders. Aust Dent J 2002;47:63-65

428. Ohayon MM, Li KK, Guilleminault C: Risk factors for sleep bruxism in the general population. Chest 2001;119:53-61

429. Ohmure H, Miyawaki S, Nagata J, Ikeda K, Yamasaki K, Al-Kalaly A: Influence of forward head posture on condylar position. J Oral Rehabil 2008;35:795-800

430. Ohrbach R: Assessment and further development of RDC/TMD Axis II biobehavioural instruments: a research programme progress report. J Oral Rehabil 2010;37:784-798

431. Ohrbach R: Symposia IADR 2010 v2 - Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). http://www.rdc-tmdinternational.org/LinkClick.aspx?fileticket=UJOU653jyuM%3Dandtabid=97andmid=1307 , 25.02.2011

432. Okeson JP: Management of temporomandibular disorders and occlusion. MosbyElsevier, Saint Louis Mo 2008

433. Oliveras-Moreno J, Hernandez-Pacheco E, Oliveras-Quintana T, Infante-Cossio P, Gutierrez-Perez J: Efficacy and Safety of Sodium Hyaluronate in the Treatment of Wilkes Stage II Disease. J Oral Maxillofac Surg 2008;66:2243-2246

434. Olivo SA, Bravo J, Magee DJ, Thie NMR, Major PW, Flores-Mir C: The association between head and cervical posture and temporomandibular disorders: a systematic review. J Orofac Pain 2006;20:9-23

435. Olmos SR, Kritz-Silverstein D, Halligan W, Silverstein ST: The effect of condyle fossa relationships on head posture. Cranio 2005;23:48-52

436. Olthoff LW, van der Zel JM, Ruiter WJ de, Vlaar ST, Bosman F: Computer modeling of occlusal surfaces of posterior teeth with the CICERO CAD/CAM system. J Prosthet Dent 2000;84:154-162

437. Ommerborn MA, Kollmann C, Handschel J, Depprich RA, Lang H, Raab WH: A survey on German dentists regarding the management of craniomandibular disorders. Clin Oral Invest 2010;14:137-144

438. Ommerborn MA, Schneider C, Giraki M, Schäfer R, Handschel J, Franz M, Raab WH: Effects of an occlusal splint compared with cognitive-behavioral treatment on sleep bruxism activity. Eur J Oral Sci 2007;115:7-14

439. Österberg T, Carlsson GE: Relationship between symptoms of temporomandibular disorders and dental status, general health and psychosomatic factors in two cohorts of 70-year-old subjects. Gerodontology 2007;24:129-135

440. Ottl P; Lauer H-C [Occlusal splint therapy for functional damage]. Zahnärztliche Praxis 1991;42:458-60, 462

441. Pahkala RH, Laine-Alava MT: Do early signs of orofacial dysfunctions and occlusal variables predict development of TMD in adolescence? J Oral Rehabil 2002;29:737-743

442. Pahkala R, Qvarnström M: Can TMD signs be predicted by early morphological or functional variables. Eur J Orthod 2004;26:367-373

443. Pearce JMS: Myofascial Pain, Fibromyalgia or Fibrositis? Eur Neurol 2004;52:67-72

444. Peck C, Murray G, Gerzina T: How does pain affect jaw muscle activity? The Integrated Pain Adaptation Model. Aust Dent J 2008;53:201-207

445. Pekkan G, Aksoy S, HekImoglu C, Oghan F: Comparative audiometric evaluation of temporomandibular disorder patients with otological symptoms. Journal of Cranio-Maxillofacial Surgery 2010;38:231-234

446. Pereira LJ, Gavião MBD, Bonjardim LR, Castelo PM, Andrade AdS: Ultrasonography and electromyography of masticatory muscles in a group of adolescents with signs and symptoms of TMD. J Clin Pediatr Dent 2006;30:314-319

447. Peretta R, Melison M, Meneghello R et al.: Unilateral masseter muscle hypertrophy: morphofunctional analysis of the relapse after treatment with botulinum toxin. Cranio 2009;27:200-210

448. Pergamalian A, Rudy TE, Zaki HS, Greco CM: The association between wear facets, bruxism, and severity of facial pain in patients with temporomandibular disorders. J Prosthet Dent 2003;90:194-200

449. Peterson AL, Dixon DC, Talcott GW, Kelleher WJ: Habit reversal treatment of temporomandibular disorders: a pilot investigation. J Behav Ther Exp Psychiatry 1993;24:49-55

450. Piquero K, Sakurai K: A clinical diagnosis of diurnal (non-sleep) bruxism in denture wearers. J Oral Rehabil 2000;27:473-482

451. Plesh O, Curtis D, Levine J, McCall WD: Amitriptyline treatment of chronic pain in patients with temporomandibular disorders. J Oral Rehabil 2000;27:834-841

452. Plesh O, Sinisi SE, Crawford PB, Gansky SA: Diagnoses based on the Research Diagnostic Criteria for Temporomandibular Disorders in a biracial population of young women. J Orofac Pain 2005;19:65-75

453. Pow EH, Leung KC, McMillan AS: Prevalence of symptoms associated with temporomandibular disorders in Hong Kong Chinese. J Orofac Pain 2001;15:228-234

454. Pullinger AG, Seligman DA: Quantification and validation of predictive values of occlusal variables in temporomandibular disorders using a multifactorial analysis. J Prosthet Dent 2000;83:66-75

455. Racine M, Tousignant-Laflamme Y, Kloda LA, Dion D, Dupuis G, Choinière M: A systematic literature review of 10years of research on sex/gender and pain perception – Part 2: Do biopsychosocial factors alter pain sensitivity differently in women and men? Pain 2012;153:619-635

456. Racine M, Tousignant-Laflamme Y, Kloda LA, Dion D, Dupuis G, Choinière M: A systematic literature review of 10years of research on sex/gender and experimental pain perception – Part 1: Are there really differences between women and men? Pain 2012;153:602-618

457. Rantala MA, Ahlberg J, Suvinen TI, Savolainen A, Könönen M: Symptoms, signs, and clinical diagnoses according to the research diagnostic criteria for temporomandibular disorders among Finnish multiprofessional media personnel. J Orofac Pain 2003;17:311-316

458. Raphael KG, Marbach JJ: Widespread pain and the effectiveness of oral splints in myofascial face pain. J Am Dent Assoc 2001;132:305-316

459. Raphael KG, Marbach JJ, Gallagher RM, Dohrenwend BP: Myofascial TMD does not run in families. Pain 1999;80:15-22

460. Raphael KG, Marbach JJ, Wolford LM, Keller SE, Bartlett JA: Self-reported systemic, immune-mediated disorders in patients with and without proplast-teflon implants of the temporomandibular joint. J Oral Maxillofac Surg 1999;57:364-70; discussion 370-1

461. Raphael KG, Marbach JJ, KLAUSNER J: Myofascial face pain. Clinical characteristics of those with regional vs. widespread pain. J Am Dent Assoc 2000;131:161-171

462. Raphael KG, Marbach JJ, Klausner JJ, Teaford MF, Fischoff DK: Is bruxism severity a predictor of oral splint efficacy in patients with myofascial face pain? J Oral Rehabil 2003;30:17-29

463. Rauso R, Santagata M, Colella G, Nesi N, Gherardini G, Tartaro G: Can occlusal devices prolong the effect of botulinum toxin type A in the contouring of the lower face? Eur J Plast Surg 2010;33:35-40

464. Reißhauer A, Mathiske-Schmidt K, Küchler I, Umland G, Klapp BF, Mazurek B: Funktionsstörungen der Halswirbelsäule bei Tinnitus. HNO 2006;54:125-131

465. Reißmann D, John M, Schierz O, Wassell R: Functional and psychosocial impact related to specific temporomandibular disorder diagnoses. J Dent 2007;35:643-650

466. Reißmann D, John M, Schierz O, Hirsch C: Eine Kurzversion der RDC/TMD. Schmerz 2009;23:618-627

467. Reiter S, Eli I, Gavish A, Winocur E: Ethnic differences in temporomandibular disorders between Jewish and Arab populations in Israel according to RDC/TMD evaluation. J Orofac Pain 2006;20:36-42

468. Reyes-Velázquez J, Espinosa-Robles C, Salinas-Chapa E: Indometacina-betametasona-metocarbamol como alternativa medica en el síndrome doloroso disfuncional de la ATM. Med Oral 2007;9:17-19

469. Richter M, Ferrari R, Otte D, Kuensebeck H, Blauth M, Krettek C: Correlation of clinical findings, collision parameters, and psychological factors in the outcome of whiplash associated disorders. J Neurol Neurosurg Psychiatr 2004;75:758-764

470. Ries LGK, Bérzin F: Analysis of the postural stability in individuals with or without signs and symptoms of temporomandibular disorder. Braz Oral Res 2008;22:378-383

471. Riley JL, Gilbert GH, Heft MW: Socioeconomic and demographic disparities in symptoms of orofacial pain. J Public Health Dent 2003;63:166-173

472. Riley JL, Gilbert GH: Orofacial pain symptoms: an interaction between age and sex. Pain 2001;90:245-256

473. Riley JL, Robinson ME, Wise EA, Myers CD, Fillingim RB: Sex differences in the perception of noxious experimental stimuli: a meta-analysis. Pain 1998;74:181-187

474. Roark AL, Glaros AG, O'Mahony AM: Effects of interocclusal appliances on EMG activity during parafunctional tooth contact. J Oral Rehabil 2003;30:573-577

475. Robert C, Caillieux N, Wilson CS, Gaudy JF, Arreto CD: World orofacial pain research production: a bibliometric study (2004-2005). J Orofac Pain 2008;22:181-189

476. Roberts CA, Tallents RH, Katzberg RW, Sanchez-Woodworth RE, Espeland MA, Handelman SL: Comparison of internal derangements of the TMJ with occlusal findings. Oral Surg Oral Med Oral Pathol 1987;63:645-650

477. Rocabado Seaton M, Iglarsh ZA: Musculoskeletal approach to maxillofacial pain. Lippincott, Philadelphia 1991

478. Rodrigues D, Siriani AO, Bérzin F: Effect of conventional TENS on pain and electromyographic activity of masticatory muscles in TMD patients. Braz Oral Res 2004;18:290-295

479. Rompré P, Daigle-Landry D, Guitard F, Montplaisir J, Lavigne G: Identification of a Sleep Bruxism Subgroup with a Higher Risk of Pain. J Dent Res 2007;86:837-842

480. Rosenbaum M, Ayllon T: Treating bruxism with the habit-reversal technique. Behav Res Ther 1981;19:87-96

481. Rosted P: Practical recommendations for the use of acupuncture in the treatment of temporomandibular disorders based on the outcome of published controlled studies. Oral Dis 2001;7:109-115

482. Rugh JD, Solberg WK: Oral health status in the United States: temporomandibular disorders. J Dent Educ 1985;49:398-406

483. Rutkiewicz T, Könönen M, Suominen-Taipale L, Nordblad A, Alanen P: Occurrence of clinical signs of temporomandibular disorders in adult Finns. J Orofac Pain 2006;20:208-217

484. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS: Evidence based medicine: what it is and what it isn't. BMJ 1996;312:71-2

485. Sae-Lee D, Wanigaratne K, Whittle T, Peck C, Murray G: A method for studying jaw muscle activity during standardized jaw movements under experimental jaw muscle pain. J Neurosci Meth 2006;157:285-293

486. Sáez-Yuguero MdR, Linares-Tovar E, Calvo-Guirado JL, Bermejo-Fenoll A, Rodríguez-Lozano FJ: Joint hypermobility and disk displacement confirmed by magnetic resonance imaging: A study of women with temporomandibular disorders. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;107:e54

487. Saito ET, Akashi PMH, Sacco IdCN: Global body posture evaluation in patients with temporomandibular joint disorder. Clinics 2009;64, doi: 10.1590/S1807-59322009000100007

488. Sakurai Y, Yamaguchi M, Abiko Y: Inhibitory effect of low-level laser irradiation on LPS-stimulated prostaglandin E2 production and cyclooxygenase-2 in human gingival fibroblasts Eur J Oral Sci 2000;108:29-34

489. Salazar H, Jara-Oseguera A, Rosenbaum T: El canal TRPV1 como diana para tratar el dolor. Rev Neurol 2009;48:357-364

490. Saletu A, Parapatics S, Saletu B, Anderer P, Prause W, Putz H, Adelbauer J, Saletu-Zyhlarz GM: On the Pharmacotherapy of Sleep Bruxism: Placebo-Controlled Polysomnographic and Psychometric Studies with Clonazepam. Neuropsychobiology 2005;51:214-225

491. Saletu A, Parapatics S, Anderer P, Matejka M, Saletu B: Controlled clinical, polysomnographic and psychometric studies on differences between sleep bruxers and controls and acute effects of clonazepam as compared with placebo. Eur Arch Psychiatry Clin Neurosci 2010;260:163-174

492. Sari S, Kucukesmen C, Sonmez H: Evaluation of the applicability of temporomandibular opening index in Turkish children with and without signs and symptoms of temporomandibular joint disorders. Cranio 2008;26:197-201

493. Sarlani E, Garrett PH, Grace EG, Greenspan JD: Temporal summation of pain characterizes women but not men with temporomandibular disorders. J Orofac Pain 2007;21:309-317

494. Sarlani E, Greenspan J: Gender differences in temporal summation of mechanically evoked pain. Pain 2002;97:163-169

495. Sasaki K, Tamura H, Watahiki R, Takeda Y, Tomura K, Noma H, Kameda S: Clinical study of the pumping pressure changes in the temporomandibular joint space before and after arthroscopic surgery. Bull Tokyo Dent Coll 1999;40:149-155

496. Sato C, Sato S, Takashina H, Ishii H, Onozuka M, Sasaguri K: Bruxism affects stress responses in stressed rats. Clin Oral Invest 2010;14:153-160

497. Savabi O, Nejatidanesh F, Khosravi S: Effect of occlusal splints on the electromyographic activities of masseter and temporal muscles during maximum clenching. Quintessence Int 2007;38:e129-32

498. Schierz O, John MT, Schroeder E, Lobbezoo F: Association between anterior tooth wear and TMD pain in a German population. J Prosthet Dent 2007;97:305-309

499. Schiavone V, Adamo D, Ventrella G, Morlino M, Notaris EB, Ravel MG, Kussman F, Piantadosi M, Pollio A, Fortuna G, Mignogna MD: Anxiety, depression, and pain in burning mouth syndrome:first chicken or egg?. Headache 2012;52:1019-1025

500. Schiffman E, Look J, Hodges J et al.: Randomized Effectiveness Study of Four Therapeutic Strategies for TMJ Closed Lock. J Dent Res 2007;86:58-63

501. Schindler HJ, Rong Q, Spieß W: Der Einfluss von Aufbissschienen auf das Rekrutierungsmuster des Musculus temporalis. Dtsch Zahnarztl Z 2000;55:575-581

502. Schindler H, Rues S, Türp J, Schweizerhof K, Lenz J: Jaw Clenching: Muscle and Joint Forces, Optimization Strategies. J Dent Res 2007;86:843-847

503. Schindler HJ, Türp JC: Kiefermuskelschmerz - Neurobiologische Grundlagen. Schmerz 2002;16:346-354

504. Schindler HJ, Türp Jc, Blaser R, Lenz J: Differential activity patterns in the masseter muscle under simulated clenching and grinding forces. J Oral Rehabil 2005;32:552-563

505. Schindler HJ, Türp JC, Sommer C, Kares H, Nilges P, Hugger A: Therapie bei Schmerzen der Kaumuskulatur. Schmerz 2007;21:102-115

506. Schmitter M, Balke Z, Hassel A, Ohlmann B, Rammelsberg P: The prevalence of myofascial pain and its association with occlusal factors in a threshold country non-patient population. Clin Oral Invest 2007;11:277-281

507. Schmitter M, Kress B, Ohlmann B, Henningsen P, Rammelsberg P: Psychosocial behaviour and health care utilization in patients suffering from temporomandibular disorders diagnosed on the basis of clinical findings and MRI examination. Eur J Pain 2005;9:243-250

508. Schmitter M, Rammelsberg P, Hassel A: The prevalence of signs and symptoms of temporomandibular disorders in very old subjects. J Oral Rehabil 2005;32:467-473

509. Schubert R, Frank S: Zur Epidemiologie der Myoarthropathie. Eine Längsschnittstudie über fünf Jahre. Dtsch Zahnarztl Z 1980;35:303-305

510. Schüller BK, Neugebauer EAM: Evidenz zur Laserakupunktur bei orthopädischen Erkrankungen. Ein systematisches Review. Schmerz 2008;22:9-15

511. Scott NA, Guo B, Barton PM, Gerwin RD: Trigger point injections for chronic non-malignant musculoskeletal pain: a systematic review. Pain Med 2009;10:54-69

512. Seedorf H, Weitendorf H, Scholz A, Kirsch I, Heydecke G: Effect of non-working occlusal contacts on vertical condyle position. J Oral Rehabil 2009;36:435-441

513. Seedorf H, Scholz A, Kirsch I, Fenske C, Jüde HD: Pivot appliances? Is there a distractive effect on the temporomandibular joint? J Oral Rehabil 2007;34:34-40

514. Sessle BJ: Acute and chronic craniofacial pain. Brainstem mechanism of nociceptive transmission and neuroplasticity, and their clinical correlates. Crit Rev Oral Biol Med 2000;11:57-91

515. Shankland WE: Patients seeking treatment for craniofacial pain: a retrospective study of 300 patients. Cranio 2008;26:241-245

516. Shedden Mora MC, Bleichhardt G, Weber D, Neff A, Rief W: Biofeedback bei kraniomandibulären Dysfunktionen. Psychotherapeut 2010;55:217-224

517. Sheean G: Botulinum toxin for the treatment of musculoskeletal pain and spasm. Curr Pain Headache Rep 2002;6:460-469

518. Sheets DW, Okamoto T, Dijkgraaf LC, Milam SB, Schmitz JP, Zardeneta G: Free Radical Damage in Facsimile Synovium: Correlation with Adhesion Formation in Osteoarthritic TMJs. J Prosthodontics 2006;15:9-19

519. Shimizu N, Yamaguchi M, Goseki T, Shibata Y, Takiguchi H, Iwasawa T, Abiko Y: Inhibition of Prostaglandin E2 and Interleukin 1- Production by Low-power Laser Irradiation in Stretched Human Periodontal Ligament Cells. J Dent Res 1995;74:1382-1388

520. Shodadai SP, Türp JC, Gerds T, Strub JR: Is there a benefit of using an arbitrary facebow for the fabrication of a stabilization appliance? Int J Prosthodont 2001;14:517-522

521. Siccoli MM, Bassetti CL, Sándor PS: Facial pain: clinical differential diagnosis. The Lancet Neurology 2006;5:257-267

522. Simmons HC, Gibbs SJ: Anterior repositioning appliance therapy for TMJ disorders: specific symptoms relieved and relationship to disk status on MRI. Cranio 2005;23:89-99

523. Simunovic Z: Low level laser therapy with trigger points technique: a clinical study on 243 patients. J Clin Laser Med Surg 1996;14:163-167

524. Simunovic Z, Trobonjaca T, Trobonjaca Z: Treatment of medial and lateral epicondylitis--tennis and golfer's elbow--with low level laser therapy: a multicenter double blind, placebo-controlled clinical study on 324 patients. J Clin Laser Med Surg 1998;16:145-151

525. Singer E, Dionne R: A controlled evaluation of ibuprofen and diazepam for chronic orofacial muscle pain. J Orofac Pain 1997;11:139-146

526. Slade GD, Diatchenko L, Ohrbach R, Maixner W: Orthodontic Treatment, Genetic Factors and Risk of Temporomandibular Disorder. Semin Orthod 2008;14:146-156

527. Slavicek R, Sato S: Bruxismus als Stressbewältigungsfunktion des Kauorgans. Wien Med Wochenschr 2004;154:584-589

528. Sluka KA, Walsh D: Transcutaneous electrical nerve stimulation: basic science mechanisms and clinical effectiveness. J Pain 2003;4:109-121

529. Smolka W, Yanai C, Smolka K, Iizuka T: Efficiency of arthroscopic lysis and lavage for internal derangement of the temporomandibular joint correlated with Wilkes classification. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106:317-323

530. Snaith RP, Zigmond AS: The hospital anxiety and depression scale. Br Med J (Clin Res Ed) 1986; 292:344

531. Sommer C: Pharmakologische Behandlung orofazialer Schmerzen. Schmerz 2002;16:381-388

532. Song PC, Schwartz J, Blitzer A: The emerging role of botulinum toxin in the treatment of temporomandibular disorders. Oral Dis 2007;13:253-260

533. Sönmez H, Sari S, Oksak Oray G, Camdeviren H: Prevalence of temporomandibular dysfunction in Turkish children with mixed and permanent dentition. J Oral Rehabil 2001;28:280-285

534. Sorel B, Piecuch JF: Long-term evaluation following temporomandibular joint arthroscopy with lysis and lavage. Int J Oral Maxillofac Surg 2000;29:259-263

535. Soyka D: Der chronische Gesichtsschmerz. Internist (Berl) 1999;40:148-152

536. Stam HJ, McGrath PA, Brooke RI: The effects of a cognitive-behavioral treatment program on temporo-mandibular pain and dysfunction syndrome. Psychosom Med 1984;46:534-545

537. Stapelmann H, Türp JC: The NTI-tss device for the therapy of bruxism, temporomandibular disorders, and headache – Where do we stand? A qualitative systematic review of the literature. BMC Oral Health 2008;8:22

538. Sterne JA, Egger M, Smith GD: Systematic reviews in health care: Investigating and dealing with publication and other biases in meta-analysis. BMJ 2001;323:101-105

539. Sterne JAC, Egger M, Moher D (editors). Chapter 10: Addressing reporting biases. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Intervention.* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

540. Stohler CS: Craniofacial Pain and Motor Function: Pathogenesis, Clinical Correlates, and Implications Crit Rev Oral Biol Med 1999;10:504-518

541. Stowell AW, Gatchel RJ, Wildenstein L: Cost-effectiveness of treatments for temporomandibular disorders: biopsychosocial intervention versus treatment as usual. J Am Dent Assoc 2007;138:202-208

542. Stroup D, Berlin J, Morton S, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB: Meta-analysis of observational studies in epidemiology. A proposal reporting. JAMA 2000; 19:2008-2012

543. Sun W, Dong L, Kaneyama K, Takegami T, Segami N: Bacterial diversity in synovial fluids of patients with TMD determined by cloning and sequencing analysis of the 16S ribosomal RNA gene. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:566-571

544. Svensson P: Muscle pain in the head: overlap between temporomandibular disorders and tension-type headaches. Curr Opin Neurol 2007;20:320-325

545. Svensson P, Burgaard A, Schlosser S: Fatigue and pain in human jaw muscles during a sustained, low-intensity clenching task. Arch Oral Biol 2001;46:773-777

546. Svensson P, Jadidi F, Arima T, Baad-Hansen L, Sessle BJ: Relationships between craniofacial pain and bruxism. J Oral Rehabil 2008;35:524-547

547. Svensson P, Graven-Nielsen T: Craniofacial muscle pain: review of mechanisms and clinical manifestations. J Orofac 2001;15:117-145

548. Svensson P, Wang K, Sessle B, Arendt-Nielsen L: Associations between pain and neuromuscular activity in the human jaw and neck muscles. Pain 2004;109:225-232

549. Szentpétery A, Huhn E, Fazekas A: Prevalence of mandibular dysfunction in an urban population in Hungary. Community Dent Oral Epidemiol 1986;14:177-180

550. Tal M, Sharav Yair: Jaw clenching modulates sensory perception in high- but not in low-hypnotizable subjects. J Orofac 2005;19:76-81

551. Tallents RH, Katzberg RW, Murphy W, Proskin H: Magnetic resonance imaging findings in asymptomatic volunteers and symptomatic patients with temporomandibular disorders. J Prosthet Dent 1996;75:529-533

552. Tanaka A, Kawashiri S, Kumagai S, Takatsuka S, Narinobou M, Nakagawa K, Tanaka S: Expression of matrix metalloproteinase-2 in osteoarthritic fibrocartilage from human mandibular condyle. J Oral Pathol Med 2000;29:314-320

553. Tanaka A, Kumagai S, Kawashiri S, Takatsuka S, Nakagawa K, Yamamoto E, Matsumoto N: Expression of matrix metalloproteinase-2 and -9 in synovial fluid of the temporomandibular joint accompanied by anterior disc displacement. J Oral Pathol Med 2001;30:59-64

554. Tanaka E, Yamano E, Dalla-Bona DA, Watanabe M, Inubushi T, Shirakura M, Sano R, Takahashi K, van Eijden T, Tanne K: Dynamic Compressive Properties of the Mandibular Condylar Cartilage J Dent Res 2006;85:571-575

555. Tecco S, Crincoli V, Di Bisceglie B, Saccucci M, MacrÍ M, Polimeni A, Festa F: Signs and symptoms of temporomandibular joint disorders in Caucasian children and adolescents. Cranio 2011;29:71-79

556. Teel Wall R: Simple BruxGuard fabrication. Dent Equip Mat 2005;31-32

557. Tognini F, Manfredini D, Melchiorre D, Bosco M: Comparison of ultrasonography and magnetic resonance imaging in the evaluation of temporomandibular joint disc displacement. J Oral Rehabil 2005;32:248-253

558. Tojyo I, Yamaguchi A, Nitta T, Yoshida H, Fujita S, Yoshida T: Effect of hypoxia and interleukin-1ß on expression of tenascin-C in temporomandibular joint. Oral Dis 2008;14:45-50

559. Tokiwa O, Park B, Takezawa Y, Takahashi Y, Sasaguri K, Sato S: Relationship of tooth grinding pattern during sleep bruxism and dental status. Cranio 2008;26:287-293

560. Torii K, Chiwata I: Relationship between habitual occlusal position and flat bite plane induced occlusal position in volunteers with and without temporomandibular joint sounds. Cranio 2005;23:16-21

561. Torii K, Chiwata I: Occlusal adjustment using the bite plate-induced occlusal position as a reference position for temporomandibular disorders: a pilot study. Head Face Med 2010;6:5

562. Tough EA, White AR, Cummings TM, Richards SH, Campbell JL: Acupuncture and dry needling in the management of myofascial trigger point pain: a systematic review and meta-analysis of randomised controlled trials. Eur J Pain 2009;13:3-10

563. Townsend D, Nicholson RA, Buenaver L, Bush F, Gramling S: Use of a habit reversal treatment for temporomandibular pain in a minimal therapist contact format. J Behav Ther Exp Psychiatry 2001;32:221-239

564. Travell JG, Simons LS: Myofascial pain and dysfunction. The trigger point manual / David G. Simons, Janet G. Travell, Lois S. Simons ; illustrations by Barbara D. Cummings ; with contributions by Diane Abeloff and Jason Lee. Vol.1, Upper half of body (1983-1999)

565. Türker KS: Muscle pain theories: Is there a third dimension? Clin Neurophysiol 2010;121:634-635

566. Türp JC: Temporomandibular pain. Clinical presentation and impact. Quintessenz, Berlin ; London 2000

567. Türp JC, Jokstad A, Motschall E, Schindler HJ, Windecker-Gétaz I, Ettlin DA: Is there a superiority of multimodal as opposed to simple therapy in patients with temporomandibular disorders? A qualitative systematic review of the literature. Clin Oral Implants Res 2007;18:138-150

568. Türp JC, Komine F, Hugger A: Efficacy of stabilization splints for the management of patients with masticatory muscle pain: a qualitative systematic review. Clin Oral Invest 2004;8:179-195

569. Türp JC, Schindler HJ, Pritsch M, Rong Q: Antero-posterior activity changes in the superficial masseter muscle after exposure to experimental pain. Eur J Oral Sci 2002;110:83-91

570. Türp JC, Schindler H: The dental occlusion as a suspected cause for TMDs: epidemiological and etiological considerations. J Oral Rehabil 2012;39:502-512

571. Türp JC, Schindler HJ: Chronische Myoarthropathien des Kausystems. Schmerz 2004;18:109-117

572. Tullberg M, Alstergren PJ, Ernberg MM: Effects of low-power laser exposure on masseter muscle pain and microcirculation. Pain 2003;105:89-96

573. Turasi B, Ari-Demirkaya A, Biren S: Comparison of increased overjet cases and controls: normative data for condylar positions. J Oral Rehabil 2007;34:129-135

574. Turk D: Cognitive-behavioral approach to the treatment of chronic pain patients. Reg Anesth Pain Med 2003;28:573-579

575. Turner JA, Mancl L, Aaron LA: Brief cognitive-behavioral therapy for temporomandibular disorder pain: effects on daily electronic outcome and process measures. Pain 2005;117:377-387

576. Turner JA, Brister H, Huggins KH, Mancl L, La Aaron, Truelove EL: Catastrophizing is associated with clinical examination findings, activity interference, and health care use among patients with TMD. J Orofac Pain 2005;19:291-300

577. Turner JA, Holtzman S, Mancl L: Mediators, moderators, and predictors of therapeutic change in cognitive–behavioral therapy for chronic pain. Pain 2007;127:276-286

578. Turner JA, Mancl L, Aaron L: A Short- and long-term efficacy of brief cognitive-behavioral therapy for patients with chronic temporomandibular disorder pain: A randomized, controlled trial. Pain 2006;121:181-194

579. U.S. National Library of Medicine: MEDLINE® Citation Counts by Year of Publication. http://www.nlm.nih.gov/bsd/medline_cit_counts_yr_pub.html, accessed on 27.02.2011

580. Uhac I, Kovac Z, Valentić-Peruzović M, Juretić M, Moro LJ, Grzić R: The influence of war stress on the prevalence of signs and symptoms of temporomandibular disorders. J Oral Rehabil 2003;30:211-217

581. Unell L, Johansson A, Carlsson G, Halling A, Söderfeldt B: Changes in reported orofacial symptoms over a ten-year period as reflected in two cohorts of fifty-year-old subjects. Acta Odontol Scand 2006;64:202-208

582. Uysal S, Kansu H, Akhan O, Kansu O: Comparison of ultrasonography with magnetic resonance imaging in the diagnosis of temporomandibular joint internal derangements: A preliminary investigation Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;94:115-121

583. van der Meulen MJ, Lobbezoo F, Aartman IHA, Naeije M: Ethnic background as a factor in temporomandibular disorder complaints. J Orofac Pain 2009;23:38-46

584. van der Windt DA, van der Heijden GJ, van den Berg SG, ter Riet G, Winter AF de, Bouter LM: Ultrasound therapy for musculoskeletal disorders: a systematic review. Pain 1999;81:257-271

585. van der Zaag J, Lobbezoo F, Wicks DJ, Visscher CM, Hamburger HL, Naeije M: Controlled assessment of the efficacy of occlusal stabilization splints on sleep bruxism. J Orofac Pain 2005;19:151-158

586. van Selms MKA, Lobbezoo F, Wicks DJ, Hamburger HL, Naeije M: Craniomandibular pain, oral parafunctions, and psychological stress in a longitudinal case study. J Oral Rehabil 2004;31:738-745

587. van Selms MKA, Lobbezoo F, Visscher CM, Naeije M: Myofascial temporomandibular disorder pain, parafunctions and psychological stress. J Oral Rehabil 2008;35:45-52

588. van Selms M, Wang K, Lobbezoo F, Svensson P, Arendt Nielsen L, Naeije M: Effects of masticatory muscle fatigue without and with experimental pain on jaw-stretch reflexes in healthy men and women. Clin Neurophysiol 2005;116:1415-1423

589. van 't Spijker A, Kreulen CM, Creugers NHJ: Attrition, occlusion, (dys)function, and intervention: a systematic review. Clin Oral Implants Res 2007;18:117-126

590. Vanderas AP, Manetas KJ: Relationship between malocclusion and bruxism in children and adolescents: a review. Pediatr Dent 1995;17:7-12

591. Velly AM, Gornitsky M, Philippe P: Contributing factors to chronic myofascial pain: a case-control study. Pain 2003;104:491-499

592. Venâncio RA de, Alencar FGPJ, Zamperini C: Different substances and dry-needling injections in patients with myofascial pain and headaches. Cranio 2008;26:96-103

593. Venancio RA, Alencar FG, JR, Zamperini C: Botulinum toxin, lidocaine, and dry-needling injections in patients with myofascial pain and headaches.pdf. Cranio 2009;27:46-53

594. Verhagen A, de Vet HCW, de Bie RA, Kessels AGH, Boers M, Bouter LM, Knipschild PG: The Delphi List: A Criteria List for Quality Assessment of Randomized Clinical Trials for Conducting Systematic Reviews Developed by Delphi Consensus. J Clin Epidemiol 1998;51:1235-1241

595. Vierola A, Suominen AL, Ikavalko T et al.: Clinical signs of temporomandibular disorders and various pain conditions among children 6 to 8 years of age: the PANIC study. J Orofac Pain 2012;26:17-25

596. Visscher CM, Boer W de, Lobbezoo F, Habets LLMH, Naeije M: Is there a relationship between head posture and craniomandibular pain? J Oral Rehabil 2002;29:1030-1036

597. Visscher C, Hofman N, Mes C, Lousberg R, Naeije M: Is temporomandibular pain in chronic whiplash-associated disorders part of a more widespread pain syndrome? Clin J Pain 2005;21:353-357

598. Waldeyer A: Anatomie des Menschen. 17 Auflage. De Gruyter, Berlin 2003

599. Wang J, Chao Y, Wan Q, Zhu Z: The possible role of estrogen in the incidence of temporomandibular disorders. Med Hypotheses 2008;71:564-567

600. Wang M, He J, Chen C, Widmalm SE: A preliminary anatomical study on the association of condylar and occlusal asymmetry. Cranio 2011;29:111-116

601. Wang K, Svensson P, Arendt-Nielsen L: Effect of tonic muscle pain on short-latency jaw-stretch reflexes in humans. Pain 2000;88:189-197

602. Warren MP, Fried JL: Temporomandibular disorders and hormones in women. Cells Tissues Organs 2001;169:187-192

603. Wassell, R. W.; Moufti, M. A.; Meechan, J. G.; Steen, in; Steele, J. G. A method for clinically defining improvers in chronic pain studies. J Orofac Pain 2008;22:30-40

604. Watanabe T, Ichikawa K, Clark GT: Bruxism levels and daily behaviors: 3 weeks of measurement and correlation. J Orofac Pain 2003;17:65-73

605. Wei L, Xiong H, Li B et al.: Change of HA molecular size and boundary lubrication in synovial fluid of patients with temporomandibular disorders. J Oral Rehabil 2010;37:271-277

606. Wheeler AH: Myofascial pain disorders: theory to therapy. Drugs 2004;64:45-62

607. Wig AD, Aaron LA, Turner JA, Huggins KH, Truelove E: Short-term clinical outcomes and patient compliance with temporomandibular disorder treatment recommendations. J Orofac Pain 2004;18:203-213

608. Williams, Amanda C. de C.; Eccleston, Christopher; Morley, StephenPsychological therapies for the management of chronic pain (excluding headache) in adultsCochrane Database Syst 11, CD007407 doi:10.1002/14651858.CD007407.pub3

609. Winocur E, Gavish A, Halachmi M, Bloom A, Gazit E: Generalized joint laxity and its relation with oral habits and temporomandibular disorders in adolescent girls. J Oral Rehabil 2000;27:614-622

610. Winocur E, Gavish A, Halachmi M, Eli I, Gazit E: Topical application of capsaicin for the treatment of localized pain in the temporomandibular joint area. J Orofac Pain 2000;14:31-36

611. Winocur E, Gavish A, Emodi-Perlman A, Halachmi M, Eli I: Hypnorelaxation as treatment for myofascial pain disorder: a comparative study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;93:429-434

612. Winocur E, Steinkeller-Dekel M, Reiter S, Eli I: A retrospective analysis of temporomandibular findings among Israeli-born patients based on the RDC/TMD. J Oral Rehabil 2009;36:11-17

613. Winocur E, Uziel N, Lisha T, Goldsmith C, Eli I: Self-reported Bruxism - associations with perceived stress, motivation for control, dental anxiety and gagging*. J Oral Rehabil 2011;38:3-11

614. Wirz S, Wartenberg HC, Wittmann M et al.: Versorgung von Patienten mit chronischem orofazialem Schmerz. Schmerz 2003;17:325-331

615. Wise EA, Price DD, Myers CD, Heft MW, Robinson ME: Gender role expectations of pain: relationship to experimental pain perception. Pain 2002;96:335-342

616. Woda A, Pionchon P: A unified concept of idiopathic orofacial pain. Clinical features. J Orofac Pain 1999;13:172-184

617. Woda A, Pionchon P: A unified concept of idiopathic orofacial pain. Pathophysiologic features. J Orofac Pain 2000;14:196-212

618. Woolf C, Salter M: Neuronal Plasticity: Increasing the Gain in Pain. Science 2000;288:1765-1768

619. Wright EF: Referred craniofacial pain patterns in patients with temporomandibular disorder. J Am Dent Assoc 2000;131:1307-1315

620. Wright E, Anderson G, Schulte J: A randomized clinical trial of intraoral soft splints and palliative treatment for masticatory muscle pain. J Orofac Pain 1995;9:192-199

621. Wu YW, Bi YP, Kou XX et al.: 17-Beta-estradiol enhanced allodynia of inflammatory temporomandibular joint through upregulation of hippocampal TRPV1 in ovariectomized rats. J Neurosci 2010;30:8710-8719

622. Wu YW, Bi YP, Kou XX, Xu W, Ma LQ, Wang KW, Gan YH, Ma XC; 17-Beta-estradiol enhanced allodynia of inflammatory temporomandibular joint through upregulation of hippocampal TRPV1 in ovariectomized rats. J Neurosci 2010;30:8710-8719

623. Yanez-Vico RM, Iglesias-Linares A, Torres-Lagares D, Gutierrez-Perez JL, Solano-Reina E: Association between condylar asymmetry and Temporo- mandibular disorders using 3D-CT. Med Oral 2012:e852–e858

624. Yap AUJ, Chua EK, Tan KBC, Chan YH: Relationships between depression/somatization and self-reports of pain and disability. J Orofac Pain 2004;18:220-225

625. Yap AUJ, Dworkin SF, Chua EK, List T, Tan KBC, Tan HH: Prevalence of temporomandibular disorder subtypes, psychologic distress, and psychosocial dysfunction in Asian patients. J Orofac Pain 2003;17:21-28

626. Yatani H, Studts J, Cordova M, Carlson CR, Okeson JP: Comparison of sleep quality and clinical and psychologic characteristics in patients with temporomandibular disorders. J Orofac Pain 2002;16:221-228

627. Yoshida K, Takatsuka S, Tanaka A, Hatada E, Nakamura H, Nakagawa K, Okada Y: Aggrecanase analysis of synovial fluid of temporomandibular joint disorders. Oral Dis 2005;11:299-302

628. Yoshida K, Takatsuka S, Hatada E, Nakamura H, Tanaka A, Ueki K, Nakagawa K, Okada Y, Yamamoto E, Fukuda R: Expression of matrix metalloproteinases and aggrecanase in the synovial fluids of patients with symptomatic temporomandibular disorders. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102:22-27

629. Yoshida K, Iizuka T: Botulinum toxin treatment for upper airway collapse resulting from TMJ dilocation due to jaw-opening dystonia. Cranio 2006;24:217-222

630. Yoshihara T, Shigeta K, Hasegawa H, Ishitani N, Masumoto Y, Yamasaki Y: Neuroendocrine responses to psychological stress in patients with myofascial pain. J Orofac Pain 2005;19:202-208

631. Yoshimi H, Sasaguri K, Tamaki K, Sato S: Identification of the occurrence and pattern of masseter muscle activities during sleep using EMG and accelerometer systems. Head Face Med 2009;5:7

632. Younger JW, Shen YF, Goddard G, Mackey SC: Chronic myofascial temporomandibular pain is associated with neural abnormalities in the trigeminal and limbic systems. Pain 2010;149:222-228

633. Yu XM, Sessle BJ, Vernon H, Hu JW: Effects of inflammatory irritant application to the rat temporomandibular joint on jaw and neck muscle activity. Pain 1995;60:143-149

634. Yuasa H, Kurita K, Westesson P: External validity of a randomised clinical trial of temporomandibular disorders: analysis of the patients who refused to participate in research. Br J Oral Maxillofac Surg 2003;41:129-131

635. Zhang C, Chen L, Zhang F, Zhang H, Feng H, Dai G: A New Virtual Dynamic Dentomaxillofacial System for Analyzing Mandibular Movement, Occlusal Contact, and TMJ Condition. Digital Human Modeling LNCS 4561, Springer 2007, 747-756

636. Zhang X: Acupuncture: Review and analysis reports on controlled clinical trials. 2002 http://site.ebrary.com/lib/academiccompletetitles/home.action

637. Zhang SY, Huang D, Liu XM, Yang C, Undt G, Haddad M, Chen ZZ: Arthroscopic treatment for intra-articular adhesions of the TMJ. J Oral Maxillofac Surg 2011;69:2120-2127

638. Ziegler CM, Wiechnik J, Mühling J: Analgesic Effects of Intra-Articular Morphine in Patients With Temporomandibular Joint Disorders: A Prospective, Double-Blind, Placebo-Controlled Clinical Trial. J Oral Maxillofac Surg 2010;68:622-627

639. Zwijnenburg A, John M, Reiber T: Schmerz als bestimmender Faktor für den subjektiven Behandlungsbedarf kraniomandibulärer Dysfunktionen. In: Lipp MDW (Hrsg): Kiefer- und Gesichtsschmerz. Diagnose und Therapie in der zahnärztlichen Praxis ; Referate der 7. Jahrestagung des Interdisziplinären Arbeitskreises Zahnärztliche Anästhesie. Schlüter, Hannover 2002, 44-46

640. http://auricularacupuncturetraining.com/auricular-acupuncture/

641. http://www.cvdentus.com.br/English/oclusal.html

642. http://www.dentistry.unc.edu/acupuncture/

643. http://www.dgfdt.de/zahnaerzte-mitglieder/dokumente-formulare/

644. http://www.exodontia.info/Bruxism.html

645. http://www.ncbi.nlm.nih.gov

Appendices

Appendix I. Search strategy of Acupuncture for Myofacial pain

MEDLINE via PubMed. Database entry date: 01.11.2012

#1 Myofascial Pain Syndromes [MeSH]
#2 Craniomandibular Disorders [MeSH]
#3 Temporomandibular Joint Dysfunction Syndrome [MeSH]
#4 Temporomandibular Joint Disorders [MeSH]
#5 myofascial [tiab] AND pain [tiab] AND syndrom* [tiab]
#6 myofascial [tiab] AND trigger point [tiab] AND pain [tiab]
#7 craniomandibular [tiab] AND disorder* [tiab]
#8 craniomandibular disease* [tiab]
#9 temporomandibular joint dysfunction syndrome [tiab] OR myofascial pain dysfunction syndrome, temporomandibular joint [tiab]
#10 TMJ [tiab] AND syndrome [tiab]
#11 Costen* [tiab] AND syndrome [tiab]
#12 temporomandibular [tiab] AND joint [tiab] AND syndrome [tiab]
#13 temporomandibular [tiab] AND joint [tiab] AND disorder* [tiab]
#14 TMJ [tiab] AND disorder* [tiab]
#15 temporomandibular [tiab] AND disorder* [tiab]
#16 temporomandibular [tiab] AND joint [tiab] AND disease* [tiab]
#17 TMJ [tiab] AND disease* [tiab]
#18 craniofacial pain [tiab]OR masticatory muscle disorder [tiab] OR masticatory muscle pain [tiab] OR orofacial muscle pain [tiab] OR chronic muscle pain [tiab] OR myofacial pain [tiab]OR myogenous facial pain [tiab]OR myofunctional pain [tiab] OR orofacial myofunctional disorder* [tiab] OR myofunctional disorder [tiab]OR myoarthropat*[tiab]
#19 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
#20 Acupuncture [MeSH]
#21 Acupuncture therapy [MeSH]
#22 Acupuncture analgesia [MeSH]
#23 acupunctur* [tiab]
#24 acupunctur therap* [tiab]
#25 acupunctur* [tiab] AND analgesi* [tiab]
#26 acupunctur*[tiab] AND anesthesi* [tiab]
#27 dry needl* [tiab]
#28 #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27
#29 #19 AND #28
The above described search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision); PubMed format as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of *The Cochrane Handbook for Systematic Reviews of Interventions,* Version 5.0.2 [updated March 2011].

Appendix II. Search strategy of LLLT for Myofacial pain
MEDLINE via Pubmed. Database entry date: 01.11.2012
#1 Myofascial Pain Syndromes [MeSH]
#2 Craniomandibular Disorders [MeSH]
#3 Temporomandibular Joint Dysfunction Syndrome [MeSH]
#4 Temporomandibular Joint Disorders [MeSH]
#5 myofascial [tiab] AND pain [tiab] AND syndrom* [tiab]
#6 myofascial [tiab] AND trigger point [tiab] AND pain [tiab]

#7 craniomandibular [tiab] AND disorder* [tiab]
#8 craniomandibular disease* [tiab]
#9 temporomandibular joint dysfunction syndrome [tiab] OR myofascial pain dysfunction syndrome, temporomandibular joint [tiab]
#10 TMJ [tiab] AND syndrome [tiab]
#11 Costen* [tiab] AND syndrome [tiab]
#12 temporomandibular [tiab] AND joint [tiab] AND syndrome [tiab]
#13 temporomandibular [tiab] AND joint [tiab] AND disorder* [tiab]
#14 TMJ [tiab] AND disorder* [tiab]
#15 temporomandibular [tiab] AND disorder* [tiab]
#16 temporomandibular [tiab] AND joint [tiab] AND disease* [tiab]
#17 TMJ [tiab] AND disease* [tiab]
#18 craniofacial pain [tiab]OR masticatory muscle disorder [tiab] OR masticatory muscle pain [tiab] OR orofacial muscle pain [tiab] OR chronic muscle pain [tiab] OR myofacial pain [tiab]OR myogenous facial pain [tiab]OR myofunctional pain [tiab] OR orofacial myofunctional disorder* [tiab] OR myofunctional disorder [tiab]OR myoarthropat*[tiab]
#19 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
#15 laser Therapy, Low-Level [MeSH]
#16 laser therap*[tiab] AND low-level [tiab]
#17 laser therap* [tiab] AND low level [tiab]
#18 laser [tiab] AND irradiation [tiab] AND low-power [tiab]
#19 laser [tiab] AND phototherap* [tiab]
#20 low-power [tiab] AND laser therap* [tiab]
#21 low power [tiab] AND laser therap* [tiab]
#22 LLLT [tiab] OR low-power laser irradiation [tiab] OR low power laser irradiation [tiab]
#23 laser [tiab] AND biostimulation [tiab]
#24 #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR#22 OR #23
#25 #19 AND #24
The above described search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision); PubMed format as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of *The Cochrane Handbook for Systematic Reviews of Interventions,* Version 5.0.2 [updated March 2011].

Appendix III. Search strategy of Drugs for Myofacial Pain
MEDLINE via Pubmed. Database entry date: 01.11.2012
#1 Myofascial Pain Syndromes [MeSH]
#2 Craniomandibular Disorders [MeSH]
#3 Temporomandibular Joint Dysfunction Syndrome [MeSH]
#4 Temporomandibular Joint Disorders [MeSH]
#5 myofascial [tiab] AND pain [tiab] AND syndrom* [tiab]
#6 myofascial [tiab] AND trigger point [tiab] AND pain [tiab]
#7 craniomandibular [tiab] AND disorder* [tiab]
#8 craniomandibular disease* [tiab]
#9 temporomandibular joint dysfunction syndrome [tiab] OR myofascial pain dysfunction syndrome, temporomandibular joint [tiab]
#10 TMJ [tiab] AND syndrome [tiab]
#11 Costen* [tiab] AND syndrome [tiab]
#12 temporomandibular [tiab] AND joint [tiab] AND syndrome [tiab]
#13 temporomandibular [tiab] AND joint [tiab] AND disorder* [tiab]
#14 TMJ [tiab] AND disorder* [tiab]
#15 temporomandibular [tiab] AND disorder* [tiab]
#16 temporomandibular [tiab] AND joint [tiab] AND disease* [tiab]

#17 TMJ [tiab] AND disease* [tiab]
#18 craniofacial pain [tiab]OR masticatory muscle disorder [tiab] OR masticatory muscle pain [tiab] OR orofacial muscle pain [tiab] OR chronic muscle pain [tiab] OR myofacial pain [tiab]OR myogenous facial pain [tiab]OR myofunctional pain [tiab] OR orofacial myofunctional disorder* [tiab] OR myofunctional disorder [tiab]OR myoarthropat*[tiab]
#19 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
#20 Analgesics [MeSH]
#21 Anti-inflammatory agents, non-steroidal [MeSH]
#22 Anticonvulsants [MeSH]
#23 Benzodiazepines [MeSH]
#24 Capsaicin [MeSH]
#25 Neuromuscular agents [MeSH]
#26 Propanolol [MeSH]
#27 analgesic* [tiab] OR anodyne* [tiab] OR antinociceptive agent* [tiab]
#28 analgesic* [tiab] AND drug* [tiab]
#29 analgesic* [tiab] AND agent* [tiab]
#30 anti-inflammatory [tiab] AND agent* [tiab] AND non-steroidal [tiab]
#31 anti inflammatory [tiab] AND agent* [tiab] AND non steroidal [tiab]
#32 anti inflammatory [tiab] AND agent*[tiab] AND nonsteroidal [tiab]
#33 NSAIDs [tiab]
#34 antiinflammatory [tiab] AND agent* [tiab] AND non steroidal [tiab]
#35 antiinflammatory [tiab] AND agent* [tiab] AND nonsteroidal [tiab]
#36 anti-inflammatory [tiab] agent* [tiab] AND [tiab] non-steroidal [tiab]
#37 anti-inflammatory [tiab] agent* [tiab] AND nonsteroidal [tiab]
#38 anti-rheumatic [tiab] AND agent* [tiab] AND non-steroidal [tiab]
#39 anti rheumatic [tiab] AND agent* [tiab] AND non steroidal [tiab]
#40 anti rheumatic [tiab] AND agent* [tiab] AND non-steroidal [tiab]
#41 antirheumatic [tiab] AND agent* [tiab] non-steroidal [tiab]
#42 antirheumatic [tiab] AND agent* [tiab] non steroidal [tiab]
#43 aspirin-like [tiab] AND agent* [tiab]
#44 analgesic* [tiab] AND anti-inflammatory [tiab]
#45 analgesic*[tiab] AND anti inflammatory [tiab]
#46 pain killer* [tiab]
#47 anticonvuls* [tiab] OR antiepileptic* [tiab]
#48 anticonvuls* [tiab] AND drug* [tiab]
#49 anticonvuls* [tiab] AND agent* [tiab]
#50 antiepileptic [tiab] AND agent* [tiab]
#51 antiepileptic [tiab] AND drug* [tiab]
#52 benzodiazepine* [tiab] OR benzodiazepine compound* [tiab]
#53 capsaicin* [tiab] OR 8-methyl-N-vanillyl-6-nonenamide [tiab] OR 8 methyl N vanillyl 6 nonenamide [tiab] OR axsain [tiab] OR zacin [tiab] OR elan brand of capsaicin [tiab] OR capsicum farmaya [tiab] OR alacan brand of capsaicin [tiab] OR capsidol [tiab] OR vinas brand of capsaicin [tiab] OR zostrix [tiab] OR medicis brand of capsaicin [tiab] OR link brand of capsaicin [tiab] capzasin [tiab] OR Thompson brand of capsaicin [tiab] OR gelcen [tiab] OR centrum brand of capsaicin [tiab] OR katrum [tiab] OR smaller brand of capsaicin [tiab] OR NGX-4010 [tiab] OR NGX 4010 [tiab] OR NGX4010 [tiab] OR antiphlogistine Rub A-535 capsaicin [tiab] OR carter horner brand of capsaicin [tiab] OR capsin [tiab] OR flemming brand of capsaicin
#54 neuromuscular [tiab] AND agent* [tiab]
#55 skeletal [tiab] AND muscle [tiab] AND relaxant* [tiab]
#56 neuromuscular [tiab] AND effect* [tiab]
#57 propanolol [tiab] OR avlocardyl [tiab] OR AY-20694 [tiab] OR AY 20694 [tiab] OR AY20694 [tiab] OR betadren [tiab] OR dexpropanolol [tiab] OR inderal [tiab] OR obsidan [tiab] OR obzidan [tiab] OR rexigen [tiab] OR anaprilin* [tiab] OR dociton [tiab]

#58 propanolol [tiab] AND hydrochloride [tiab]
#59 #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58
#60 #19 AND #59
The above described search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision); PubMed format as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of *The Cochrane Handbook for Systematic Reviews of Interventions,* Version 5.0.2 [updated March 2011].

Appendix IV. Search strategy of Physiotherapeutical interventions for Myofacial pain
MEDLINE via Pubmed. Database entry date: 01.11.2012
#1 Myofascial Pain Syndromes [MeSH]
#2 Craniomandibular Disorders [MeSH]
#3 Temporomandibular Joint Dysfunction Syndrome [MeSH]
#4 Temporomandibular Joint Disorders [MeSH]
#5 myofascial [tiab] AND pain [tiab] AND syndrom* [tiab]
#6 myofascial [tiab] AND trigger point [tiab] AND pain [tiab]
#7 craniomandibular [tiab] AND disorder* [tiab]
#8 craniomandibular disease* [tiab]
#9 temporomandibular joint dysfunction syndrome [tiab] OR myofascial pain dysfunction syndrome, temporomandibular joint [tiab]
#10 TMJ [tiab] AND syndrome [tiab]
#11 Costen* [tiab] AND syndrome [tiab]
#12 temporomandibular [tiab] AND joint [tiab] AND syndrome [tiab]
#13 temporomandibular [tiab] AND joint [tiab] AND disorder* [tiab]
#14 TMJ [tiab] AND disorder* [tiab]
#15 temporomandibular [tiab] AND disorder* [tiab]
#16 temporomandibular [tiab] AND joint [tiab] AND disease* [tiab]
#17 TMJ [tiab] AND disease* [tiab]
#18 craniofacial pain [tiab]OR masticatory muscle disorder [tiab] OR masticatory muscle pain [tiab] OR orofacial muscle pain [tiab] OR chronic muscle pain [tiab] OR myofacial pain [tiab]OR myogenous facial pain [tiab]OR myofunctional pain [tiab] OR orofacial myofunctional disorder* [tiab] OR myofunctional disorder [tiab]OR myoarthropat*[tiab]
#19 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
#20 Exercise therapy[MeSH]
#21 Massage [MeSH]
#22 Myofunctional therapy [MeSH]
#23 exercise [tiab] AND therap* [tiab]
#24 massage [tiab] OR reflexology [tiab] OR rolfing [tiab] OR bodywork* [tiab]
#25 zone [tiab] AND therap* [tiab]
#26 craniosacral [tiab] AND massage [tiab]
#27 myofunctional therap* [tiab] OR therap* myofunctional [tiab] OR oral myotherap* [tiab] OR myotherap*, oral [tiab] OR orofacial myotherap* [tiab] OR myotherap*, orofacial [tiab]
#28 jaw exercises [tiab] OR posture training [tiab] OR EMG biofeedback [tiab] OR electromyograph* biofeedback [tiab]
#29 #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28
#30 #19 AND #29
The above described search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision); PubMed format as referenced in Chapter 6.4.11.1 and detailed in box

6.4.c of *The Cochrane Handbook for Systematic Reviews of Interventions,* Version 5.0.2 [updated March 2011].

Appendix V. Search strategy of Occlusal appliances for Myofacial pain
MEDLINE via Pubmed. Database entry date: 01.11.2012
#1 Myofascial Pain Syndromes [MeSH]
#2 Craniomandibular Disorders [MeSH]
#3 Temporomandibular Joint Dysfunction Syndrome [MeSH]
#4 Temporomandibular Joint Disorders [MeSH]
#5 myofascial [tiab] AND pain [tiab] AND syndrom* [tiab]
#6 myofascial [tiab] AND trigger point [tiab] AND pain [tiab]
#7 craniomandibular [tiab] AND disorder* [tiab]
#8 craniomandibular disease* [tiab]
#9 temporomandibular joint dysfunction syndrome [tiab] OR myofascial pain dysfunction syndrome, temporomandibular joint [tiab]
#10 TMJ [tiab] AND syndrome [tiab]
#11 Costen* [tiab] AND syndrome [tiab]
#12 temporomandibular [tiab] AND joint [tiab] AND syndrome [tiab]
#13 temporomandibular [tiab] AND joint [tiab] AND disorder* [tiab]
#14 TMJ [tiab] AND disorder* [tiab]
#15 temporomandibular [tiab] AND disorder* [tiab]
#16 temporomandibular [tiab] AND joint [tiab] AND disease* [tiab]
#17 TMJ [tiab] AND disease* [tiab]
#18 craniofacial pain [tiab]OR masticatory muscle disorder [tiab] OR masticatory muscle pain [tiab] OR orofacial muscle pain [tiab] OR chronic muscle pain [tiab] OR myofacial pain [tiab]OR myogenous facial pain [tiab]OR myofunctional pain [tiab] OR orofacial myofunctional disorder* [tiab] OR myofunctional disorder [tiab]OR myoarthropat*[tiab]
#19 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
#20 occlusal splints [MeSH]
#21 occlusal [tiab] AND splint* [tiab]
#22 oral splint* [tiab] OR oral appliance* [tiab] OR occlusal appliance* [tiab] OR bite splint* [tiab] OR bite plate* [tiab]
#23 stabilization splint* [tiab] OR stabilization splint* [tiab]
#24 standard treatment [tiab] OR usual treatment [tiab] OR standard care [tiab] OR usual care [tiab]
#25 #20 OR #21 OR #22 OR #23 OR #24
#26 #19 AND #25
The above described search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized trials in MEDLINE: sensitivity- maximizing version (2008 revision); PubMed format as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of *The Cochrane Handbook for Systematic Reviews of Interventions,* Version 5.0.2 [updated March 2011].

Appendix VI. Search strategy of Psychosocial interventions for Myofacial pain
MEDLINE via Pubmed. Database entry date: 01.11.2012
#1 Myofascial Pain Syndromes [MeSH]
#2 Craniomandibular Disorders [MeSH]
#3 Temporomandibular Joint Dysfunction Syndrome [MeSH]
#4 Temporomandibular Joint Disorders [MeSH]
#5 myofascial [tiab] AND pain [tiab] AND syndrom* [tiab]
#6 myofascial [tiab] AND trigger point [tiab] AND pain [tiab]
#7 craniomandibular [tiab] AND disorder* [tiab]

#8 craniomandibular disease* [tiab]
#9 temporomandibular joint dysfunction syndrome [tiab] OR myofascial pain dysfunction syndrome, temporomandibular joint [tiab]
#10 TMJ [tiab] AND syndrome [tiab]
#11 Costen* [tiab] AND syndrome [tiab]
#12 temporomandibular [tiab] AND joint [tiab] AND syndrome [tiab]
#13 temporomandibular [tiab] AND joint [tiab] AND disorder* [tiab]
#14 TMJ [tiab] AND disorder* [tiab]
#15 temporomandibular [tiab] AND disorder* [tiab]
#16 temporomandibular [tiab] AND joint [tiab] AND disease* [tiab]
#17 TMJ [tiab] AND disease* [tiab]
#18 craniofacial pain [tiab]OR masticatory muscle disorder [tiab] OR masticatory muscle pain [tiab] OR orofacial muscle pain [tiab] OR chronic muscle pain [tiab] OR myofacial pain [tiab]OR myogenous facial pain [tiab]OR myofunctional pain [tiab] OR orofacial myofunctional disorder* [tiab] OR myofunctional disorder [tiab]OR myoarthropat*[tiab]
#19 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
#20 cognitive therapy [MeSH]
#21 hypnosis, dental [MeSH]
#22 self care [MeSH]
#23 cogniti* [tiab] AND therap* [tiab]
#24 cogniti* [tiab] AND psychotherap* [tiab]
#25 cogniti* [tiab] AND behavio* [tiab] AND therap* [tiab]
#26 dental [tiab] AND hypnos* [tiab]
#27 self [tiab] AND care [tiab]
#28 self-care [tiab] OR self-management [tiab] OR self management [tiab]
#29 CBT [tiab] OR cogniti* biobehavio* therap* [tiab]OR cogniti* behavio* [tiab]
#30 oral habit reversal [tiab] OR hypnos* [tiab]
#31 self-care treatment* [tiab] OR self care treatment* [tiab] OR self-care strateg* [tiab] OR self care strateg* [tiab]
#32 relaxation training [tiab] OR self-efficacy enhancement [tiab] OR fear-avoidance technique* [tiab]
#33 #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32
#34 #19 AND #33
The above described search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized trials in MEDLINE: sensitivity- maximizing version (2008 revision); PubMed format as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of *The Cochrane Handbook for Systematic Reviews of Interventions,* Version 5.0.2 [updated March 2011].

Appendix VII. Additional search strategies for all the systematic reviews

EBSCO – Dentistry and Oral Sciences Source (EBSCO – TMD pubmed)

Published data from 01/1999-04/2010, Peer-reviewed only, for each subject's term:

1. temporomandibular joint disease
2. temporomandibular disorder
3. temporomandibular dysfunction
4. craniomandibular disorder*
5. craniofacial pain
6. mandibular condyle
7. masticatory muscle disorder
8. masticatory muscle pain
9. orofacial muscle pain
10. chronic muscle pain

11. myofacial pain
12. myofacial pain
13. myogenous facial pain
14. bruxism
15. myofunctional pain
16. orofacial myofunctional disorder*
17. oral myofunctional
18. myofunctional disorder*

EMBASE:

#1. temporomandibular joint disease
#2. temporomandibular disorder
#3. temporomandibular dysfunction
#4. craniomandibular disorder*
#5. craniofacial pain
#6. mandibular condyle
#7. masticatory muscle disorder
#8. masticatory muscle pain
#9. orofacial muscle pain
#10. chronic muscle pain
#11. myofacial pain
#12. myofacial pain
#13. myogenous facial pain
#14. bruxism
#15. myofunctional pain
#16. orofacial myofunctional disorder*
#17. oral myofunctional
#18. myofunctional disorder*
#19. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18

KLINISCHER FUNKTIONSSTATUS

der Deutschen Gesellschaft für Funktionsdiagnostik
und -therapie (DGFDT) in der DGZMK

Name, Vorname, Geburtsdatum	Praxisstempel
Patientennummer	
Untersuchungsdatum	

ANAMNESE (VORGESCHICHTE)

Was ist der Grund Ihres Besuches?

_____

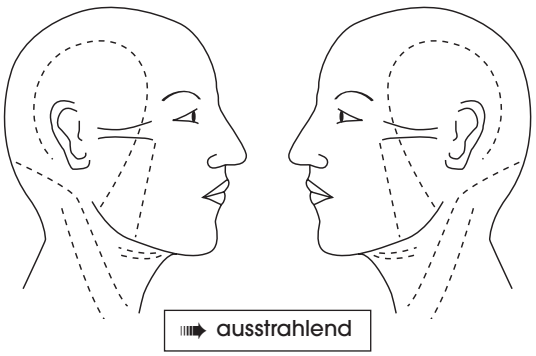
Waren Sie in letzter Zeit in Behandlung bei:	ja	nein
Zahnarzt? _____	❑	❑
Kieferorthopäde? _____	❑	❑
Arzt? _____	❑	❑
Wurde bei Ihnen bereits eine Funktionstherapie durchgeführt? Wenn ja, welcher Art?	❑	❑
_____		
Erlitten Sie einen Unfall/Schlag im Kopf-/Halsbereich?	❑	❑

Haben Sie Schmerzen, Beschwerden oder Verspannungen im/am

Kopf (allgemein)?	li ❑	re ❑	❑
Schläfen?	li ❑	re ❑	❑
Ohrbereich/Kiefergelenke?	li ❑	re ❑	❑
Nacken?	li ❑	re ❑	❑
Schulter?	li ❑	re ❑	❑
Andere (z.B. Wirbelsäule, andere Gelenke)?			❑

wo? _____

Ort und Ausbreitung der Schmerzen/Beschwerden



Qualität des Schmerzes (z. B. dumpf, stechend): _____

Zeitpunkt des Schmerzes:

morgens ❑ im Laufe des Tages ❑
abends ❑ bestimmter Anlass ❑

_____

Dauer des Schmerzes: _____ Minuten _____ Stunden

Häufigkeit des Schmerzes:

täglich ❑ 1–2 mal/Woche ❑
1–2 mal/Monat ❑ seltener ❑

Wann traten die Beschwerden erstmals auf? _____

Wie stark ausgeprägt sind die Beschwerden?

0	1	2	3	4	5	6	7	8	9	10

kein Schmerz — stärkster vorstellbarer Schmerz

Wie stark beeinflussen die Beschwerden Ihr Wohlbefinden oder Ihre Leistungsfähigkeit?

0	1	2	3	4	5	6	7	8	9	10

gar nicht — sehr stark

	ja	nein
Sind/waren Kauen ☐, Kieferöffnung ☐, Kieferschluss ☐, und/oder eine andere Unterkieferbewegung ☐ (_____) behindert (1) oder schmerzhaft (2)?	❑	❑
Kauen Sie bevorzugt auf der linken ❑, rechten ❑ Seite oder beidseitig? ❑		
Kiefergelenkgeräusche links ❑ rechts ❑ seit _____		❑
Sind die Zähne bzw. ist das Zahnfleisch schmerzhaft oder empfindlich?	❑	❑
Passen die Zähne richtig aufeinander?	❑	❑
Liegt bei Ihnen ein Taubheitsgefühl im Kopf-/Gesichtsbereich (auch Zungen-/Gaumenbrennen) vor?	❑	❑

Weitere Angaben zur Anamnese _____

BEFUNDE

1. KIEFERGELENK

1.1 Palpation

(0 = unauffällig, 1 = Missempfindung, 2 = Schmerz)

	re	li
Kiefergelenk von lateral		
Kiefergelenk von dorsal		

1.2 Auskultation

Geräusche: ja ❑ nein ❑ (R = Reiben, K = Knacken)

re Öffnen **li** **re** Schließen **li**

R	K	R	K			R	K	R	K
				initial	terminal				
				intermediär	intermediär				
				terminal	initial				

2. MUSKULATUR

(0 = unauffällig, 1 = Missempfindung, 2 = Schmerz)

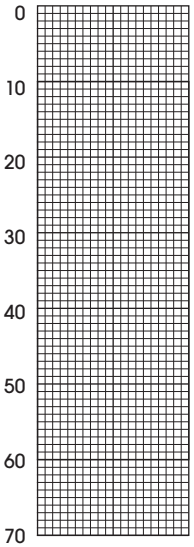
Palpation	re	li
M. temporalis Pars anterior		
M. temporalis Pars media		
M. temporalis Pars posterior		
Sehne M. temporalis		
M. masseter superficialis, Ursprung		
M. masseter superficialis, Muskelbauch		
M. masseter superficialis, Ansatz		
Regio postmandibularis		
Regio submandibularis		
Regio M. pterygoideus lateralis		
Subokzipital-/Nackenmuskulatur		

3. MOBILITÄT DES UNTERKIEFERS

(0 = unauffällig, 1 = Missempfindung, 2 = Schmerz)

	mm	re	li
Kieferöffnung aktiv			
Kieferöffnung passiv			
RL			
LL			
P			
R			

P = Protrusion
R = Retrusion



4. KIEFERRELATION UND OKKLUSION

4.1 Horizontale Kieferrelation

Gleiten zentrische Okklusion/habituelle Okklusion:

ja ❑ nein ❑

mm	mm	mm	mm
re	Mitte	li	vertikal

4.2 Vertikale Kieferrelation

❑ unauffällig ❑ erhöht ❑ zu niedrig

4.3 Okklusion

4.3.1 Statische Okklusion

(+ = Kontakt, + - = schwacher Kontakt, - = kein Kontakt, x = fehlender Zahn)

ZO															
HO															
	8	7	6	5	4	3	2	1	1	2	3	4	5	6	7	8
HO															
ZO															

ZO = zentrische Okklusion HO = habituelle Okklusion

4.3.2 Dynamische Okklusion

FZ = Frontzahn, PM = Prämolar, M = Molar

	FZ	PM re	PM li	M re	M li
RL					
LL					
P					

5. WEITERE BEFUNDE

❑ Abrasionen/Attrition ❑ keilförmige Defekte
❑ Zungenimpressionen ❑ Wangenimpressionen
❑ andere _____

WEITERE DIAGNOSTISCHE MASSNAHMEN

❑ Manuelle Strukturanalyse
❑ Orthopädisches Screening
❑ Psychosoziales Screening
❑ Instrumentelle Funktionsanalyse
❑ Instrumentelle Okklusionsanalyse
❑ Konsiliarische Untersuchung
- ❑ Magnetresonanztomographie
- ❑ Computertomographie
- ❑ Arthroskopie
- ❑ Kieferorthopädie
- ❑ Mund-Kiefer-Gesichtschirurgie
- ❑ Hals-Nasen-Ohrenheilkunde
- ❑ Orthopädie
- ❑ Rheumatologie
- ❑ Innere Medizin
- ❑ Neurologie
- ❑ Psychosomatische Medizin
- ❑ andere _____

INITIALDIAGNOSE(N)

_____

THERAPIE

Initialtherapie

❑ Okklusionsschiene/Art _____
❑ Physikalische Therapie
- ❑ Massage
- ❑ Wärmetherapie ❑ Kältetherapie
- ❑ Elektrotherapie _____
- ❑ Manuelle Therapie
- ❑ Bewegungsübungen

❑ Medikamentöse Therapie _____
❑ Entspannungsübungen
❑ andere _____

Weitere Therapie

❑ Einschleifmaßnahmen
❑ Restaurative/Prothetische Therapie
❑ Dauerschiene
❑ Psychosomatische Therapie
❑ Kieferorthopädie
❑ Kieferorthopädische Chirurgie
❑ Kiefergelenkchirurgie
❑ andere _____

Beiblatt zum Klinischen Funktionsstatus

der Deutschen Gesellschaft für Funktionsdiagnostik
und -therapie (DGFDT) in der DGZMK

Name, Vorname, Geburtsdatum	Praxisstempel
Patientennummer	
Untersuchungsdatum	

Der Klinische Funktionsstatus wurde am _____ auf dem Formblatt erhoben.
Es wurde dem Krankenblatt zur Dokumentation beigefügt.

Die GOZ-Positionen

8000 ❑ 8010 ❑ 8020 ❑ 8030 ❑ 8035 ❑ 8050 ❑ 8060 ❑ 8065 ❑ 8080 ❑ 8090 ❑ 8100 ❑

wurden aus folgender Indikation durchgeführt:

- ❑ Funktionelle Vorbehandlung bei
  - ❑ funktionell bedingten Zahn-, Kiefergelenk- und Muskelerkrankungen
  - ❑ Kiefergelenk- und Muskelerkrankungen, die mit Dysgnathien verbunden sind
  - ❑ Parodontopathien, wenn ungleichmäßige Belastungsverhältnisse die Erkrankung ungünstig beeinflussen
  - ❑ Gebisssanierungen, wenn die zentrische Okklusion durch Veränderungen in der horizontalen und/oder vertikalen Kieferrelation und/oder die Frontzahnführung verloren gegangen ist
- ❑ Diagnostik und Operationsplanung bei kieferorthopädischen und/oder kieferchirurgischen Behandlungen
- ❑ Umfangreiche restaurative und prothetische Versorgungen im Rahmen der definitiven Therapie zur Rekonstruktion und Erhaltung des Gebisses
- ❑ Adjuvante zahnärztliche Maßnahme bei multifaktoriell bedingtem chronischen Schmerz

---

PLANUNG/THERAPIE:

8	7	6	5	4	3	2	1	1	2	3	4	5	6	7	8

F = Füllung
K = Krone/Teilkrone
T = Teleskopkrone
f = fehlender Zahn
B = Brückenglied
E = ersetzter Zahn
H = Halteelement
)(= Lückenschluss

❑ **SONSTIGE INDIKATION** BEGRÜNDUNG**:** _____

_____

_____

_____

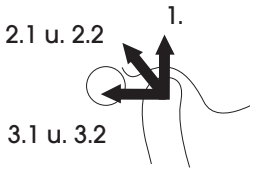
Datum: _____ Unterschrift: _____

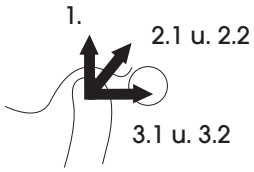
MANUELLE STRUKTURANALYSE

Deutsche Gesellschaft für Funktionsdiagnostik
und -therapie (DGFDT) in der DGZMK

KOMPRESSION IN DER STATIK (PASSIVE KOMPRESSION)

0 = unauffällig,
1 = Missempfindung
2 = Schmerz
ZKP = Zentrische Kondylenposition

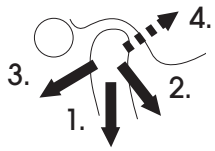


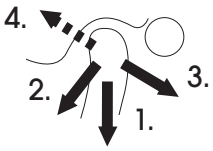


Kompression	Schmerz re	Schmerz li
1. kranial		
2.1 dorsokranial (ZKP)		
2.2 dorsokranial (Laterotrusion)		
3.1 dorsal (ZKP)		
3.2 dorsal (Laterotrusion)		

TRAKTION/TRANSLATION

0 = unauffällig
1 = Missempfindung
2 = Schmerz





	Schmerz re	Endgefühl re	Schmerz li	Endgefühl li
1. Kaudaltraktion				
2. ventrokaudale Translation				
3. laterale Translation				
4. mediale Translation				

KOMPRESSION IN DER DYNAMIK (DYNAMISCHE KOMPRESSION)

(+ = stärker bzw. später, 0 = unverändert, - = schwächer bzw. früher)

	re	li
Geräuschintensität		
Geräuschzeitpunkt		

ISOMETRIE

0 = unauffällig, 1 = Missempfindung, 2 = Schmerz
RL = Rechtslateralbewegung, LL = Linkslateralbewegung

	Schmerz re	Muskelkraft re	Schmerz li	Muskelkraft li
Kieferöffnung				
Kieferschluss				
RL				
LL				

INITIALDIAGNOSE(N)

Questionnaire of von Korff et al for Grading the Severity of Chronic Pain

Overview: The severity of chronic pain can be graded based on its characteristics and its impact on a person's activities.

Questions [text slightly modified from Appendix page 147]

(1) How would you rate your pain on a 0-10 scale at the present time (right now)? [Pain Right Now]

- responses 0 to 10
- 0 = no pain
- 10 = pain as bad as it could be

(2) During the past 6 months how intense was your worst pain? [Worst Pain]

- responses 0 to 10
- 0 = no pain
- 10 = pain as bad as it could be

(3) During the past 6 months on the average how intense was your pain? (That is your usual pain at times you were experiencing pain.) [Average Pain]

- responses 0 to 10
- 0 = no pain
- 10 = pain as bad as it could be

(4) About how many days in the past 6 months have you been kept from your usual activities (work school or housework) because of your pain? [Disability Days]

- response the total number of days disabled
- points assigned below

5) In the past 6 months how much has the pain interfered with your daily activities? [Daily Activities]

- responses 0 to 10
- 0 = no interference
- 10 = unable to carry on any activities

(6) In the past 6 months how much has the pain changed your ability to take part in recreational social and family activities? [Social Activities]

- responses 0 to 10

- 0 = no change
- 10 = extreme change

(7) In the past 6 months how much has the pain changed your ability to work (including housework)? [Work Activities]

- responses 0 to 10
- 0 = no change
- 10 = extreme change

characteristic pain intensity = (((response question 1) + (response question 2) + (response question 3)) / 3) * 10

disability score = (((response question 5) + (response question 6) + (response question 7)) / 3) * 10

disability points = (points for disability days) + (points for disability score)

Parameter	Finding	Points
disability days from question 4	0 - 6 days	0
	7 - 14 days	1
	15 - 30 days	2
	>= 31 days	3
disability score (above)	0 - 29	0
	30 - 49	1
	40 - 69	2
	>= 70	3

Interpretation

Findings	Type	Grade
no pain problems for the prior 6 months	pain free	0
characteristic pain intensity < 50 disability points < 3	low disability low intensity	I
characteristic pain intensity >= 50 disability points < 3	low disability high intensity	II
disability points 3 or 4	high disability moderately limiting	III
disability points 5 or 6	high disability severely limiting	IV

References:

Smith BH Penny KI et al. The Chronic Pain Grade questionnaire: Validation and reliability in postal research. Pain. 1997; 71: 141-147.

Von Korff M Ormel J et al. Grading the severity of chronic pain. Pain. 1992; 50: 133-149.

Von Korff M Deyo RA et al. Back pain in primary care. Spine. 1993; 18: 855-862. (Table 1 page 856).

Hospital Anxiety and Depression Scale

~ Scoring Sheet ~

	Yes definitely	Yes sometimes	No, not much	No, not at all
1. I wake early and then sleep badly for the rest of the night.	3	2	1	0
2. I get very frightened or have panic feelings for apparently no reason at all.	3	2	1	0
3. I feel miserable and sad.	3	2	1	0
4. I feel anxious when I go out of the house on my own.	3	2	1	0
5. I have lost interest in things.	3	2	1	0
6. I get palpitations, or sensations of 'butterflies' in my stomach or chest.	3	2	1	0
7. I have a good appetite.	0	1	2	3
8. I feel scared or frightened.	3	2	1	0
9. I feel life is not worth living.	3	2	1	0
10. I still enjoy the things I used to.	0	1	2	3
11. I am restless and can't keep still.	3	2	1	0
12. I am more irritable than usual.	3	2	1	0
13. I feel as if I have slowed down.	3	2	1	0
14. Worrying thoughts constantly go through my mind.	3	2	1	0

Anxiety 2, 4, 6, 8, 11, 12, 14

Depression 1, 3, 5, 7, 9, 10, 13

Scoring 3, 2, 1, 0 (For items 7 & 10 the scoring is reversed)

GRADING: 0 - 7 = Non-case 8 – 10 = Borderline case 11+ = Case

Personal Information

Schriftliche Erklärung

Ich erkläre ehrenwörtlich, dass ich die dem Fachbereich Medizin der Johann Wolfgang Goethe-Universität Frankfurt am Main zur Promotionsprüfung eingereichte Dissertation mit dem Titel

“Myofacial pain: etiological factors and therapeutical methods. A systematic literature review of the last 12 years, and a meta-analysis of the “usual treatment” vs. psychosocial interventions”

in dem Zentrum der Zahn-, Mund- und Kieferheilkunde (Carolinum) der Johann Wolfgang Goethe-Universität Frankfurt am Main
unter Betreuung und Anleitung von Prof. Dr. Hans-Christoph Lauer mit Unterstützung durch Dr. Steffani Janko ohne sonstige Hilfe selbst durchgeführt und bei der Abfassung der Arbeit keine anderen als die in der Dissertation angeführten Hilfsmittel benutzt habe. Darüber hinaus versichere ich, nicht die Hilfe einer kommerziellen Promotionsvermittlung in Anspruch genommen zu haben.

Ich habe bisher an keiner in- oder ausländischen Universität ein Gesuch um Zulassung zur Promotion eingereicht*. Die vorliegende Arbeit wurde bisher nicht als Dissertation eingereicht.

_____ _____

(Ort, Datum) (Unterschrift)

*) im Falle des Nichtzutreffens streichen

Carolina Roldán Barraza, DDS

SUMMARY

Carolina Roldán B. is a doctoral candidate at the Johann Wolfgang Goethe-University Frankfurt. She graduated in Dentistry from Universidad de Chile. After four years of experience working at public health institutions in Chile and collaborating at the Faculty of Dentistry at the University of Chile, she received a fellowship from the German Academic Exchange Service (DAAD) through the continuing education program to do a clinical study at the Frankfurt University. Hereafter she started a PhD in Dentistry at the same institution, the Johann Wolfgang Goethe- Frankfurt University. She is university lecturer in the University Cairo.

PROFESSIONAL EXPERIENCE

PhD Student
2009 - Present
Department of Prosthetic Dentistry
Zentrum der Zahn-, Mund- und Kieferheilkunde (Carolinum)
Johann Wolfgang Goethe-Universität Frankfurt am Main
Frankfurt am Main, Germany

University lecturer
2013-2014
Faculty of Dentistry
Cairo University
Cairo, Egypt

Visiting Lecturer
2013
Faculty of Dentistry
Ain Shams University
Cairo, Egypt

Dentist
2013
Private practice
Cairo, Egypt

Visiting Fellow
2008
Department of Prosthetic Dentistry
Zentrum der Zahn-, Mund- und Kieferheilkunde (Carolinum)
Johann Wolfgang Goethe-Universität Frankfurt am Main
Frankfurt am Main, Germany

Dentist *(General de zona-EDF: Odontóloga en Etapa de Destinación y Formación)*
2005 - 2008
Centro de Salud Familiar Isla de Maipo
Servicio de Salud Metropolitano Occidente
Isla de Maipo, Chile

Dentist
2005
Consultorio El Recreo
Servicio de Salud Metropolitano Sur
Santiago, Chile

Dentist
2005
Consultorio Adosado del Hospital de Agudos - Complejo Hospitalario San José de Maipo
Servicio de Salud Metropolitano Occidente
San José de Maipo, Chile

Research Associate
2005 - 2008
Department of Prosthetic Dentistry
Faculty of Dentistry, University of Chile
Santiago, Chile

EDUCATION

University of Chile
1996-2004
DDS [Cirujano Dentista]
Santiago, Chile

Internship
2004
Chile Chico Hospital
Chile Chico, Chile

Internship
2004
Barros Luco-Trudeau Hospital
Santiago, Chile

PUBLICATIONS

"A systematic review and meta-analysis of Usual treatment vs. Psychosocial interventions in the treatment of myofascial pain" Roldán C, Janko S, Villanueva J, Araya I, Lauer H-C. Journal of Orofacial Pain [in edition]

"Low Level Laser Therapy for the treatment of oral myofacial pain" Roldán C, Janko S, Lauer H-C. Journal of the Lebanese Dental Association [in edition]

"Comportamiento clínico de lechos cingulares de resina en caninos mandibulares de pacientes clase I de Kennedy [Clinical performance of cingular rest seats on mandibular canines in Kennedy class I

patients]" (2005) Roldán C., Marín J Prof. Dr, Prof. Dr. Rochefort C, Moráguez O Revista de la Facultad de Odontología de la Universidad de Chile vol. 23(2):59-68

Clinical Guide *"Diagnóstico y planificación del tratamiento en Prótesis Parcial Removible [Diagnosis and treatment planning in Prosthetic Dentistry]"* (2007) Pizarro A, Roldán C, Ocaranza D, Department of Prosthetic Dentistry, Faculty of Dentistry, Universidad de Chile

SCIENTIFIC POSTERS

"Systematic review: Exercise therapy and massages for Oral Myofacial Pain" (2014) Roldán C, Janko S, Lauer H-Ch. International Association for Dental Research (IADR), General Session 2014, Cape Town

"*Effects of speech therapy on patients with atypical swallowing patterns*" (2010) Roldán C, Janko S, Martínez B, Lauer H-Ch. *International Association for Dental Research* (IADR), General Session 2010, Barcelona

"Efecto de la rehabilitación protésica removible en masticatión y deglución [Effect of the removable dental prosthesis on mastication and deglutition]" (2007) Roldán C, Pizarro A, Vera R, Marín J, 20. *International Association for Dental Research* (IADR), Chilean Section, Santiago

"Influencia de los patrones deglutorios pre-existentes en el pronóstico de rehabilitación oral [Influence of the swallowing patterns on the oral rehabilitation prognosis]" (2007) Pizarro A, Roldán C, Vera R, Marín J, 20. *International Association for Dental Research* (IADR), Chilean Section, Santiago

"Diagnóstico funcional de la deglución en el paciente desdentado parcial [Functional diagnosis of deglutition in partially edentulous patients]" (2006) Pizarro A, Dreyer E, Roldán C, Bossart B, Vera R, 19. Annual Conference of the *International Association for Dental Research* (IADR), Chilean Section, Valparaíso, Chile

"Análisis de la deglución en el paciente desdentado parcial [Analysis of deglutition in partially edentulous patients] " (2005) Pizarro A, Bossart B, Roldán C, Vera R, XVI National Congress of Kinesiology, Santiago, Chile

MEMBERSHIPS AND ASSOCIATIONS

- *Continental European Division-International Association for Dental Research* (CED-IADR)
- *International RDC/TMD Consortium Network*
- *Goethe Graduate Academy* (GRADE) Program
- *Redciencia*

Carolina Roldán Barraza, DDS

ZUSAMMENFASSUNG

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"Low Level Laser Therapy for the treatment of oral myofacial pain" Roldán C, Janko S, Lauer H-C. Journal of the Lebanese Dental Association [in edition]

"Comportamiento clínico de lechos cingulares de resina en caninos mandibulares de pacientes clase I de Kennedy [Clinical performance of cingular rest seats on mandibular canines in Kennedy class I patients]" (2005) Roldán C., Marín J Prof. Dr, Prof. Dr. Rochefort C, Moráguez O Revista de la Facultad de Odontología de la Universidad de Chile vol. 23(2):59-68

Clinical Guide *"Diagnóstico y planificación del tratamiento en Prótesis Parcial Removible [Diagnosis and treatment planning in Prosthetic Dentistry]"* (2007) Pizarro A, Roldán C, Ocaranza D, Department of Prosthetic Dentistry, Faculty of Dentistry, Universidad de Chile

WISSENSCHAFTLICHE POSTERS

"Systematic review: Exercise therapy and massages for Oral Myofacial Pain" (2014) Roldán C, Janko S, Lauer H-Ch. International Association for Dental Research (IADR), General Session 2014, Cape Town

"*Effects of speech therapy on patients with atypical swallowing patterns*" (2010) Roldán C, Janko S, Martínez B, Lauer H-Ch. *International Association for Dental Research* (IADR), General Session 2010, Barcelona

"Efecto de la rehabilitación protésica removible en masticatión y deglución [Effect of the removable dental prosthesis on mastication and deglutition]" (2007) Roldán C, Pizarro A, Vera R, Marín J, 20. *International Association for Dental Research* (IADR), Chilean Section, Santiago

"Influencia de los patrones deglutorios pre-existentes en el pronóstico de rehabilitación oral [Influence of the swallowing patterns on the oral rehabilitation prognosis]" (2007) Pizarro A, Roldán C, Vera R, Marín J, 20. *International Association for Dental Research* (IADR), Chilean Section, Santiago

"Diagnóstico funcional de la deglución en el paciente desdentado parcial [Functional diagnosis of deglutition in partially edentulous patients]" (2006) Pizarro A, Dreyer E, Roldán C, Bossart B, Vera R, 19. Annual Conference of the *International Association for Dental Research* (IADR), Chilean Section, Valparaíso, Chile

"Análisis de la deglución en el paciente desdentado parcial [Analysis of deglutition in partially edentulous patients] " (2005) Pizarro A, Bossart B, Roldán C, Vera R, XVI National Congress of Kinesiology, Santiago, Chile

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