Effectiveness of Manual Therapy and Therapeutic Exercise for Temporomandibular Disorders: Systematic Review and Meta-Analysis

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Background. Manual therapy (MT) and exercise have been extensively used to treat people with musculoskeletal conditions such as temporomandibular disorders (TMD). The evidence regarding their effectiveness provided by early systematic reviews is outdated.

Purpose. The aim of this study was to summarize evidence from and evaluate the methodological quality of randomized controlled trials that examined the effectiveness of MT and therapeutic exercise interventions compared with other active interventions or standard care for treatment of TMD.

Data Sources. Electronic data searches of 6 databases were performed, in addition to a manual search.

Study Selection. Randomized controlled trials involving adults with TMD that compared any type of MT intervention (eg, mobilization, manipulation) or exercise therapy with a placebo intervention, controlled comparison intervention, or standard care were included. The main outcomes of this systematic review were pain, range of motion, and oral function. Forty-eight studies met the inclusion criteria and were analyzed.

Data Extraction. Data were extracted in duplicate on specific study characteristics.

Data Synthesis. The overall evidence for this systematic review was considered low. The trials included in this review had unclear or high risk of bias. Thus, the evidence was generally downgraded based on assessments of risk of bias. Most of the effect sizes were low to moderate, with no clear indication of superiority of exercises versus other conservative treatments for TMD. However, MT alone or in combination with exercises at the jaw or cervical level showed promising effects.

Limitations. Quality of the evidence and heterogeneity of the studies were limitations of the study.

Conclusions. No high-quality evidence was found, indicating that there is great uncertainty about the effectiveness of exercise and MT for treatment of TMD.

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Temporomandibular disorders (TMD) consist of a group of pathologies affecting the masticatory muscles, the temporomandibular joint, and related structures.[1,2] Temporomandibular disorders constitute a major public health problem, as they are one of the main sources of chronic orofacial pain interfering with daily activities. These disorders also are commonly associated with other symptoms affecting the head and neck region, such as headache, ear-related symptoms, cervical spine dysfunction,[3,4] and altered head and cervical posture.[5-15]

Physical therapy has been used for decades for treating craniomandibular disorders using thermal packs, vapocoolants, and transcutaneous electrical nerve stimulation (TENS).[16] In 1997, Feine and Lund[17] recognized that dentists valued physical therapy treatment for TMD, and a recent national survey in the United Kingdom showed that, despite limited evidence, 72% of respondents considered physical therapy to be an effective treatment option for TMD, with jaw exercise (79%), ultrasound (52%), manual therapy (MT) (48%), acupuncture (41%), and laser therapy (15%) as the most effective modalities for managing TMD.[18] To date, evidence supports the use of conservative and reversible treatment approaches for TMD treatment, although a multidisciplinary health care approach may be required. Physical therapy is among the 10 most commonly used treatments for TMD,[19] focused on decreasing neck and jaw pain, improving range of motion (ROM), and promoting exercise to maintain healthy function.

The goals of physical therapy in the treatment of TMD are to decrease pain, enable muscle relaxation, reduce muscular hyperactivity, and re-establish muscle function and joint mobility.[20] Physical therapy treatment is reversible and noninvasive and provides self-care management in an environment to create patient responsibility for their own health. Physical therapy modalities include electrophysical modalities (ultrasound, microwave, laser), electroanalgesic modalities (TENS, interferential current, biofeedback), acupuncture, therapeutic exercise, and MT. Therapeutic exercise and MT are used to improve strength, coordination, and mobility and to reduce pain,[21] and treatment may include and focus on poor posture, cervical muscle spasm or pain, and treatment for referred cervical origin orofacial pain (pain referred from upper levels of the cervical spine).[22] The evidence for the effect of electrophysical modalities has been questioned.[23]

Manual therapy (including joint mobilization, manipulation, or treatment of the soft tissues) and therapeutic exercises in physical therapy treatments have been increasingly used by clinicians and researched due to positive outcomes in some conditions, especially for low back pain, neck pain, and related disorders.[24] Manual therapy has been used to restore normal ROM, reduce local ischemia, stimulate proprioception, break fibrous adhesions, stimulate synovial fluid production, and reduce pain. In the area of orofacial pain, several systematic reviews have been conducted regarding physical therapy and specifically MT and exercise interventions for TMD.[19,23,25] Most of these early systematic reviews highlighted the positive effects of exercises and MT to improve symptoms and function in people with TMD. However, 2 reviews[19,23] were conducted 9 years previously and included few randomized controlled trials (RCTs). Research has expanded over the last few years, and new RCTs have been conducted, which implies that the information from earliest reviews is now outdated. Another recent systematic review[25] combined pathologies of the upper extremity and TMD. That review included several types of designs and did not focus on RCTs, which are the best evidence when looking at interventions. In addition, based on a preliminary search performed by our team, it was realized that this review missed important RCTs in the area (included only 5 studies). In addition, none of these systematic reviews provided a meta-analysis of the trials. Therefore, the objectives of this systematic review were: (1) to summarize the evidence from and evaluate the methodological quality of RCTs that examined the effectiveness of MT and therapeutic exercise interventions in the management of TMD and (2) to determine the magnitude of the effect of these interventions to manage TMD.

Method

The reporting of this systematic review is based on the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines.[26] The aim of the PRISMA statement is to help authors improve the reporting of systematic reviews and meta-analyses. It consists of a 27-item checklist and 4-phase flow diagram. This systematic review was registered in PROSPERO (CRD42013005628).

Study Selection

Inclusion criteria for this review were as follows.

Participants. This review was restricted to trials with participants meeting the following criteria: (1) diagnosis of TMD according to the research diagnostic criteria for temporomandibular disorders (RDC/TMD) established by Dworkin and LeResche[27] or any clinical diagnosis involving signs and symptoms of TMD,[28,29] (2) adult (>18 years of age), (3) musculoskeletal dysfunction, (4) pain impairment, (5) no previous surgery in the temporomandibular region, and (6) no other serious comorbid conditions (eg, fracture in region, cancer, neurological disease).

Studies. This review targeted RCTs comparing any type of MT intervention (eg, mobilization, manipulation, soft tissue mobilization) or exercise therapy alone or in combination with other therapies with a placebo intervention, controlled comparison intervention, or standard care (ie, treatment that normally is offered).

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- **eTable 1:** Characteristics of Included Studies
- **eTable 2:** Risk of Bias of Included Studies

Outcomes

The primary outcomes of interest for this systematic review were pain, ROM, and oral function. Oral function for this systematic review focused on limitations of daily activities of patients with TMD measured through different questionnaires. A secondary outcome of interest was pressure pain threshold (PPT).

The minimal clinically important difference for pain has been reported to range from 1.5 to 3.2 points.[30–34] The smallest detectable difference of maximal mouth opening in healthy people has been reported to be 5 mm, indicating that an important change of at least 5 mm can be considered clinically relevant.[35] Measurements of PPT have been shown to have good or excellent interrater and intrarater reliability.[36–38] The minimal important difference for PPTs has been reported to be ≥ 1.10 kg/cm^2/s.[39,40] This systematic review was open to all time points: immediately posttreatment and short-term, intermediate-term, and long-term follow-up.

Data Sources and Searches

A bibliographic search of 6 electronic databases was conducted:

- MEDLINE (database root [1966]–April 7, 2015),
- EMBASE (database root [1988])–April 7, 2015),
- Cochrane Library and Best Evidence (database root [1991]–April 7, 2015),
- ISI Web of Science (database root [1965]–April 7, 2015),
- EBM reviews–Cochrane Central Register of Controlled Trials (database root [1991]–April 7, 2015), and
- CINAHL (database root [1982]–April 7, 2015).

Key words and medical subject headings were identified with the assistance of a librarian who specialized in health science databases and experts in the orofacial pain field. No restrictions were made regarding the language of publication. A manual search of the references of selected studies was conducted as well (refer to the Appendix for an example of the search strategy).

Data Screening

Two independent investigators screened the titles of publications found in the databases and, if available, the abstract of the publication. The Early Review Organizing Software (EROS) (http://www.eros-systematic-review.org/) Web platform was used for screening the articles for inclusion. In order for papers to be included in the review, the paper had to meet all inclusion criteria of this systematic review on the rating form created in EROS software. Studies were analyzed with the available information. Authors were not contacted.

Disagreements between reviewers on inclusion were resolved by consensus. The kappa statistic was calculated using STATA software, version 12, (StataCorp LP, College Station, Texas) to determine the level of agreement between raters on trial inclusion before consensus. Criteria proposed by Byrt[41] were used to interpret kappa values.

Data Extraction

The information of each study included in this review was extracted and entered into Excel or Microsoft Word (Microsoft Corp, Redmond, Washington) files. For each part of the review, data extraction was carried out independently by 2 reviewers. Data were extracted on study characteristics, including the design, type of TMD, type of interventions, main and secondary outcomes, and treatment estimates. Any disagreements on data extraction were resolved by consensus.

Quality Assessment (Risk of Bias)

Assessments of quality (risk of bias) were completed by 2 independent reviewers (any 2 members of the research team). For the assessment of RCTs, our team used a compiled set of items based on the 7 tools most commonly used to evaluate the risk of bias in complex physical therapy trials.[42] In addition, the risk of bias tool was used with the main outcome of each study to make the assessments. We followed the guidelines established by the Cochrane Collaboration to perform assessments of risk of bias; however, we developed specific decision rules to make decisions as described elsewhere.[43] For the overall assessment of risk of bias, a trial was considered at low risk of bias if it was rated as low risk in all individual domains, if the rating was unclear in at least one domain and the other domains were unclear or low, or if the overall assessment of risk of bias was unclear. Finally, an overall assessment of high risk of bias was considered if at least one domain was rated as high. These criteria have been used previously by our team and other authors.[43,44]

Any discrepancies in quality ratings were resolved by discussion. If consensus could not be reached, a third member of the review team with expertise in quality assessments (S.A-O.) acted as an arbitrator and made a final decision.

Data Analysis and Synthesis

Data analysis was performed based on type of intervention (ie, exercise, mobilization, and manipulation), TMD diagnosis (myogenous TMD, arthrogenous TMD, mixed TMD), and type of outcome (eg, pain intensity, range of mouth opening [ROM], oral function (oral-related quality of life]). For analysis of continuous outcome data, we used the mean difference (MD) and the standardized mean difference (SMD) with 95% confidence interval (95% CI) to pool data. Heterogeneity was evaluated statistically using the I^2 statistic. The MD and SMD were defined according to the Cochrane Collaboration,[45] as follows:

> MD is a standard statistic that measures the absolute difference between the mean value in 2 groups in a clinical trial. It estimates the amount by which the experimental intervention changes the outcome on average compared with the control. It can be used as a summary statistic in meta-analysis when outcome measurements in all studies are made on the same scale.

> The SMD is used as a summary statistic in meta-analysis when the studies assess the same outcome but measure it in a variety of ways (ie, use different psychometric scales). In this circumstance, it is necessary to standardize the results of the studies to a uniform scale before they can be combined. The standardized mean difference expresses the size of the intervention effect in each study relative to the variability observed in that study.

We decided to pool studies based on TMD diagnosis, intervention provided, and outcome. We grouped studies that had the same diagnosis (myogenous, arthrogenous, or mixed), similar intervention of interest (ie, MT, exercises), and the same underlying outcome. Thus,

we created groups of studies that were similar in terms of these characteristics and pooled them. In the presence of clinical heterogeneity in the study population or intervention, the DerSimonian and Laird random-effects model of pooling was used based on the assumption of the presence of interstudy variability to provide a more conservative estimate of the true effect.[46,47]

Cohen's criteria were used to interpret values of effect sizes found for our pooled estimates.[48] Cohen described 0.2, 0.5, and 0.8 as small, moderate, and large effect sizes, respectively.[48] Review Manager (RevMan) version 5.0 software (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, 2008) was used to summarize the effects (ie, pooled MD values) and construct forest plots for all comparisons.

Subgroup and sensitivity analysis. In order to investigate and accommodate heterogeneity (clinical heterogeneity in the study population or intervention) as explained above, a random-effects model was used across all the comparisons. Furthermore, in order to explain the heterogeneity in terms of study-level covariates, we could have attempted a meta-regression model. However, because of the small number of studies (<10) for comparison, this analysis was not possible. We attempted to perform sensitivity analyses when possible.

We did not perform sensitivity analyses based on quality because the risk of bias of the analyzed studies was either unclear or high, with no study being classified as low risk. These factors precluded sensitivity analyses by different levels of biases. Therefore, the pooled data should be interpreted carefully.

Data synthesis. The quality of the body of the evidence was assessed using the GRADE approach.[49] The evidence was classified as high, moderate, low, and very low, as described by Guyatt et al.[49] Domains that may decrease the quality of the evidence are: (1) the study design, (2) risk of bias, (3) inconsistency of results, (4) indirectness (not generalizable), (5) imprecision (insufficient data), and (6) other factors (eg, reporting bias).

Role of the Funding Source

Results

The search of the literature resulted in a total of 3,549 published articles. Of the 3,549 published articles, 106 were considered to be potentially relevant. Independent review (in duplicate) of these 106 articles led to the inclusion of 58 articles representing 50 studies (some studies reported data from the same population in 2 manuscripts). There were 5 articles in other languages[50-54] that were not possible to translate by our study team and were not included in the final analysis. Thus, 45 studies were included for this review from the search of the databases. In addition, 3 studies[55-57] were obtained through a manual search. Therefore, a total of 48 studies were included in the final analysis (Fig. 1). The agreement between reviewers to select the articles for this review was kappa=0.98 (95% CI=0.977, 0.99). According to Byrt's criteria,[41] the agreement between reviewers was excellent. Details of included studies are provided in eTable 1 (available at ptjournal.apta.org).

Diagnosis

There was considerable diversity in the clinical presentations and diagnoses of participants with TMD among the included studies (eTab. 1). Fourteen of the studies examined the effectiveness of the exercise or MT interventions in muscular TMD (myogenous TMD), 14 studies examined the effectiveness in patients with articular TMD (arthrogenous TMD), and 19 studies examined the effectiveness in patients with mixed diagnoses of TMD (including both myogenous and arthrogenous TMD).[28,29] One study looked at both myogenous and arthrogenous TMD.[58] Twenty-one of the studies[57-76] used the RDC/TMD established by Dworkin and LeResche[27] to classify the patients as having TMD. The remaining 27 studies used their own diagnostic criteria, based on signs and symptoms of the patients.

Methodological Quality Assessment

The results of the critical appraisal of the selected studies are presented in eTable 2 (available at ptjournal.apta.org). Only 6 studies accomplished more than 60% of the items listed in eTable 2.[57,66,67,76-78] Most of the studies did not accomplish items with important methodological indicators of risk of bias, such as randomization, allocation concealment, blinding, and intention to treat (ITT). For example, study flaws regarding patient selection were mainly related to description and appropriateness of the randomization procedure and concealment of allocation, with only 20 (41.6%) and 4 (8.3%) of the studies meeting these criteria, respectively. As expected, items related to blinding were not achieved by the majority of the studies. Only 3 of the studies used a double-blinded design and could blind participants. These studies used a placebo arm, which is hard to obtain in these types of interventions. In addition, only 12 (25%) of the studies used blinded assessment of outcomes, and none of the studies blinded the therapist. Thus, blinding was the area that was the hardest section to be met by the analyzed studies. When analyzing issues regarding intervention, we found that although it is expected that interventions would be well described to be reproducible, only 64.6% (n=30) of the studies described the main intervention to be tested. In addition, most studies failed to control for cointerventions. Only 6 studies met this item.

Testing participants' adherence to intervention and having adequate adherence was another issue that was not met by many studies (only 11 and 7 studies, respectively). Furthermore, adverse
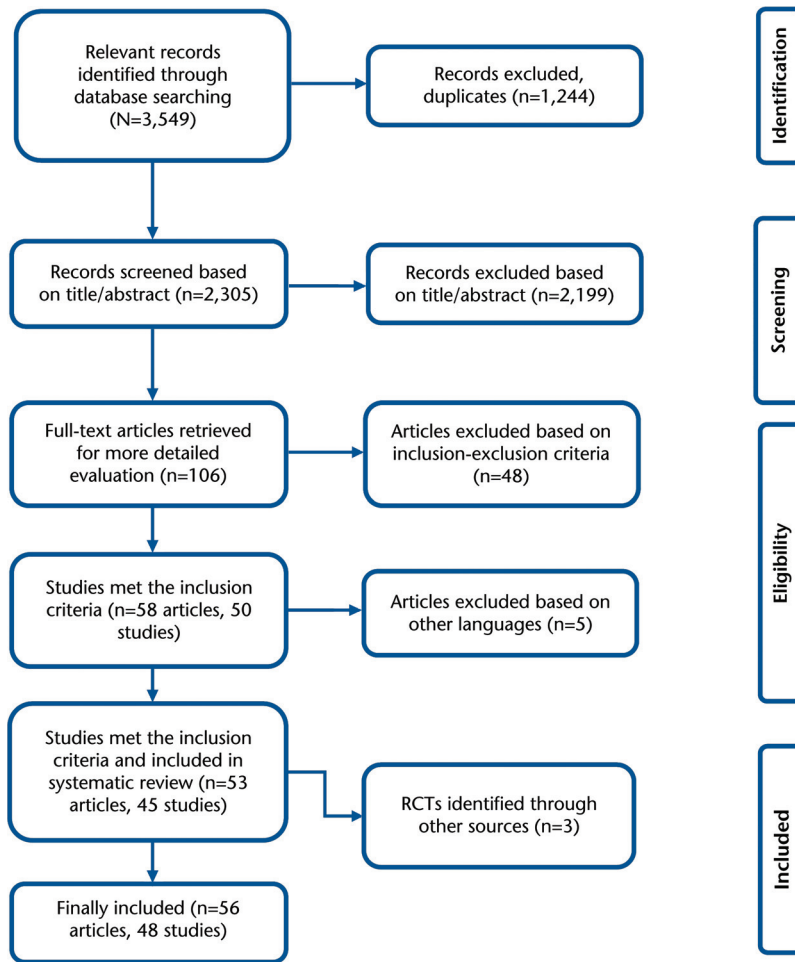
Figure 1.
Flowchart of trial selection based on PRISMA guidelines.

rater reliability of the assessors who performed outcome measurements. Regarding statistical issues, it was uncertain if sample size was adequate in 30 of the studies, and only 18 studies reported an evaluation of the clinical significance of their results. Risk of bias assessments using the risk of bias tool determined that none of the studies was considered as low risk of bias. Most of them were classified as either unclear (58.4%) or high risk of bias (41.6%).

Effectiveness of Intervention by TMD Diagnoses: Posture Correction Exercises in Myogenous TMD

Two studies[59,60] evaluated the effectiveness of posture correction exercises for patients with myofascial pain. Both studies showed positive results of postural exercises for improving symptoms of muscular TMD. When pooling the data for these 2 studies, which had similar interventions, diagnoses, and outcomes, maximum pain-free mouth opening significantly increased in patients receiving postural training compared with a control group. The MD in maximum pain-free mouth opening was 5.54 mm (95% CI=2.93, 8.15) (Fig. 2), which was clinically significant in favor of postural training.[35] Furthermore, patients treated with postural training had significantly fewer symptoms and disturbance with daily living compared with a control group. The SMD in symptoms and disturbance of symptoms with daily life was 1.13 (95% CI=0.48, 1.78), indicating a large, clinically significant effect size for this pooled outcome.

effects were reported on only 10 of the studies, but there was no specific description of such events when they occurred in all of the studies.

Despite the fact that the adequate handling of dropouts is considered an important method used to prevent bias in data analysis, only 17 of the analyzed studies included information regarding the reasons of withdrawals and dropouts, and only 16 studies used intention-to-treat analysis. The outcome measures were not described well in terms of validity, reliability, or responsiveness. Only a few studies reported these items (11, 17, and 3 studies, respectively). Moreover, the authors did not report intrarater or inter-

Study or Subgroup	Postural Correction X̄	SD	Total	Control X̄	SD	Total	Weight	Mean Difference IV, Random [95% CI]	Mean Difference IV, Random, 95% CI
Komiyama et al,[59] 1999	16.35	5.06	20	9.58	6	20	53.8%	6.77 [3.33, 10.21]	
Wright et al,[60] 2000	5.3	8.8	30	1.2	5.6	30	46.2%	4.10 [0.37, 7.83]	
Total (95% CI)			50			50	100.0%	5.54 [2.93, 8.15]	

Heterogeneity: tau²=0.21, χ²=1.06, df=1 (P=.30), I²=6%
Test for overall effect: Z=4.16 (P<.0001)

−10 −5 0 5 10
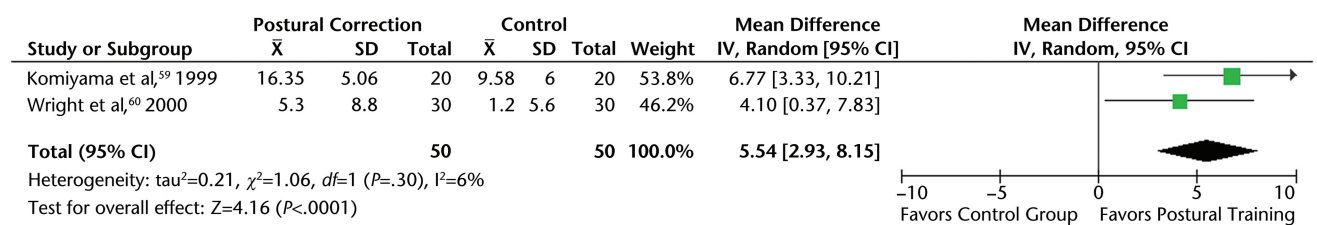Favors Control Group   Favors Postural Training

Figure 2.
Maximum pain-free opening: postural training versus control group in patients with myogenous temporomandibular disorders. CI=confidence interval, IV=inverse variance.

General Jaw Exercises Alone or Combined With Neck Exercise Program in Myogenous TMD

Eight studies[56–58,62,63,66,79,80] looked at the effect of exercises alone or combined with other therapies for myogenous TMD. The results of these studies were equivocal. Five of them did not find significant differences between a general physical therapy exercise program targeted to the jaw[56,62,79,80] or jaw and neck[57] compared with a control or other active treatments, such as biofeedback, TENS, use of the TheraBite Jaw Motion Rehabilitation System (ATOS Medical AB, Hörby, Sweden), or oral splint therapy. However, 3 studies[58,63,66] showed better outcomes, especially on pain and ROM, compared with control groups.

Data were pooled from studies that had similar outcomes and diagnoses and compared an exercise program and other forms of therapy, such as education,[62,66] or splint therapy.[56,58] Data from these studies[56,58,62,66] indicated that there was a trend to favor exercise therapy for pain-free maximum mouth opening and pain intensity compared with a control group. The MD for pain-free maximum mouth opening was 5.94 mm (95% CI=−1.0, 12.87), which is considered clinically relevant.[35] The SMD for pain intensity pooling 5 studies[57,58,62,63,66] was 0.43 (95% CI=−0.02, 0.87), with a moderate effect size according to Cohen's guidelines.[48] When performing sensitivity analyses, grouping studies comparing exercise therapy and education,[62,66] a nonsignificant effect was found on pain-free maximum mouth opening (1.92 mm; 95% CI=−0.57, 4.41). However, when comparing exercises and splint therapy,[56,58] a statistically and clinically meaningful effect was found (12.31 mm; 95% CI=7.73, 16.89).

Manual Therapy Targeted to the Orofacial Region in Myogenous TMD

Four studies[64,65,77,81] looked at MT techniques, such as facial manipulation versus botulinum toxin[81] or intraoral myofascial therapy versus waiting list, and self-care education and exercises for people with myogenous TMD.[64,65,77] The results of these studies support the use of MT to treat myogenous TMD, as people

treated with all of these approaches had improved mouth opening and reduced jaw pain from baseline. Although the results for the intraoral myofascial therapy and exercise groups were superior to the results for the waiting-list control group, there was no statistically significant difference between them. In addition, facial manipulation had an equivalent effect as botulinum toxin. However, at 3 months after treatment, facial manipulation was slightly superior in reducing subjective pain perception, and botulinum toxin injections were slightly superior in increasing ROM. When pooling the results from 3 of these studies based on similar outcomes and diagnoses and comparing similar interventions regarding MT,[64,65,81] we found that MT significantly reduced pain at 4 to 6 weeks of treatment compared with botulinum toxin or waiting list, approaching a clinically relevant value. The MD for pain intensity was 1.35 cm (95% CI=0.91, 1.78). When pooling the studies that considered the comparison of MT versus a waiting list only, similar results were obtained (1.31 cm; 95% CI=0.86, 1.76).

Manual Therapy Mobilization of the Cervical Spine and Myogenous TMD

A recent RCT conducted by La Touche et al[67] testing a more specific approach directed to the cervical spine to treat patients with cervico-craniofacial pain of myofascial origin was performed. This preliminary study showed that mobilizations targeted to the cervical spine drastically decreased pain intensity and pain sensitivity (via PPT evaluation) in patients with cervico-craniofacial pain of myofascial origin immediately after the application of the technique compared with placebo treatment. The effect sizes found in this study for pain intensity (28.75 points; 95% CI=21.65, 35.85) and PPT (1.12 kg/cm^2; 95% CI=0.96, 1.29) were considered clinically relevant.

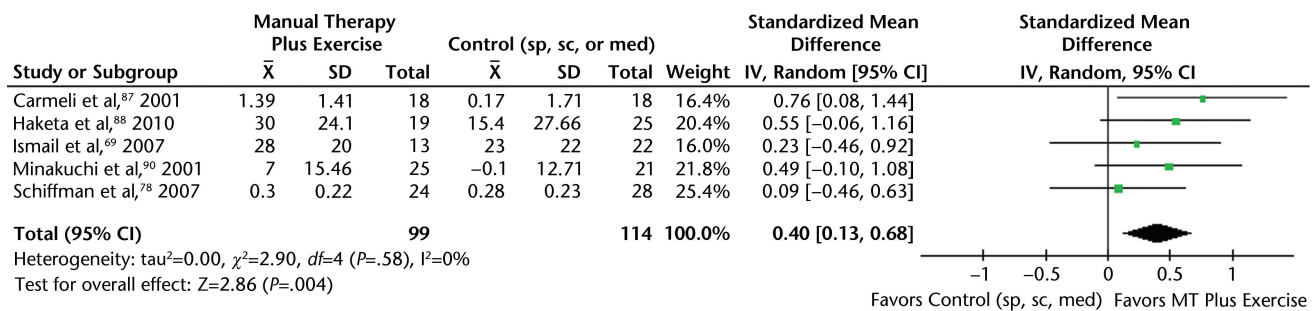## Jaw and Neck Exercises Alone or as Part of a Conservative Regimen in Arthrogenous TMD

Eight studies[58,61,68,82–86] that examined patients with arthrogenous TMD focused on jaw and neck exercises alone or combined with other therapies, such as medications, surgery, or self-care rec-

ommendations. Six studies[58,61,68,84–86] focused on exercise therapy alone,[85,86] exercise therapy combined with conventional treatment,[61] or the combination of jaw exercises with TheraBite[58] or myofunctional therapy.[68] The remaining 2 studies[82,83] looked at the effectiveness of surgery (arthrocentesis or arthroscopy) combined with conservative treatment including exercises for the jaw versus jaw exercises alone.

Although the results were mixed, most of the studies favored the use of exercises alone or as part of a general regimen to treat people with arthrogenous TMD, including disk displacements with or without reduction.[58,68,84–86] However, one study[61] did not find that exercises were superior to a control group involving general physical therapy treatment.

Data were pooled from studies with similar outcomes and diagnoses that compared an exercise program with other forms of therapy, such as education[61] or splint therapy,[58] or with a control group.[68,86] When pooling the results of the studies investigating the effectiveness of exercise alone or in combination with other conservative therapies on pain intensity,[58,61,68,86] we found that there was no statistically significant difference in pain between exercise and control groups. Nevertheless, there was a trend to favor the exercise group compared with the control group. The SMD for pain intensity was 0.68 (95% CI=−0.04, 1.40), with a moderate effect size according to Cohen's guidelines.[48] When pooling was focused on those studies including only a control group,[68,86] similar results were found, although the SMD increased (SMD=1.11; 95% CI=−0.73, 2.94). Regarding active mouth opening, a nonsignificant effect was found between general jaw exercises and education, splint therapy, or a control group when pooling 3 studies.[58,61,86] The MD for active mouth opening was 3.13 mm (95% CI=−1.96, 8.23). A trend favoring exercises was observed based on the 95% CI values.

When pooling the studies[82,83] that looked at exercises plus arthrocentesis or arthroscopy versus conservative ther-

Study or Subgroup	Manual Therapy Plus Exercise			Control (sp, sc, or med)			Weight	Standardized Mean Difference IV, Random [95% CI]	Standardized Mean Difference IV, Random, 95% CI
	X̄	SD	Total	X̄	SD	Total			
Carmeli et al,[87] 2001	1.39	1.41	18	0.17	1.71	18	16.4%	0.76 [0.08, 1.44]	
Haketa et al,[88] 2010	30	24.1	19	15.4	27.66	25	20.4%	0.55 [−0.06, 1.16]	
Ismail et al,[69] 2007	28	20	13	23	22	22	16.0%	0.23 [−0.46, 0.92]	
Minakuchi et al,[90] 2001	7	15.46	25	−0.1	12.71	21	21.8%	0.49 [−0.10, 1.08]	
Schiffman et al,[78] 2007	0.3	0.22	24	0.28	0.23	28	25.4%	0.09 [−0.46, 0.63]	
Total (95% CI)			**99**			**114**	**100.0%**	**0.40 [0.13, 0.68]**	

Heterogeneity: tau²=0.00, χ²=2.90, df=4 (P=.58), I²=0%
Test for overall effect: Z=2.86 (P=.004)

Favors Control (sp, sc, med)   Favors MT Plus Exercise

Figure 3.
Pain intensity at 4 weeks to 3 months: manual therapy plus excercises versus control group in patients with arthrogenous temporomandibular disorders. CI=confidence interval, IV=inverse variance, sp=splint, sc=standard care, med=medications.

apy including exercises alone on active mouth opening at 6 months, we found no differences between these approaches. The MD was −1.01 mm (95% CI=−5.43, 3.42), implying that conservative treatment plus exercises is appropriate to treat disk displacement without reduction or when patients have restricted mandibular movement. The results indicate noninvasive procedures as a first line of treatment.

Manual Therapy Plus Jaw Exercises in Arthrogenous TMD

Seven studies[69,70,78,87-91] looked at the combined effect of MT plus jaw exercises for people with arthrogenous TMD. Three studies[69,87,88] compared MT and exercises versus splint therapy, 1 study[89,90] compared MT and exercise with self-care and advice regarding prognosis, and 2 studies[78,91] used medication as a comparison. In addition, one study[70] compared anesthetic blockage of the auriculotemporal nerve and MT and exercises in addition to blockage of the auriculotemporal nerve.

In general, we found that MT plus exercises reduced symptoms and increased ROM for patients with arthrogenous TMD, particularly for those with reduced ROM due to disk displacements without reduction ("closed lock"). Five of these studies[69,78,87,88,91] favored the use of MT in conjunction with exercises compared with splints[69,87,88] or with medications[91] or other nonconservative treatments for arthrogenous TMD, such as arthroscopy and arthroplasty.[78]

When pooling the results from the studies with homogeneous interventions and

similar outcomes, diagnoses, and available data,[69,78,87,88,90] we found that pain was significantly reduced in patients receiving MT combined with exercises compared with splint therapy, self-care, or medications. The SMD for pain intensity at 4 weeks to 3 months was 0.40 (95% CI=0.13, 0.68), with a moderate effect size according to Cohen's guidelines[48] (Fig. 3).

When looking at active mouth opening,[69,87,88,90] we found that MT plus exercises significantly increased active mouth opening compared with splint therapy, self-care, or medications. The MD for active mouth opening at 4 weeks to 3 months was 3.58 mm (95% CI=1.46, 5.70).

General Jaw Exercise Program in Mixed TMD

Eleven studies[55,71-74,92-99] looked at exercises alone or as part of a general conservative therapeutic regimen to treat patients with mixed TMD. In general, exercises for mixed TMD compared with control groups had better results for decreasing pain and improving function and pain sensitivity of the masticatory muscles.[55,71,96,97] However, compared with other forms of active treatments, such as splints, a global postural re-education program, or acupuncture,[72-74,95,95,98,99] no significant differences between these treatments were found.

When pooling the results of studies with available data and similar interventions and outcomes,[55,71,73,93,94] we found that exercises in the form of general jaw exercises plus conventional treatment or

with the addition of an oral device[94] were not superior to other treatment modalities, such as splint therapy, global re-education posture, splint plus counseling, acupuncture, or standard conservative care, in improving pain intensity. The SMD for pain intensity was −0.06 (95% CI=−0.50, 0.38), with a very small effect size according to Cohen's guidelines.[48]

When pooling results for mouth opening,[55,71,73,92,94,95,97] nonsignificant differences were obtained between general jaw exercises and splint therapy, global re-education posture, splint plus counseling, or standard conservative care. The MD for mouth opening was −0.25 mm (95% CI=−2.08, 1.57) (Fig. 4).

Manual Therapy and Mixed TMD

Six studies[76,100-104] looked at MT alone, such as mobilization of atlantoaxial joint,[101,103] mobilization at the level of cervical spine,[102] manipulation of the upper thoracic spine (D1),[76] massage to masticatory muscles,[104] or mobilizations at the level of TMJ joint,[100] for treating patients with mixed TMD. Results were mixed. The studies by Mansilla-Ferragud et al[101] and Otano and Legal[103] showed positive results at improving mouth ROM and increasing PPT in the orofacial region when comparing mobilization of the atlantoaxial joint versus placebo. However, no statistical differences were found between MT targeted to the jaw and jaw exercises plus splint therapy,[100] between cervical chiropractic adjustment and cervical trigger point therapy,[102] upper thoracic manipulation and placebo,[76] or masticatory muscle mas-

Study or Subgroup	Exercises (General)			Control			Weight	Mean Difference IV, Random [95% CI]
	X̄	SD	Total	X̄	SD	Total		
Burgess et al,[55] 1988	0.7	9.2	9	−1.67	10.96	10	4.1%	2.37 [−6.70, 11.44]
de Felicio et al,[68] 2008	2.82	10.23	10	1.63	8.55	10	4.9%	1.19 [−7.07, 9.45]
Grace et al,[94] 2002	0.1	8.4	11	0.4	8.9	12	6.7%	−0.30 [−7.37, 6.77]
Klobas et al,[95] 2006	0	7.14	20	0.8	6.8	27	20.4%	−0.80 [−4.85, 3.25]
Niemela et al,[73] 2012	1.3	8.9	39	0.1	7.65	37	24.0%	1.20 [−2.53, 4.93]
Raustia and colleagues,[92,99] 1985, 1986	0.6	5.5	25	3.2	8.08	25	22.7%	−2.60 [−6.43, 1.23]
Tegelberg and Kopp,[97] 1996	4.96	6.7	18	4.51	6.58	17	17.2%	0.45 [−3.95, 4.85]
Total (95% CI)			132			138	100.0%	−0.25 [−2.08, 1.57]

Heterogeneity: tau^2=0.00, χ^2=2.63, df=6 (P=.85), I^2=0%
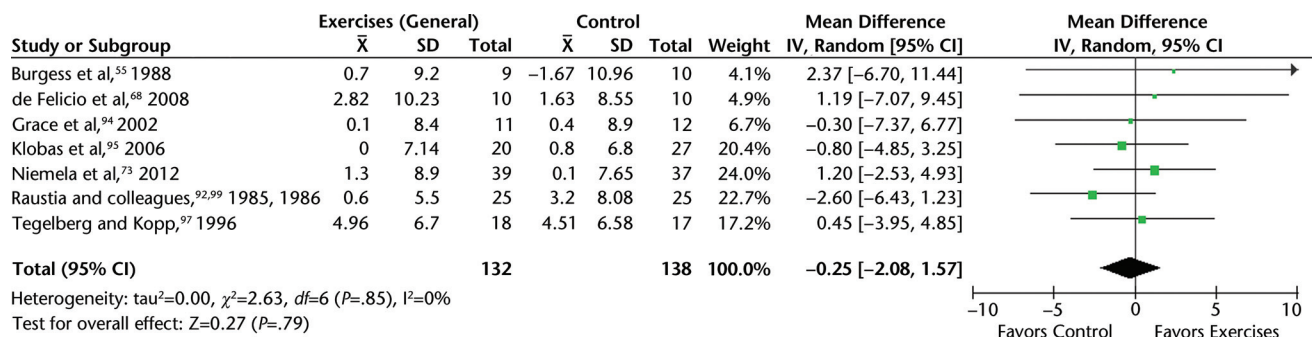Test for overall effect: Z=0.27 (P=.79)

Figure 4.
Mouth opening: general jaw exercises versus splint therapy, global re-education posture, splint plus counseling, or standard conservative care in patients with mixed temporomandibular disorders. CI=confidence interval, IV=inverse variance.

sage and splint[104] for improving symptoms of patients with mixed TMD.

When pooling data from the 2 studies that looked at similar manual techniques, TMD diagnoses, and outcomes,[101,103] although there was no significant difference between mobilization of atlantoaxial joint or control group receiving no mobilization, the MD in mouth opening between control and MT groups was 17.33 mm (95% CI=−10.39, 45.06). This difference can be considered as a clinically relevant improvement in mouth opening favoring MT treatment.

Manual Therapy Plus Exercises for Mixed TMD

Two studies[75,105,106] investigated the effect of MT combined with exercises in people with mixed TMD. Tuncer et al[75] looked at the specific effect of orofacial and cervical MT combined with stretching techniques for the masticatory and neck muscles compared with exercises for the jaw and neck alone and education (home physical therapy). Von Piekartz and Ludtke[106] compared the effect of orofacial physical therapy and neck exercises and MT techniques targeted to both orofacial and cervical regions plus home exercises compared with treatment targeted to the cervical spine only in people with mixed TMD. Pooling the results of the 2 studies[75,105,106] with similar interventions, outcomes, and diagnoses, we found that MT targeted to the orofacial region or in combination with cervical treatment was better than home exercises for the jaw and neck alone or treatment to cervical spine alone for improving mouth opening. The mouth opening

between control and MT groups was 6.10 mm (95% CI=1.11, 11.09) favoring MT groups. This difference was clinically relevant.[35]

Adverse Events

Adverse effects were reported in only 10 of the 48 included trials. Eight of the trials[57,65,67,74,75,77,87,88] reported no adverse events with the treatments. Nascimento et al[70] reported some adverse events due to the anesthetic blockages procedure. In that study, 29.4% of the patients (66/224) had temporary facial nerve paralysis, 0.44% (1/224) had hematoma, and 2.23% (5/224) had positive aspirations. Niemela et al[73] reported that pain on TMJ palpation increased significantly in the splint group compared with the control group. No adverse events regarding exercise therapy or MT treatments were reported among the trials included.

Data Synthesis

The overall quality of evidence for most comparisons was low to moderate according to the GRADE approach.[49] The trials included in this review had unclear or high risk of bias. Thus, the evidence was generally downgraded for 3 reasons: (1) risk of bias, 2) level of heterogeneity (inconsistency), and (3) some imprecision surrounding the effect estimate. Details of GRADE assessment of the included studies are displayed in the Table. From the 14 analyses performed, most of the evidence was considered moderate (9 analyses). The rest of the evidence was considered low. Thus, we can say that the total evidence was considered low.

Discussion
Main Results

Although the quality of the evidence is mostly uncertain and low, the results of our systematic review showed positive results when using postural exercises and jaw exercises to treat both myogenous and arthrogenous TMD disorders. Manual therapy alone or in combination with exercises shows promising effects. Manual therapy targeted to the cervical spine decreased pain and increased mouth ROM in patients with myogenous TMD. Exercises did not show superiority over other treatments for treating mixed TMD. A general exercise program was effective compared with arthrocentesis or arthrography for treatment of arthrogenous TMD, with conservative treatments as a first line of treatment. There remain limited RCTs of high quality that have investigated the effectiveness of MT and exercises to treat TMD.

Effect of Exercise for Treating TMD

Exercise programs are advocated for treating people with musculoskeletal disorders. Therapeutic exercises are prescribed to address TMD. Passive and active stretching of muscles are performed to increase mouth ROM and reduce pain. Postural exercises are helpful.[21] The results of our systematic review are consistent with previous reviews,[19,23] showing positive effects when using exercises to treat myogenous and arthrogenous TMD. In particular, interventions including exercises to correct head and neck posture and active and passive oral exercises can be effec-

Table.
GRADE Evidence Profile[a]

Number of Studies (Design)	Quality Assessment					Summary of Findings — Number of Patients			
	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Patients in Treatment Group	Patients in Control Group	Estimate (SMD or MD) [95% CI]	Quality
Posture Correction Exercises in Myogenous TMD									
Outcome: maximum pain-free opening									
2 (RCTs)	Unclear risk of bias for both studies. Concealment of allocation not clear for both studies, no intention-to-treat analysis.	P value on test for heterogeneity $P=.30$, $I^2=6\%$ No inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	50	50	MD=5.54 mm [2.93, 8.15]	Moderate quality because of risk of bias
Outcome: disturbance of symptoms with daily life									
2 (RCTs)	Unclear risk of bias for both studies. Concealment of allocation not clear for both studies, no intention-to-treat analysis.	P value on test for heterogeneity $P=.15$, $I^2=51\%$ No serious inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	50	50	SMD=1.13 [0.48, 1.78]	Moderate quality because of risk of bias. Upgrading because of large effect size and narrow CI.
General Jaw Exercises Alone or Combined With Exercise Program in Myogenous TMD									
Outcome: pain-free maximum opening									
4 (RCTs)	Unclear risk of bias for most of the studies. Concealment of allocation not clear for 3 studies, and 1 study was not concealed. All studies did not perform intention-to-treat analysis.	P value on test for heterogeneity $P<.00001$, $I^2=88\%$ High heterogeneity	No serious indirectness	No serious imprecision	No serious publication bias	64	67	MD=5.94 mm [−1.0, 12.87]	Low quality because of risk of bias and inconsistency
Outcome: pain intensity									
5 (RCTs)	High risk of bias for most of the studies. Concealment of allocation not clear for 4 studies, and 1 study was not concealed. Adherence and cointerventions unclear for most of the studies. No intention to treat for 4 studies.	P value on test for heterogeneity $P=.10$, $I^2=49\%$ No serious inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	85	90	SMD=0.43 [−0.02, 0.87]	Moderate quality because of risk of bias

(Continued)

Table.
Continued

Number of Studies (Design)	Quality Assessment					Summary of Findings			
	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Number of Patients		Estimate (SMD or MD) [95% CI]	Quality
						Patients in Treatment Group	Patients in Control Group		
Manual Therapy Targeted to the Orofacial Region in Myogenous TMD									
Outcome: pain intensity									
3 (RCTs)	Concealment of allocation not clear for 2 of the studies, and 1 study was not concealed. Adherence and cointerventions unclear for all of the studies. No intention to treat analysis for 2 studies.	P value on test for heterogeneity P=.78, I²=0% No serious inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	44	44	MD=1.35 cm [0.91, 1.78]	Moderate quality because of risk of bias
Jaw/Neck Exercises Alone or as Part of a Conservative Regimen in Arthrogenous TMD									
Outcome: pain intensity									
4 (RCTs)	Concealment of allocation not clear for all of the studies. Blinding was unclear for 3 of the studies, and 1 study did not have appropriate blinding. Adherence and cointerventions unclear for all of the studies. No intention-to-treat analysis for 2 studies.	P value on test for heterogeneity P=.01, I²=73% High inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	73	73	SMD=0.68 [−0.04, 1.40]	Low quality because of risk of bias and inconsistency
Outcome: active mouth opening									
3 (RCTs)	Concealment of allocation not clear for all of the studies. Blinding was unclear for 2 of the studies, and 1 study did not have appropriate blinding. Adherence and cointerventions unclear for all of the studies.	P value on test for heterogeneity P=.009, I²=79% High inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	63	63	3.13 mm [−1.96, 8.23]	Low quality because of risk of bias and inconsistency
Jaw/Neck Exercises Alone or as Part of a Conservative Regimen vs Surgery in Arthrogenous TMD									
2 (RCTs)	Concealment of allocation not appropriate for both studies. Blinding was not appropriate for both studies. Adherence and cointerventions unclear for both studies.	P value on test for heterogeneity P=.04, I²=76% High inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	68	63	MD=−1.01 mm [−5.43, 3.42]	Low quality because of risk of bias and inconsistency

(Continued)

Table.
Continued

Number of Studies (Design)	Quality Assessment					Summary of Findings			
	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Number of Patients			Quality
						Patients in Treatment Group	Patients in Control Group	Estimate (SMD or MD) [95% CI]	

Manual Therapy Plus Jaw Exercises in Arthrogenous TMD

Outcome: pain intensity

| 5 (RCTs) | Concealment of allocation unclear for most of the studies. Blinding was appropriate for most of the studies. Adherence unclear for most of the studies. No or unclear intention to treat for 2 studies. | P value on test for heterogeneity P=.58, I²=0% No inconsistency | No serious indirectness | No serious imprecision | No serious publication bias | 99 | 114 | SMD=0.40 [0.13, 0.68] | Moderate quality because of risk of bias |

Outcome: active mouth opening

| 4 (RCTs) | Concealment of allocation unclear for all of the studies. Blinding was appropriate for most of the studies. Adherence unclear for all of the studies. | P value on test for heterogeneity P=.93, I²=0% No inconsistency | No serious indirectness | No serious imprecision | No serious publication bias | 75 | 77 | 3.58 mm [1.46, 5.70] | Moderate quality because of risk of bias |

General Jaw Exercise Program in Mixed TMD

Outcome: pain intensity

| 5 (RCTs) | Concealment of allocation unclear for 4 of the studies. One study did not have appropriated allocation concealment. Appropriate blinding was unclear for most of the studies. Adherence and cointerventions unclear for all of the studies. | P value on test for heterogeneity P=.14, I²=41% No serious inconsistency | No serious indirectness | No serious imprecision | No serious publication bias | 81 | 81 | SDM=−0.06 [−0.50, 0.38] | Moderate quality because of risk of bias |

Outcome: mouth opening

| 7 (RCTs) | Concealment of allocation unclear for 4 of the studies. Three studies did not have appropriate allocation concealment. Appropriate blinding was unclear for most of the studies. Adherence and cointerventions unclear for all of the studies. Most of the studies did not perform an intention-to-treat analysis. | P value on test for heterogeneity P=.85, I²=0% No inconsistency | No serious indirectness | No serious imprecision | No serious publication bias | 132 | 138 | MD=−0.25 [−2.08, 1.57] | Moderate quality because of risk of bias |

(Continued)

Table.
Continued

Number of Studies (Design)	Quality Assessment					Summary of Findings			Quality
	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Number of Patients			
						Patients in Treatment Group	Patients in Control Group	Estimate (SMD or MD) [95% CI]	
Manual Therapy and Mixed TMD									
Outcome: mouth opening									
2 (RCTs)	Concealment of allocation unclear for both studies. Appropriate blinding was unclear for one study. Intention to treat unclear for one study.	P value on test for heterogeneity P=.000001, I²=100% Serious inconsistency	No serious indirectness	Moderate imprecision	No serious publication bias	47	49	MD=17.33 mm [−10.39, 45.08]	Low quality because of risk of bias, inconsistency, and imprecision
Manual Therapy Plus Exercises for Mixed TMD									
Outcome: mouth opening									
2 (RCTs)	Concealment of allocation unclear for both studies. Appropriate blinding was unclear for one study and not appropriate for the other study. Intention to treat unclear for one study and not performed by the other study.	P value on test for heterogeneity P=.02, I²=82% Serious inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	42	41	MD=6.10 mm [1.11, 11.09]	Moderate quality because of inconsistency

ᵃ SMD=standardized mean difference, MD=mean difference, CI=confidence interval, RCT=randomized controlled trial.

tive for reducing musculoskeletal pain and improving oromotor function.[59,60] However, most of these exercise programs were part of a general conservative treatment regimen including other therapies and did not provide clear information regarding dosage, frequency, or adherence, so the isolated effect of exercise to treat TMD and the optimal regimen are uncertain at this time. General aerobic exercises have been shown to improve muscle strength, flexibility, and functional capacity and could induce analgesia.[107] Further research is needed to investigate the usefulness of aerobic exercise and focused muscular training, especially exercises targeted to cervical muscles in people with TMD.

Effect of Manual Therapy for Treating TMD

Manual therapy has been used to restore normal ROM, reduce local ischemia, stimulate proprioception, break fibrous adhesions, stimulate synovial fluid production, and reduce pain. Based on the results of this systematic review, MT shows promising results for treatment of myogenous, arthrogenous, and mixed TMD, although the evidence is limited and low. A combination of MT for the orofacial region plus MT of the cervical spine was more effective than home exercises or treatment to cervical spine alone in people with mixed TMD. Research, to date, suggests that a mixed therapy involving MT techniques and exercises improves patient outcome. Other systematic reviews have shown similar results.[24]

Mobilization of the cervical spine resulted in decreases in pain intensity and pain sensitivity (via PPT evaluation) in patients with myogenous TMD that exceed suggested values for minimum clinically important differences for pain and treatment of the cervical spine. Manual therapy techniques such as mobilization of the cervical spine could have an influence on orofacial pain and movement in the jaw through the connections of these 2 systems in the trigeminocervical nucleus.[108]

Methodological Elements and Overall Quality of the Evidence Affecting Observed Effect

The overall rating of the evidence for this review was low. This finding was due mainly to the risk of bias of the analyzed studies. The methodological biases common to the included studies could have an impact on results. Selection bias could have existed, as only 20 trials reported appropriate randomization and only 4 reported concealment of allocation.

Another important bias was the lack of blinding, especially of the patients and assessors. Only 12 studies used blinded assessment of clinician-assessed outcomes such as mouth opening. However, we also were interested in pain, which is a subjective outcome and dependent on the patient's report. It is likely that lack of blinding could have affected the results of these studies. However, because of the nature of the interventions investigated, blinding would not be possible in many of them. There is empirical evidence showing that trials without appropriate randomization, concealment of allocation, and blinding tend to report an inaccurate treatment effect compared with trials that include these features.[109] Thus, the results of this systematic review should be interpreted with caution, especially in trials with subjective self-reported outcomes.

Other potential biases that could potentially have affected observed effects were inappropriate handling of withdrawals and dropouts (only 16 trials used ITT analysis). Effect sizes from trials that excluded participants in their analysis or that used a modified ITT protocol tended to be more beneficial than those from trials without exclusions, demonstrating that the ITT principle is important to preserve the benefits of randomization and keep unbiased estimates when the objective of the trial is to investigate effectiveness.[110]

Studies did not report interventions in sufficient detail to be reproducible. In addition, they did not control for cointerventions and did not have adequate adherence to treatment. These issues are of importance for this study, as it is unclear if the effects on selected outcomes were due to the effect of exercise, MT, or other cointerventions. In addition, it is unclear if the participants received enough dosage of treatments, as adequate adherence was accomplished by only a very small proportion of studies (15.2%). Adherence testing should be systematically studied in future studies with exercise prescriptions.

The present study used a compilation of items from all of the scales used in the reviewed physical therapy literature in addition to the risk of bias tool. Our recent analysis of health scales used to evaluate methodological quality determined that none of these scales are adequate for use alone.[44,111] Therefore, we decided to use all of the scales, using a compilation of their items, to provide a comprehensive and sensitive evaluation of the quality of individual trials. Research investigating methodological predictors for determining trial quality in physical therapy is needed.

Limitations

The findings of this review are specific to TMD (nonsurgical) and to exercise and MT. As with any systematic review, there is the potential for selection bias, yet our group used a comprehensive search strategy and included databases as well as manual search. There was a small proportion of studies in other languages that our team could not translate. However, we believe that most of the representative studies were included in the final analysis of this systematic review. In addition, it has been reported that language-restricted meta-analyses only minimally overestimate treatment effects (~2% on average) compared with language-inclusive meta-analyses.[112] Therefore, language-restricted meta-analyses do not appear to lead to biased estimates of intervention effectiveness.[112,113]

The heterogeneity among studies, particularly with respect to TMD diagnosis, study intervention, and chosen control or comparison intervention was a challenge. Many studies included the use of exercises or MT as part of a general treatment program, which made the evaluation of these treatments in isolation difficult. Moreover, different diagnostic criteria for TMD were used. Only 21 out of 48 studies included a diagnostic tool that had been demonstrated as being valid, reliable, and reproducible to diagnose TMD. Thus, diagnoses used for the analyzed studies might not be appropriate. Despite this lack of standardized diagnosis, the study populations in all trials appeared to be representative of patients seen in clinical practice. We encourage clinicians and researchers using the new diagnostic criteria for TMD (RDC/TMD) in future studies to allow consistent diagnoses according to the same criteria, taxonomy, and nomenclature to avoid confusion and misunderstanding.[114]

Research Implications

No high-quality evidence was found, indicating that there is great uncertainty about the effectiveness of exercise and manual MT for TMD. There is a clear need for well-designed RCTs examining exercise and MT interventions for TMD. Specifically, it is necessary that trials be performed isolating the type of exercise and manual technique that is under testing to allow understanding the effectiveness of this type of treatment. In addition, details of exercise, dosage, and frequency as well as details on manual techniques should be reported to create reproducible results. High-quality trials with larger sample sizes are needed.

Clinical Implications

Although the overall level of evidence is low, exercises and MT are safe and simple interventions that could potentially be beneficial for patients with TMD. Active and passive exercise for the jaw, postural exercises, and neck exercises appear to have favorable effects for patients with TMD. Manual therapy alone or in combination with exercises shows promising effects. Exercises did not show clear superiority over other conservative treatments for TMD.

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Appendix.

Search Strategy Example: Ovid MEDLINE in Process and Other Nonindexed Citations and Ovid MEDLINE, 1946–Present

No.	Searches	Results
1	temporomandibular disorders.mp. or exp Temporomandibular Joint Disorders/	14,629
2	exp Temporomandibular Joint/ or craniomandibular disorders.mp. or exp Temporomandibular Joint Dysfunction Syndrome/ or exp Craniomandibular Disorders/ or exp Temporomandibular Joint Disorders/	20,872
3	exp Temporomandibular Joint/	10,155
4	temporomandibular joint syndrome.mp. or exp Temporomandibular Joint Dysfunction Syndrome/	4,662
5	exp Facial Pain/	7,137
6	exp Temporomandibular Joint Disorders/ or TMD.mp.	15,668
7	exp Temporomandibular Joint Disorders/ or TMD.mp. or exp Temporomandibular Joint Dysfunction Syndrome/	15,668
8	TMJ.mp. or exp Temporomandibular Joint/	13,266
9	myofascial pain syndrome.mp. or exp Myofascial Pain Syndromes/	5,922
10	exp Temporomandibular Joint Dysfunction Syndrome/ or exp Facial Pain/ or exp Myofascial Pain Syndromes/ or exp Masticatory Muscles/ or myofascial pain.mp.	22,449
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	37,590
12	exp Manipulation, Orthopedic/ or manipulation.mp. or exp Manipulation, Chiropractic/ or exp Manipulation, Spinal/	66,454
13	exp Manipulation, Spinal/ or exp Chiropractic/ or spinal adjustment.mp.	4,130
14	exp Manipulation, Osteopathic/ or exp Osteopathic Medicine/ or osteopathic.mp.	3,812
15	orthopedic.mp. or exp Orthopedics/	58,939
16	exp Orthopedics/ or orthopaedic*.mp.	37,827
17	musculoskeletal therapy.mp.	14
18	exp Musculoskeletal Manipulations/ or musculoskeletal therapy.mp.	12,254
19	manual therapy.mp. or exp Musculoskeletal Manipulations/	12,850
20	manual ther*.mp.	1,315
21	exp Physical Therapy Modalities/ or physical therapy.mp. or exp Exercise Therapy/	131,424
22	physiotherapy.mp.	11,552
23	exp Exercise/ or exp Exercise Movement Techniques/ or exercise.mp. or exp Exercise Therapy/	277,733
24	rehabilitation.mp. or exp "Physical and Rehabilitation Medicine"/ or exp Mouth Rehabilitation/ or exp Rehabilitation/	230,191
25	manipula*.mp.	129,940
26	relaxation therapy.mp. or exp Relaxation Therapy/	7,438
27	relaxation training.mp.	1,093
28	exp Physical Therapy Modalities/ or exp Posture/ or posture training.mp.	184,092
29	passive jaw motion device.mp. or exp Exercise Therapy/	30,403
30	continuous passive motion.mp.	513
31	physiotherap*.mp.	15,563
32	physical Therap*.mp.	37,928
33	12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 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	803,497
34	randomized controlled trial.mp. or exp Randomized Controlled Trial/	400,223
35	exp Random Allocation/ or randomised controlled trial.mp.	93,682
36	34 or 35	467,379
37	11 and 33 and 36	270
38	exp Clinical trial/ or randomized.tw. or placebo.tw. or dt.fs. or randomly.tw. or trial.tw. or groups.tw.	3,645,258
39	11 and 33 and 38	772