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REVIEW

Effectiveness of manual therapy applied to craniomandibular structures in temporomandibular disorders: A systematic review

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Abstract

Background: Within physical therapy, manual therapy is known to be effective for managing temporomandibular disorders (TMDs). However, manual therapy is a broad term including different approaches applied to different body regions.

Aims: This is the first systematic review that aims to evaluate the effectiveness of manual therapy applied specifically to the craniomandibular structures (Cranio-Mandibular Manual Therapy [CMMT]) on pain and maximum mouth opening in people with TMD.

Material and methods: This systematic review was developed based on a pre-determined published protocol which was prospectively registered with PROSPERO (CRD42019160213). A search of MEDLINE, Embase, CINAHL, ZETOC, Web of Science, SCOPUS, PEDro, PubMed, Cochrane Library and Best Evidence, EBM reviews–Cochrane Central Register of Controlled Trials, Index to Chiropractic Literature ChiroAccess and Google Scholar databases was conducted from inception until October 2020. Randomised controlled trials comparing the effect of CMMT on pain and maximum mouth opening versus other types of treatment in TMDs were included. Two reviewers independently screened articles for inclusion, extracted data, assessed risk of bias with the revised Cochrane risk of bias tool for randomised trials and evaluated the overall quality of evidence with the Grading of Recommendations, Assessment, Development and Evaluations.

Results: A total of 2720 records were screened, of which only 6 (293 participants) satisfied the inclusion criteria. All studies showed some concerns in risk of bias, except for one, which was high risk of bias. The overall quality of evidence was very low for all outcomes because of high heterogeneity and small sample sizes. All studies showed a significant improvement in pain and maximum mouth opening for CMMT from baseline in the mid-term, but only two showed superiority compared to other interventions. Given the high heterogeneity and small sample sizes of the included studies, a quantitative synthesis was not performed.

Discussion and conclusion: There is the need for future high methodology research investigating different manual therapy techniques applied to different regions and different populations (e.g., chronic versus acute TMD) to determine what is most effective for pain and maximum mouth opening in patients with TMDs.

KEYWORDS
manual therapy, masticatory muscles, pain, physical therapy, temporomandibular disorder, temporomandibular joint

1 | BACKGROUND

The masticatory muscles, temporomandibular joints (TMJs) and associated structures are typically affected in people with temporomandibular disorders (TMDs),[1,2] and the principal symptoms are pain and restricted jaw mobility. Temporomandibular pain and functional limitations are often associated with various comorbidities including pain in other body regions such as the neck or low back.[3] In developed countries, TMDs are one of the most common chronic orofacial pain conditions and can have a negative impact on quality of life.[4,5]

Multidisciplinary management with careful consideration of conservative treatment modalities is currently recommended for patients with TMDs.[6,7] Over the last few decades, several therapeutic approaches for TMDs have been described, which take into consideration the multifactorial aetiology of the disorder. Physical therapy remains one of the most commonly applied interventions given its ability to decrease pain, improve joint mobility and address abnormal motor function.[8–10] In particular, hands-on treatment such as manual therapy (MT) intends to recover joint range of motion, mobilise or manipulate soft tissues and joints, and alleviate pain.[11,12] Several MT techniques have been examined in randomised controlled trials (RCTs), including massage and soft tissue techniques applied to the neck and masticatory muscles,[13–15] TMJ mobilisation[16] and cervical spine manipulation and mobilisation.[13,17] These studies demonstrated the positive effects of MT for patients with TMD evidenced by reduced pressure pain sensitivity, increased maximum mouth opening (MMO), and reduced pain.[13,14]

Systematic reviews and meta-analyses have been performed to investigate the effect of physical therapy for people with TMD,[18–23] and these reviews have confirmed that physical therapy has a positive impact on pain and function.[18–20] However, the authors considered combined physical therapy treatments (eg exercise combined with MT) and as such, did not provide specific knowledge on the effectiveness of individual approaches such as MT.[18–20] For this reason, two of the systematic reviews could not provide generalisable conclusions about the effectiveness of MT.[19,20] Armijo-Olivo et al. conducted a systematic review on physical therapy for TMD and included a specific sub-analysis considering different treatments. Nevertheless, the heterogeneity of MT interventions prevented them from reaching a conclusion on the effectiveness of MT.[18]

Calixtre et al. and Martins et al. performed systematic reviews to investigate the effectiveness of MT alone for TMDs.[21,22] Their conclusions reported low levels of evidence related to methodological biases, poor external and internal validity of the included RCTs and heterogeneity of MT interventions. Both systematic reviews included papers with MT directed to diverse areas such as the cervical or thoracic regions and/or craniomandibular structures.[21,22] Although MT generally includes different approaches in different body regions, the effectiveness of techniques targeted on specific regions (eg neck, trunk, TMJ) is essential information for manual therapists planning TMD treatments. To date, there has not been a systematic review investigating the effects on pain and TMJ range of motion following MT applied specifically to the craniomandibular structures (Craniomandibular manual therapy [CMMT]).

Therefore, this systematic review aimed to evaluate the effectiveness of CMMT on pain and TMJ range of motion in people with TMD.

2 | METHODS

2.1 | Protocol and registration

This systematic review was developed based on a pre-determined published protocol, which was prospectively registered with PROSPERO (CRD42019160213) and is reported in line with the updated version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Data S1).[24,25]

2.2 | Eligibility criteria

2.2.1 | Inclusion criteria

The inclusion criteria followed the PICO framework as suggested by the PRISMA checklist.[25]

Participants

Adult participants (aged >18 years) with a diagnosis of TMD according to the Research Diagnostic Criteria for TMD (RDC/TMD)[26] or with Diagnostic Criteria for TMD (DC/TMD),[27] or any trials with a population reporting signs and symptoms of TMD.[1,2,28]

Outcome measures

MMO and pain intensity are the primary outcomes. MMO is defined as the measure, in millimetres, of the interincisal distance during an active MMO. Only trials with MMO measurement methods in line with the DC/TMD clinical examination protocol (eg using a ruler) were included.[27] With regards to pain intensity, it is defined as pain reported in the masticatory muscles, TMJ area, with possible spread to adjacent regions. Only trials with pain intensity measurement methods in line with recommendations of the Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT) (eg visual analogue scale, numeric rating scale) were included.[29]

Type of intervention

Any trials reporting CMMT as one of the interventions investigated were included. CMMT is defined as 'any hands-on treatment provided by the physical therapist'[11] (p.8) [as defined by the American Academy of Orthopaedic Manual Physical Therapists] directed to masticatory muscles (eg masseter, temporal and pterygoid muscles), TMJs, suprahyoid muscles and other sites on the head.

Study design and comparison

RCTs examining CMMT alone vs comparison groups not including CMMT were included. Any comparison group was included (eg standard care, sham therapy). RCTs with multiple interventions were included and managed in line with the Cochrane Handbook for Systematic Reviews of Interventions.[30]

Timing and setting

No restriction on length of studies, assessment time points or setting of study was considered.

2.2.2 | Exclusion criteria

Any trials reporting the effects of CMMT combined with other treatment modalities (eg exercise) and/or not only targeting the craniomandibular area were excluded. Trials reporting history of Eagle's syndrome, surgery in the craniomandibular area, rheumatic diseases and other severe comorbidities (eg neurological disease, cancer) were excluded. Papers with full text not written in English were excluded.

2.3 | Information sources

The search strategy took place from 1 September to 31 October 2020. The following electronic databases were searched: MEDLINE (OVID interface), Embase (OVID interface), Scopus, Web of Science, CINAHL (EBSCO interface), PEDro, ZETOC, PubMed, Cochrane Library and Best Evidence, Index to Chiropractic Literature ChiroACCESS and Google Scholar. References from past systematic reviews and RCTs on this topic were examined for supplementary papers to be included. Hand searching was conducted of key journals (Journal of Oral Rehabilitation, Musculoskeletal Science and Practice, The Journal of Oral & Facial Pain and Headache, Journal of Manual and Manipulative Therapy, Journal of Applied Oral Science). Grey literature for unpublished research was checked on the British National Bibliography and EthOS.

2.4 | Search strategy

The search strategy was created for each database using medical subject headings (MESH) if possible and significant text words dealing with TMD, TMJ, MT, physical therapy and pain. The full search strategies for all databases are reported in Data S2.

2.5 | Selection process

Two reviewers (GA/LP) separately screened titles and abstracts by scoring them as eligible/not eligible/unsure, thanks to the predetermined eligibility criteria.[31] The priority of the eligibility criteria sequence was as follows: (1) participants, (2) study design, (3) type of intervention, (4) outcome measures and (5) absence of exclusion criteria. Papers that cannot be excluded based on title and abstract were judged potentially includible, and full texts were examined.[32] The full-text assessment was managed in the same independent way. Papers were included if both reviewers agreed on eligibility. Any disagreement was solved through discussion; however, a third reviewer (DF) was available to mediate in case of discrepancies between reviewers. The agreement between reviewers is reported in Data S3.

2.6 | Data collection process

Two reviewers (GA/LP) independently extracted the review data using a standardised form based on the Cochrane model.[30] Before starting the data extraction process, the form was applied to five papers for familiarisation.

2.7 | Data items

The extracted data items from the included papers covered: (1) trial information (authors, year of publication, location), (2) population (sample size, type of TMD, TMD diagnostic criteria, inclusion/exclusion criteria), (3) intervention (duration, frequency, detail of the manual therapy techniques), (4) comparison group (type of comparison), (5) outcome measures (pain outcome measures, MMO outcome measures), (6) follow-up assessment points (detail of timing of follow-up assessments) and (7) results (between-group differences at follow-up assessments).

2.8 | Risk of bias in individual studies

Two reviewers (GA/LP) independently applied the revised Cochrane risk-of-bias tool for randomised trials (RoB 2) to estimate the risk of bias of the included papers.[33–35] The reviewers followed the full guidance document from the ROB2 Development Group.[34] Any RoB2 disagreement was managed with the same procedure used in the inclusion/exclusion process and a third reviewer (DF) was available to mediate in case of discrepancies. Agreement between reviewers for RoB2 is reported in Data S4.

2.9 | Effect measures

MMO and pain intensity data for the included papers were analysed calculating the mean difference (MD) and 95% confidence intervals (CI). MD and CI were calculated from data reported in each paper by following the Cochrane Handbook for Systematic Reviews of Interventions Version.[30]

2.10 | Synthesis methods

Due to heterogeneity of comparators and time assessment-point, a meta-analysis was not feasible. Consequently, a narrative synthesis was developed following the synthesis without meta-analysis (SwiM) in systematic review guidelines.[36] The small number of included papers showed heterogeneity of TMD type (eg chronic, acute, myogenic, arthrogenic, mixed), so the studies were grouped for outcome measures instead of TMD type as stated in the protocol.[24] For each outcome measure, forest plots were displayed with MD and CI of individual included papers. No additional or sensitivity analysis was performed because of the heterogeneity and the small number of included papers.

2.11 | Reporting bias assessment

A search for unpublished studies, protocols and trial registration was conducted. No unpublished studies were found. None of the included papers was preceded by a protocol. There was consistency between trial registrations with the included papers. Possible competing interests from authors groups were not found.

2.12 | Certainty assessment

Two independent reviewers evaluated the overall strength and quality of evidence by applying the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) according to the GRADE Handbook.[37]

3 | RESULTS

3.1 | Study selection

Figure 1 shows the included studies at each phase of the review. A total of 2720 articles were screened by title and abstract, and 15 were assessed by full text. Six articles met the eligibility criteria and were included in the systematic review.[14,15,38–41] The main reasons for exclusion were: no TMD population ($n = 1016$); no MT intervention ($n = 860$); not an RCT ($n = 694$); intervention consisted of a combined treatment ($n = 63$); MT was not applied to the craniomandibular area ($n = 27$), other reasons ($n = 45$). One article was excluded[42] because participants were the same as included in another article.[14] Another article was excluded because the MT intervention was mainly directed to the craniomandibular area but with the possibility for the therapist to also involve the neck region.[43]

3.2 | Study characteristics

Apart from one article published in 1994,[38] all other articles were published between 2012 and 2014 or in 2018.[14,15,39–41] Three studies were conducted in Australia, two in Brazil and one in Poland. A range of TMD diagnoses were considered in the included studies (eg myogenic, arthrogenic, chronic form or not).[44] The TMD diagnostic criteria chronologically reflect the gold standard of the time for diagnosing TMD (eg RCD/TMD, DC/TMD)[26,27] except for Gomes et al.[15] using the Fonseca anamnestic index and Taylor et al.[38] relying on the clinical experience of the recruiter. With regards to the applied interventions, the included studies investigated different types of CMMT: (1) intraoral myofascial therapy (IMT), (2) oscillatory Grade IV TMJ mobilisation, (3) facial massage, (4) MT applied to TMJ and masticatory muscles and (5) masticatory muscle trigger points release. There was also heterogeneity in the comparator type (eg sham treatment, control group, self-care and exercise, splint, kinesio tape and photobiomodulation therapy) and assessment-point (immediate post-treatment, five days and from 4 weeks to 1 year). Two studies analysed MMO as the only outcome only, one pain intensity only and the others examined both outcomes. Table 1 summarises the study characteristics of the six included papers.

3.3 | Risk of bias and certainty of evidence

All studies showed 'Some Concerns' in risk of bias, except for one, which was of 'high risk' of bias.[40] No studies presented biases related to missing outcome data. On the other hand, all studies had moderate-to-high risk of bias in the selection of the reported results. Figure 2 displays the risk-of-bias assessment for each study in all domains.

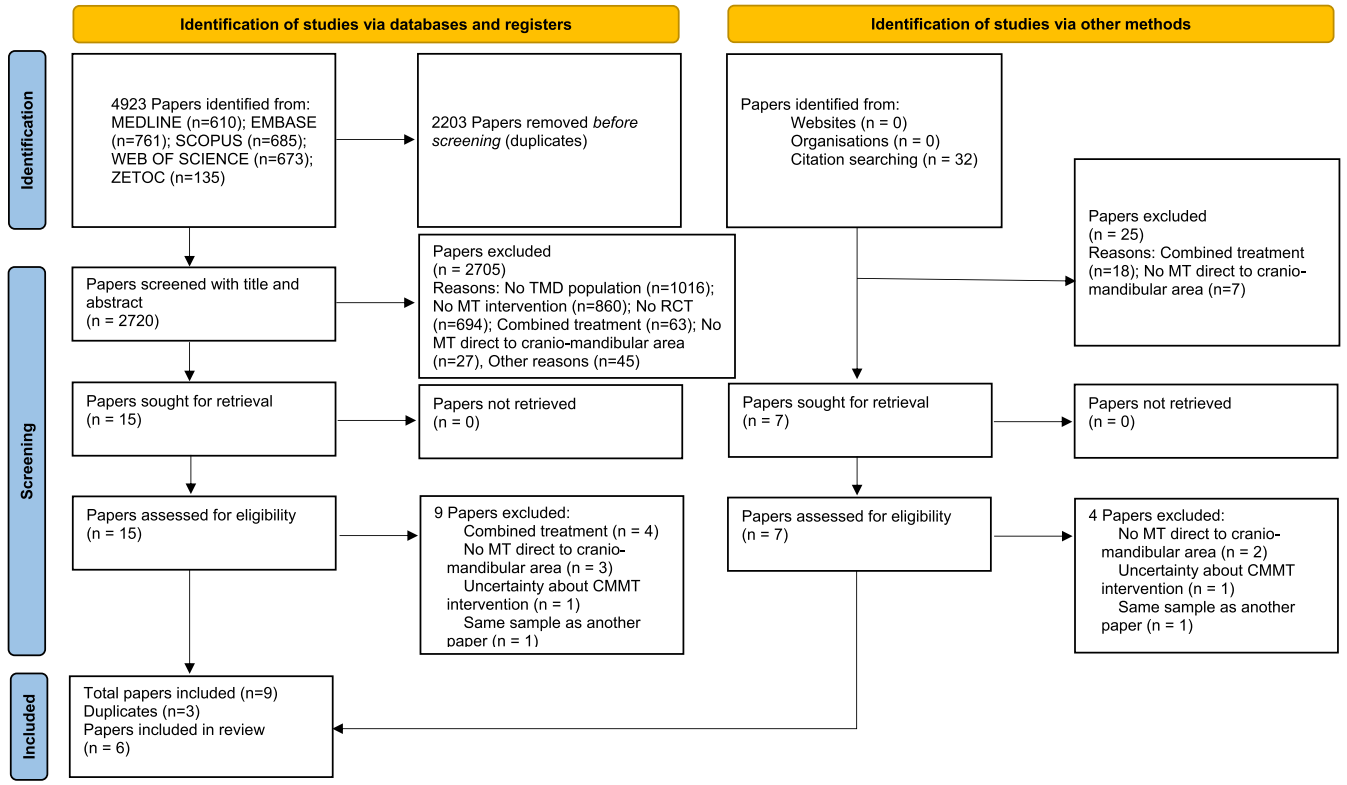

FIGURE 1 PRISMA flow diagram which included searches of databases and other sources. Page et al.[25] For more information, visit: http://www.prisma-statement.org/

Overall, there is very low quality of evidence scored with the GRADE assessment for pain intensity and MMO.[37] All studies showed serious inconsistency because of the heterogeneity of comparator and assessment time-point. Due to the restricted sample size and unsatisfactory confidence interval, the imprecision is scored as 'Serious'. No limitations were found about indirectness and publication bias. Table 2 reports the GRADE quality assessment for each outcome.

3.4 | Results of individual studies

3.4.1 | Pain

The studies by Kalamir et al. in 2012 and in 2013 found that CMMT effectively reduces pain intensity in the medium term compared to self-care with exercise and control interventions[14,39] whereas in contrast, Brochado et al.[40] showed no difference compared to photobiomodulation therapy. According to Lietz-Kijak et al.,[41] CMMT is less effective at reducing pain in the short term compared to kinesio tape. Figure 3 displays the forest plot, which illustrates the effects of CMMT on pain intensity compared to other interventions. Very low quality of evidence supports CMMT for patients with TMD for successfully improving pain in the mid-term.[14,15,38–41] However, the overall results in comparison to other interventions remain unclear because of the heterogeneity and small sample sizes of the included studies.

3.4.2 | MMO

Taylor et al.[38] found that CMMT is effective at improving MMO immediately post-treatment compared to a sham treatment. Kalamir et al.[39] showed that CMMT effectively improves MMO in the medium term compared to a control group; in contrast, other authors found no difference in the effect of CMMT on MMO compared to self-care and exercise, splint or photobiomodulation therapy.[14,15,40] Figure 4 displays the forest plot, which illustrates the effects of CMMT on MMO compared to other interventions. Very low quality of evidence suggests that CMMT applied to patients with TMD, increases MMO in the short and mid-term.[14,15,38–41] However, the overall effect in comparison to other interventions remain unclear because of the heterogeneity and small sample sizes of the included studies.

4 | DISCUSSION

This is the first systematic review analysing the effectiveness of CMMT on pain intensity and MMO in people with TMDs. All of the included studies showed a significant improvement in pain and MMO following CMMT in the mid-term, but only two showed the superiority of CMMT compared to other interventions.[14,15,38–41] Quantitative synthesis was not deemed possible and the overall the quality of evidence was very low because of moderate-to-high risk of bias, high heterogeneity and small sample sizes.

TABLE 1 Characteristics of studies comparing CMMT vs other interventions for improving pain intensity and MMO in TMDs

Trial information	Population	Intervention
Taylor et al.[38] Year: 1994 Country: Australia	*Sample*: 15 (14 female, 1 male; age 20–35 years) *TMD type*: TMPD both chronic TMJ and associated muscle symptoms and signs TMD diagnostic criteria: experienced clinician diagnosis of TMPD *Inclusion criteria*: aged 20–35; symptoms including pain in the region of the TMJs and masticatory and associated muscles and limited mandibular movement for at least six months; mandibular opening <40 mm; palpable tenderness in the masseter muscles *Exclusion criteria*: severe head trauma or surgery, known cervical pathology, not fluent in the English language, taking any medication except for occasional analgesics, no complete dentition to provide stable and repeatable base points for jaw measurements	*Intervention group*: Oscillatory Grade IV TMJ mobilisation technique, taking the joint into resistance (Maitland, 1984), which was performed three times; each procedure lasted 60 s separated by an interval of 10 s
Kalamir et al.[14] Year: 2012 Country: Australia	*Sample*: 93 (52 female, 41 male; age 34.6 ± 5.9 years) *TMD type*: chronic myogenous TMD *TMD diagnostic criteria*: RDC/TMD *Inclusion criteria*: 18–50 years; a daily history of peri-auricular pain with or without joint sounds of at least 3 months in duration; confirmed diagnosis of myogenous TMD with RDC/TMD; minimum baseline graded chronic pain score of 3 of 10 on each of the 3 symptom outcome measures *Exclusion criteria*: previous attendance at the primary author's clinic; edentulous (toothless) applicants; malignancy in the last 5 years; other physical contra-indications such as inflammatory arthritides, fracture, dislocations, or known instability of the jaws or neck; metabolic diseases; connective tissue diseases and rheumatic disorders; and hematologic disorders; severe depression on the RDC psychosocial assessment. According to RCD/TMD mixed trait and arthrogenous TMD diagnoses	*Intervention group*: IMT group underwent 2 treatment sessions per week for 5 weeks of approximately 10–15 min: (1) Intraoral temporalis release; (2) Intraoral medial and lateral pterygoid (origin) technique; (3) Intraoral sphenopalatine ganglion technique
Kalamir et al.[39] Year: 2013 Country: Australia	*Sample*: 46 (29 female, 17 male; age 27.5 ± 8.1 years) *TMD type*: chronic myogenous TMD *TMD diagnostic criteria*: RDC/TMD *Inclusion criteria*: age restriction between 18 and 50 years old, a daily history of peri-auricular pain (with or without joint sounds) for at least the last three months; confirmed diagnosis of myogenous TMD with RDC/TMD; minimum baseline graded chronic pain score of 3 of 10 on each of the 3 symptom outcome measures *Exclusion criteria*: use of dentures; a history of malignancy in the last five years; other physical contra-indications such as active inflammatory arthritides, fractures, dislocations, known instability of the jaw or neck; metabolic, connective tissue, haematologic and rheumatologic diseases; severe depression or somatisation on the RDC psychosocial assessment. According to RCD/TMD mixed trait and arthrogenous TMD diagnoses were excluded	*Intervention group*: 2 treatment sessions per week for 5 weeks of approximately 10–15 min: (1) Intraoral temporalis release; (2) Intraoral medial and lateral pterygoid (origin) technique; (3) Intraoral sphenopalatine ganglion technique

Comparison group	Outcome measures	Follow-up assessment points	Results
Comparison group: Sham treatment: barely perceptible superficial massage performed in the TMJ region, three times, each lasting 60 s and separated by an interval of 10 s	*Pain outcome measures*: N/A MMO outcome measures: One set of vernier callipers was used to measure jaw movements using the mesial incisal angles of the upper and lower right central incisor teeth as the points of reference	*Pain*: N/A *MMO*: pre-treatment; post-treatment	*Pain*: N/A *MMO*: Mandibular opening was significantly increased following mobilisation compared with the sham treatment Mean changes in MMO for the sham group was −0.98 with a SD of 1.1; mean changes in MMO for the intervention group was +2.48 with a SD of 3.3 ($p = .01$)
Comparison group: (1) no treatment; (2) IMTESC: short lecture on topics including basic TMJ anatomy, biomechanics, disk displacement and dysfunction, the role of psycho emotional factors in TMD particularly relating to parafunctional activity, and mandibular exercises to be performed at home twice a day: (1) Mandibular body condylar cross-pressure chewing technique, (2) Post-isometric relaxation stretches-laterotrusion and opening	*Pain outcome measures*: 3 pain measures: jaw pain at rest, jaw pain upon maximal active opening, and jaw pain upon clenching. These measures were based on an 11-point graded chronic pain scale reported by the participant *MMO outcome measures*: interincisal range of opening in millimetres, measured by vernier callipers	*Pain*: baseline, 6 week, 6 month, 1 year *MMO*: baseline, 6 week, 6 month, 1 year	*Pain*: Both treatment groups had significantly lower pain scores than the control group after the baseline period at the 6-week, 6-month and 1-year follow-up assessment points (p 05) *MMO*: Both treatment groups improved MMO significantly compared to the control group at the 6-week, 6-month and 1-year follow-up assessment points ($p < .05$)
Comparison group: (1) ESC: short scripted lectures on the basic anatomy, biomechanics and pathophysiology of the TMJ, the role of stress; slow, diaphragmatic breathing exercises and general advice on relaxation awareness and avoidance of potentially problematic foods, teaching and supervision self-care exercises that were performed both during the session and at home twice a day (morning and night): (1) Mandibular body—condylar cross-pressure chewing technique, (2) Post-isometric relaxation stretches-laterotrusion and opening	*Pain outcome measures*: 3 pain measures: jaw pain at rest, jaw pain upon maximal active opening, and jaw pain upon clenching. These measures were based on an 11-point graded chronic pain scale reported by the participant *MMO outcome measures*: interincisal range of opening in millimetres	*Pain*: baseline, 6 week *MMO*: baseline, 6 week	*Pain*: At 6 weeks, results indicated strong evidence of a statistically significant difference between groups in favour of IMT Average change in pain over time (with 95% confidence interval) was −1.22 (−1.64, −0.80) for the ESC group, and −2.48 (−2.90, −2.06) for the IMT group ($p < .001$) *MMO*: Results for MMO showed that, at 6 weeks, the average adjusted difference between groups in opening ranges was not significant Average change in MMO over time (with 95% confidence interval) was 2.52 (1.37, 3.67) for the ESC group, and 3.00 (1.85, 4.15) for the IMT group ($p >.05$)

Trial information	Population	Intervention
Gomes et al.[15] Year: 2014 Country: Brazil	*Sample*: 28 (28 female; age 29.9 ± 4.5 years) *TMD type*: all TMD type *TMD diagnostic criteria*: Fonseca anamnestic index *Inclusion criteria*: aged 18–40 years; Fonseca anamnestic index >20 *Exclusion criteria*: occurrence of missing teeth (except third molars); current use of orthodontic appliance; history of neuromuscular disease; current use of analgesic, anti-inflammatory agent, or muscle relaxant; and currently undergoing physical therapy for TMD	*Intervention group*: The massage group underwent to 3 weekly 30-min sessions of massage of the masticatory muscles for 4 consecutive weeks
Brochado et al.[40] Year: 2018 Country: Brazil	*Sample*: 51 (48 female, 3 male; age 44.5 ± 17.1) *TMD type*: myogenic and arthrogenic TMD based on RDC/TMD Axis I analysis *TMD diagnostic criteria*: RDC/TMD *Inclusion criteria*: 21 years or older, be diagnosed with myogenic and arthrogenic TMD based on RDC/TMD Axis I analysis, present pain TMJ and limited mouth opening *Exclusion criteria*: current dental therapies that could affect TMJ, rheumatic diseases, and use of anti-inflammatory drugs and muscle relaxants	Intervention group: GMT: 3 weekly 21-min sessions of MT on masticatory muscles and TMJ for 4 consecutive weeks. Temporal, masseter, and medial pterygoid muscles from both sides were submitted to MT for 3 min in each muscle group. MT was performed on the TMJ by placing the thumb on the second or third molar and performing a caudal distraction with anterior projection, intermittently for 1 min and 3 repetitions
Lietz-Kijak et al.[41] Year: 2018 Country: Poland	*Sample*: 60 (31 female, 29 male; age 25.9 ± 4.9) *TMD type*: masticatory muscles myofascial TMD *TMD diagnostic criteria*: RDC/TMD *Inclusion criteria*: 18–35 years old; confirmed diagnosis of myofascial TMD according to RDC/TMD *Exclusion criteria*: regular drug therapy, mental illness, coagulopathy, diabetes, or chronic infections..e subjects were not addicted to nicotine, alcohol, or drugs. Participants with joint clicking and a clinical diagnosis of disc displacement were also excluded, and they were asked to refrain or not to use self-treatment during the therapy	Intervention group: TrP Group: release of trigger points by the iscahemic compression method. Trigger point therapy was performed within the upper and lower attachment of the masseter, on the right and left sides. The procedure was performed three times, on the first, third, and fifth days of therapy

Abbreviations: ESC, education and self-care exercises; GCT, combined therapy group; GMT, manual therapy group; GPBM, photobiomodulation group; IMT, intraoral myofascial therapy; IMTESC, IMT with education and self-care exercises; KT, kinesio taping; MMO, maximum mouth opening; MT, manual therapy; RDC/TMD, research diagnostic criteria for TMD; SD, standard deviation; TMD, temporomandibular disorder; TMJ, temporomandibular joint; TMPD, temporomandibular pain-dysfunction disorder; TrP, trigger point; VAS, Visual analogue scale.

Comparison group	Outcome measures	Follow-up assessment points	Results
Comparison group: (1) The occlusal splint group was submitted to treatment with an occlusal splint for 4 weeks. (2) The asymptomatic comparison group was not submitted to any form of intervention	*Pain outcome measures*: N/A *MMO outcome measures*: Mandibular ROM (maximum active mouth opening) was evaluated by a blinded examiner using a digital calliper	*Pain*: N/A *MMO*: Baseline, 4 week	*Pain*: N/A *MMO*: In the intragroup analysis, significant increases in MMO were found in the massage and occlusal splint groups The mean of MMO with standard deviation at baseline for the massage group was 43.84 (3.99); at follow-up was 50.32 (5.63). On the other hand, the same values for the splint group were 42.41 (3.12) at baseline and 47.17 (3.53) at follow-up
Comparison group: (1) GPBM: PBM was applied by a single professional using a continuous wave of GaAlAs diode laser with a wavelength of 808 nm. PBM was applied 12 times (3 times a week for 4 consecutive weeks). (2) GCT: In each session, patients were submitted to PBM and MT protocols 3 times a week for 4 consecutive weeks	*Pain outcome measures*: VAS *MMO outcome measures*: maximum mouth opening measured in mm	*Pain*: baseline, day 7, day 14, day 21, day 28, day 60, day 90 *MMO*: Baseline, day 28, day 60, day 90	*Pain*: All groups experienced a significant reduction in pain by day 14 ($p < .05$). The change in mean VAS scores did not differ significantly between groups during evaluation time Mean pain VAS scores (with IC95%) at baseline were 4.1 (2.91–5.38) for the PBM group and 4.4 (2.46–6.31) for the MT group. At D28 PBM group reached 1.1 (0.43–1.71) and MT group 1.3 (0.17–2.44). In D90, all groups maintained a stable mean similar to D28 *MMO*: Maximum opening analysis revealed that PBM and MT promoted improvements between day 0 and day 90 MMO mean scores were (IC95%) from 29.64 (27.17–32.35) to 36.86 (34.51–39.36) for PBM group and from 27.92 (24.97–31.23) to 33.38 (30.78–36.21) for the MT group
Comparison group: KT Group: Muscular application was used for the region of the masseter with a tape (5 cm wide) cut into 2 parts, called tails, which covered the treatment sites without tension. All participants of the study were obliged to wear the kinesiology tape for a period of 5 days and were advised to carry out everyday activities without unnecessary care	*Pain outcome measures*: VAS *MMO outcome measures*: N/A	*Pain*: baseline, day 5 *MMO*: N/A	*Pain*: Both methods proved to be effective ($p < .001$) The mean values of VAS pain changes after KT range from 6.50 ± 1.74 at baseline, to 3.10 ± 1.35 at follow-up The mean values of VAS pain changes after TrP are 6.27 ± 1.41 at baseline and 4.17 ± 1.36 at follow-up. The KT method gave a greater improvement in the reduction of pain. The unpaired sample Welch *t* test confirms this ($p < .001$) *MMO*: N/A

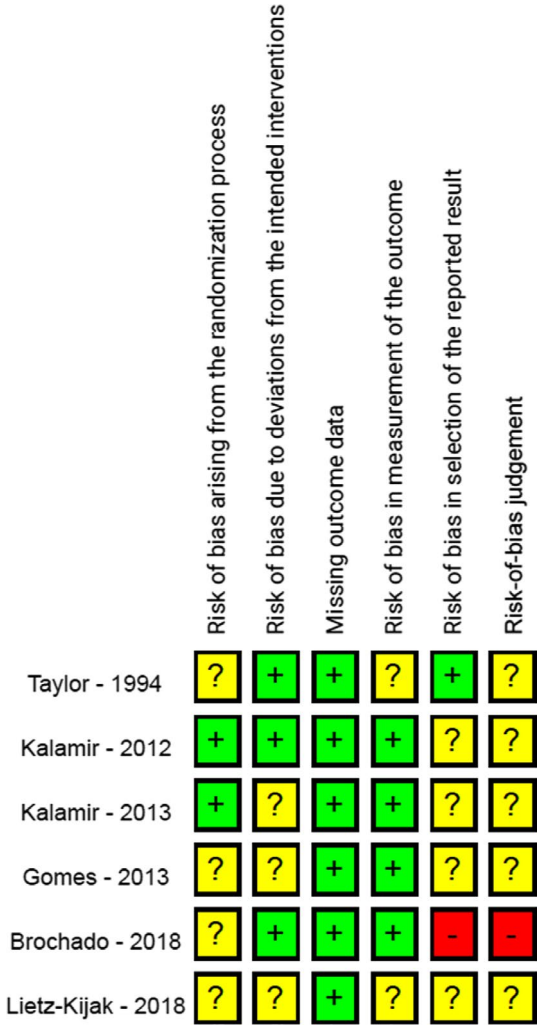

FIGURE 2 Risk of Bias 2. Summary of risk of bias for each study. A plus sign denotes low risk or bias; minus sign denotes high risk of bias; and question mark denotes moderate risk of bias

MT can modulate pain via the activation of low-threshold Aβ fibres that inhibit nociceptive input from Aδ and C afferent fibres.[45,46] In addition, MT can induce affective responses activating opioid, oxytocin and dopaminergic pathways.[45,46] Since TMDs are disorders involving the masticatory muscles, TMJs and associated structures,[2] it is reasonable to hypothesise that MT applied to craniomandibular structures positively affects the perception of pain. The quality of evidence to support this hypothesis is very low even though the available evidence supports the use of CMMT for pain relief in patients with TMD. According to the IMMPACT recommendations, the mean reduction in pain intensity observed in the included studies is clinically significant.[29] However, it is important to note that CMMT is not superior to other types of pain relieving treatments such as kinesio tape or photobiomodulation therapy,[40,41] even though it appears to be superior to sham therapy and self-care with exercise.[38,39] Other systematic reviews have revealed that different treatment interventions significantly reduce pain in people with TMDs, including education and counselling, exercise or splint therapy.[47–49] Thus, clinicians can consider that CMMT, as with other treatment modalities, can significantly reduce pain intensity in the short and mid-term.

Although the quality of evidence is very low, our results suggest that CMMT also significantly improves MMO in people with TMDs. The mean improvement in MMO reported in the included studies following CMMT is clinically significant.[50] The neurophysiological responses following MT can decrease tissue spasm and increase range of motion.[10,45] It should be noted that CMMT significantly reduces MMO compared to sham therapy and no treatment,[14,38] but it is not superior to self-care with exercise, splint therapy, or photobiomodulation therapy.[15,39,40] These findings are in accordance with several studies reporting that different conservative interventions are effective at improving MMO in people with TMDs.[47–49] Similar to the conclusions for treatment selection for pain relief, clinicians planning treatment should consider CMMT as one effective, low-cost, option for MMO improvement in the short and mid-term.

In a previous systematic review of CMMT, Armijo-Olivo et al.[18] included four studies in their subgroup analysis investigating MT targeted to the orofacial region.[14,39,42,43] Compared to this review, in the current systematic review we excluded (1) Kalamir et al.[42] because the participants were the same as included in another article[39] and (2) Guarda-Nardini et al. because the MT intervention was directed to the craniomandibular area, however, with the possibility for the therapist to also apply MT to the neck region. We, however, included more recent papers that were not available at the time of this earlier review by Armijo-Olivo et al. in 2016.[40,41] Our findings strengthen Armijo-Olivo et al.'s findings by supporting the use of MT to treat myogenous TMD for improving MMO and pain. However, the current review has also provided further evidence about the effectiveness of CMMT for all TMD types based on the more recent papers included.

The small number of included studies did not allow us to perform a subgroup analysis for TMD type. Three studies included all TMD types, two studies included chronic myogenous TMD and one study included both acute and chronic myogenous TMD.[14,15,38–41] Similarly, subgroup analysis for MT techniques was not possible. Two studies investigated IMT, one investigated TMJ mobilisation, one facial massage, one trigger points release and one MT applied to masticatory muscles and the TMJs.[14,15,38–41] There is low-to-moderate quality of evidence in the literature that supports using myofascial MT techniques targeted to the cervico-cranial region to treat myogenous TMD with improvement in MMO and jaw pain from baseline.[18] Our current results cannot support or refute this finding. On the other hand, there is no existing evidence investigating the best MT techniques for arthrogenous TMD. Manual therapists managing patients with TMDs should apply clinical reasoning to identify tissue and muscle dysfunction and target their treatment accordingly.[49] Regarding age and gender, all of the included studies involved adult participants; two studies included adults up to 35 years,[38,41] two studies up to 50 years[14,39] and two studies with no maximum age limit.[15,40] One study included only female participants,[15] whilst the others examined both male and female participants but with a high predominance of females. Subgroup analysis for age and gender was

TABLE 2 GRADE Assessment of studies comparing CMMT vs other interventions for improving pain intensity and MMO in TMDs

Quality assessment – CMMT							
N° of studies (design)	**Participants in CMMT and in comparison groups**	**Limitations [RoB2]**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication Bias**	**Quality of evidence grades**
Outcomes: Pain intensity							
4 studies (RCTs) Kalamir et al. 2012[14] Kalamir et al. 2013[39] Brochado et al. 2018[40] Lietz-Kijak et al. 2018[41]	CMMT group: 100 Comparison group: 102	Unclear[a]	Serious[c]	Not serious	Serious[d]	Undetected	Very low
Outcomes: MMO							
5 studies (RCTs) Taylor et al. 1994[38] Kalamir et al. 2012[14] Kalamir et al. 2013[39] Gomes et al. 2014[15] Brochado et al. 2018[40]	CMMT group: 99 Comparison group: 101	Not serious[b]	Serious[c]	Not serious	Serious[d]	Undetected	Very low

Abbreviations: CMMT, craniomandibular manual therapy; MMO, maximum mouth opening; RCT, randomised controlled trial; RoB2, risk of Bias 2.

[a]Overall risk of bias: 3 studies 'Some Concerns'; 1 study 'High'.

[b]Overall risk-of-bias: 5 studies 'Some Concerns'.

[c]Heterogeneity of comparator and assessment time-point.

[d]Small sample size and unsatisfactory confidence interval.

not possible due to the large amount of heterogeneity present between studies.

The level of evidence of the included studies is very low for several reasons. There were four studies with a moderate risk of bias related to randomisation.[15,38,40,41] The authors did not specify how the randomisation sequence was generated. Secondly, no authors published a study protocol to openly state research questions and methods a priori. Consequently, there is a moderate-to-high risk of bias in the selection of reported results. In addition, three studies had moderate risk of bias due to deviations from the intended interventions because participants were aware of their assigned intervention during the trial.[15,39,41] Moreover, two studies presented moderate risk of bias in measuring outcomes because the assessors were aware of the intervention received by the participants.[38,41] No included study showed a risk of bias in missing outcome data. Finally, the small sample size of included studies produced a large and unsatisfactory confidence interval with a loss in the statistical power of results. All of these factors contributed to the 'very low' quality of evidence based on the GRADE assessment.

The knowledge provided by this systematic review should be considered cautiously due to some limitations. First, the choice to include any assessment-point time and any comparator vs CMMT led to inconsistent results because of heterogeneity. For this reason, a meta-analysis was not performed, and minimal clinical implications could be drawn. Secondly, different diagnostic criteria for TMD were considered. In addition, no study setting criteria were placed, and this decision led to the inclusion of two studies conducted by the same group of authors in a private clinic, which limits the external validity. Moreover, our very restrictive inclusion criteria about the interventions (ie CMMT without combined treatment) resulted in a small number of included studies. The total sample size for CMMT and comparator interventions was approximately 100 participants, which is too low considering the number of people that have TMDs.[5,51–54]

The current systematic review revealed the limited amount of literature on this topic and especially the lack of studies with high methodology quality. In the last decade, the results from systematic reviews have supported the effectiveness of physical therapy in managing people with TMDs with an adequate level of evidence.[8,9,18–20] This knowledge has contributed to making physical therapy one of the most common treatments for the successful management of TMDs[8] also because a physical therapy approach fits with TMD treatment recommendation (eg conservative, evidence based, promoting behaviour changes).[55] However, additional studies are required to determine the most effective form or combination of physical therapy interventions (eg strengthening exercises, stretching exercises or MT). With regards to MT, studies are needed to examine different MT techniques, applied to different regions and different populations (eg chronic or acute TMD) to determine what is most effective at relieving pain and improving TMJ range of motion. Based on observations from this systematic review, future studies should (1) publish a study protocol, which clearly presents the planned methodology; (2) clearly specify the randomisation process and generation of the random sequence of allocation; (3) develop solutions so that both participants and assessors are blinded; (4) use DC/TMD or RDC/TMD diagnostic inclusion criteria only[26,27]; (5) determine an appropriate sample size to reach adequate statistical power.

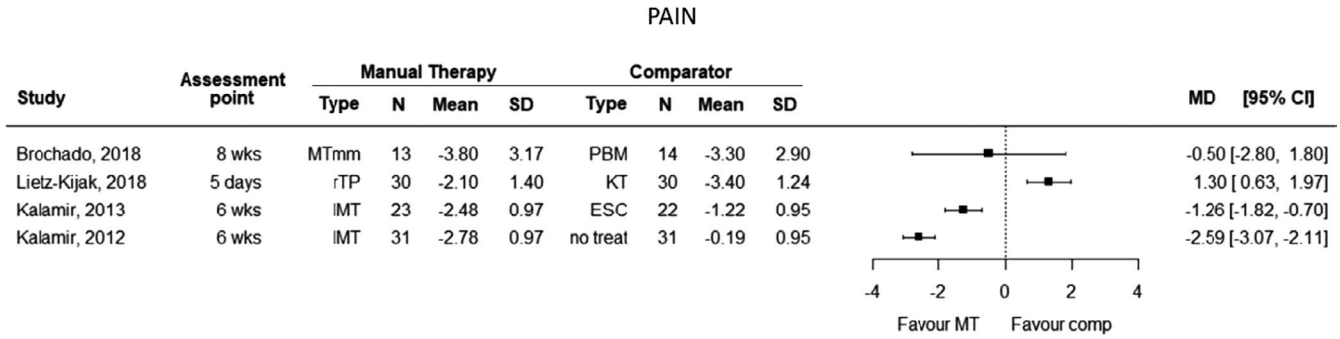

FIGURE 3 Results of individual studies: Pain. Forest plot, without meta-analysis, showing the effects of manual therapy compared to other interventions on pain intensity (0/10). Mean value changes (with standard deviation) between pre- and post-intervention are reported for comparators and manual therapy interventions. ESC, self-care and exercise; IMT, intraoral myofascial therapy; KT, kinesiotaping; MTmm, manual therapy on masticatory muscles; PBM, photobiomodulation; rTP, release of trigger points on masticatory muscles. *Note*: Standard deviation in Kalamir 2012 imputed from SDs in Kalamir 2013; Data in Kalamir 2012 obtained from median and IQ range following Wan et al. 2014. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range

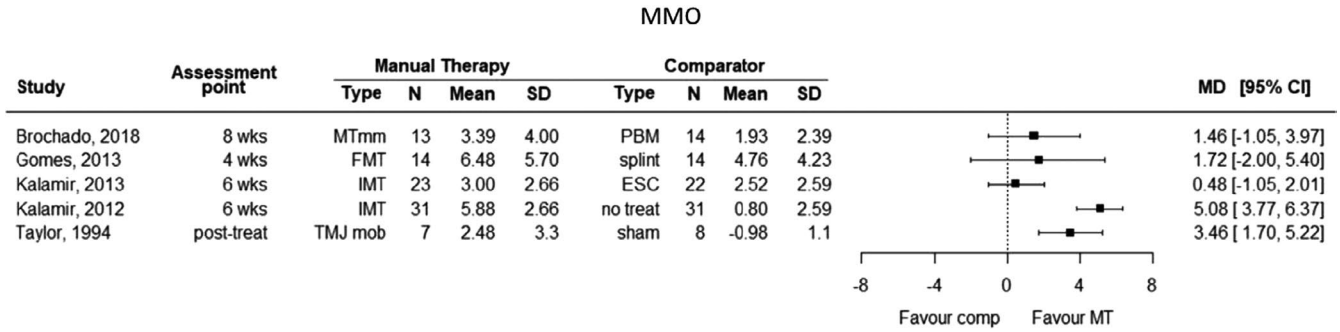

FIGURE 4 Results of individual studies: MMO. Forest plot, without meta-analysis, showing the effects of manual therapy compared to other interventions on maximum mouth opening (MMO) in mm. Mean value changes (with standard deviation) between pre- and post-intervention are reported for comparators and manual therapy interventions. FMT, facial massage therapy; IMT, intraoral myofascial therapy; KT, kinesiotaping; MTmm, manual therapy on masticatory muscles; PBM, photobiomodulation; TMJ mob, temporomandibular joint mobilisation. *Note*: Standard deviation in Kalamir 2012 imputed from SDs in Kalamir 2013; Data in Kalamir 2012 obtained from median and IQ range following Wan et al. 2014. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range

In conclusion, very low quality of evidence supports CMMT for patients with TMD for successfully reducing pain and improving MMO in the mid-term. Whether CMMT is superior to other interventions remains unclear. Clinicians planning treatment of patients with TMD may consider CMMT, in addition to other treatment modalities, as one effective, low-cost, conservative option to manage pain and improve MMO in the mid-term.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

All authors contributed to the manuscript. GA is an MRes Spinal Pain student with DF as supervisor. GA and DF were responsible for conception of the review. GA and LP were the two reviewers on each stage supported by DF in case of disagreement. All authors have contributed to data interpretation, conclusions and dissemination. All authors have read, contributed to and agreed upon the final manuscript. DF is guarantor.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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