Trigger point manual therapy for the treatment of chronic non-cancer pain in adults: a systematic review.

Authors

Diarmuid Denneny[1,5], Katrine Petersen[1], Rebecca McLoughlin[1], Suzanne Brook[4], Salma Hassan[1], Helena C Frawley[3,6], Amanda C de C Williams[2]

1: Pain Management, UCLH NHS Foundation Trust, London, UK

2: Research Department of Clinical, Educational & Health Psychology, University College London, London, UK

3: Department of Physiotherapy, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Australia

4: Independent Physiotherapy Practitioner, Kent, UK

5: Centre for Primary Care and Public Health, Blizard Institute, Queen Mary, University of London, UK

6: Centre for Allied Health Research and Education, Cabrini Health, Melbourne, Australia

Trigger point manual therapy for the treatment of chronic non-cancer pain in adults: a systematic review.

Abstract

Background. Myofascial pain is a type of chronic pain attributed to the development of trigger points in muscles. Trigger point manual therapy (TPMT) is widely used, but as a stand-alone treatment its effect on chronic pain is uncertain.

Objectives. To determine the effectiveness of TPMT for reducing chronic non-cancer pain and associated problems in adults, by analysing all relevant randomised controlled trials (RCTs).

Search methods and selection criteria. We searched databases and clinical trials registers from their inception to May 2017. We included RCTs in any language that recruited patients over the age of 18, with pain of three months duration or more. We assessed pain, function, and patient-reported improvement as outcomes. We combined all data using a random-effects model and assessed the quality of evidence using GRADE.

Data collection and analysis. Two authors independently extracted and verified data. Meta-analysis was completed where possible, otherwise data were synthesised narratively.

Main results. 19 trials (involving 1047 participants) met inclusion criteria, representing TPMT treatment for musculoskeletal, pelvic and facial pain. No effect was found for short-term pain relief (mean standardized difference -0.53, 95% CI -1.08 to 0.02). One small study showed a longer-term benefit for pain (mean standardized difference --2.00 (95% CI -3.40 to -0.60) but with low confidence in the effect. Significant gains emerged for function (mean standardized difference -0.77, 95% CI -1.27 to -0.26, and in patient global response (odds ratio 3.79, 95% CI 1.86 to 7.71) from four studies, but not for health-related quality of life.

Conclusions. Evidence for TPMT for chronic non-cancer pain is weak and it cannot currently be recommended.

Key Words: Chronic Pain; Myofascial, Physical Therapy

Trigger point manual therapy for the treatment of chronic non-cancer pain in adults: a systematic review.

Background

Chronic pain is pain that lasts more than three months, persisting beyond expected healing times [1]. Myofascial pain syndrome (MPS) is chronic pain perceived in myofascia; which consists of muscle and the surrounding highly innervated connective tissue [2,3]. Myofascial trigger points have been described as "small, highly sensitive areas in muscle" [3]. Myofascial pain is reportedly caused by muscle injury, overuse or repetitive strain [2] with the subsequent development of trigger points in muscles. Trigger points (TrPs) are described as nodules in muscle, located within taut bands, that are painful to palpation, reproduce the patient's symptoms, and cause referred pain [3]. Estimates of TrP incidence vary from 30%-93% in adults [4,5,6]. Research exists to support TrP as a cause of MPS [7,8,9] but other studies dispute the existence, assessment, clinical significance and underlying mechanisms of TrPs [,10,11,12,13]. The identification and diagnosis of TrPs by palpation has been reported to lack reliability [13,14]. An explanation for this lack of reliability may be that tenderness on palpation may be due to other known clinical phenomena associated with chronic pain conditions, such as allodynia and hyperalgesia.

The pathophysiology of MPS remains unclear and without agreed definitive explanation. Early focus on bio-medical explanations that concentrated on peripheral mechanisms has been superseded by improved understanding of the complex nature of chronic pain. Currently MPS is considered a form of neuromuscular dysfunction, consisting of soft tissue and sensory abnormalities involving both peripheral and central nervous systems [16,]. Referred pain, a characteristic of TrPs, is postulated to be a central phenomenon initiated and activated by peripheral sensitization, whereby peripheral nociceptive input from muscle can sensitize previously silent dorsal horn neurons [10].

Many current treatments for MPS originate from the early model and target local pain symptoms rather than addressing central nervous system or psychosocial factors. Current treatments include trigger point manual therapy (TPMT), dry needling, local injection, laser,

stretching, and massage [3, 15,16,17,18]. Limited evidence that deep needling into TrPs has an overall treatment benefit, when compared with standardised care, was found by one systematic review [18] that also suggested that there was no logical basis for choosing treatments for MPS until different interventions were compared directly. Analgesic medication, as with all chronic pain conditions, is often unsatisfactory, and side effects common.

Currently no systematic review has compared the effects of TPMT with other forms of treatment or no treatment. This review aimed to determine the effectiveness of TPMT for treating chronic, non-cancer, pain in adults.

TPMT description and mechanism of action

The clinical criteria used to diagnose TrPs vary and the six most commonly used criteria reported in the literature are: a tender spot in a taut band of skeletal muscle, patient pain recognition and predicted pain referral pattern on tender spot palpation, painful and limited range of movement, and identification of a local twitch response on muscle palpation [12]. Ischaemic compression to ablate the TrP is the predominant theory used to explain the effect of TPMT [17,19]. Manual application of pressure to TrPs, usually involving sustained digital pressure, as described by Travell and Simons [20], is typically used to perform this compression. Theories relating to effect of TPMT on the CNS have been postulated. D'Ambrogio [21] described adjustments to pain threshold in the spinal cord following TPMT. The therapist may place the muscle containing the TrP into positions of longitudinal tension or stretch whilst performing TPMT. Optimal duration of applied pressure, patient positioning, and treatment frequency are not clearly defined in the literature.

Methods:

A protocol for this review was published prior to commencement [22]. There were a few minor deviations from the protocol: XX carried out the data extraction with XX (XX was on leave). XX and XX also carried out the risk of bias assessment. XX joined the team and acted as an independent advisor, contributing to the review manuscript. Sensitivity analysis was planned, as per protocol [22], to assess the effect of the different methodological decisions made throughout the review process by removal of cluster RCTs to leave individually

randomised trials. As no cluster RCTs were identified we did not perform this analysis. We also planned to conduct a sensitivity analyses on risk of bias where sufficient data were available (investigating the influence of excluding studies classified as high risk of bias). We were able to perform this analysis for pain relief, and functional outcomes, based on power calculations for sample size.

We performed narrative synthesis of the evidence using the GRADE system (Appendix ii), as described in Chapter 12 of the Cochrane Handbook for Systematic Reviews of Interventions [23]:

- High quality: we are very confident that the true effect lies close to that of the estimate of the effect
- Moderate quality: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different
- Low quality: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect
- Very low quality: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Devices that penetrate the skin, such as acupuncture needles, were not included in our definition of TPMT. We excluded treatments that did not specifically address the TrP by using ischaemic compression techniques, such as transverse friction massage, muscle energy techniques, mobilisation, massage, manipulations, and spray and stretch therapies. Table 1 provides more detail of inclusion, exclusion and outcome criteria used for this review.

Searches

We searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL,); Ovid MEDLINE; Ovid EMBASE; EBSCO CINAHL; Ovid PsycINFO; Ovid AMED; LILACS; PEDro; Web of Science (ISI); SciVerse SCOPUS; Database of Abstracts of Reviews of Effects (DARE), The Cochrane Library; Health Technology Assessments, from inception to May 2017: with search

domains consisting of the condition (trigger points), the intervention (manual therapy) and the population (chronic pain). See Appendix i for MEDLINE search.

Table 1. Inclusion criteria and Primary and Secondary Outcome Measures

Design
- Randomised, controlled trial
- Full-text articles published in peer-reviewed journal

Participants
- Chronic non-cancer pain (>3 months)
- Adults (> 18 years old)

Intervention
- TPMT

Exclusion
- Headaches and progressive neurological conditions
- Studies where it is not possible to separate the chronic pain data from acute pain data

Primary outcome measure
- Changes in pain severity/intensity; measured using VAS, NRS, verbal rating scale or Likert scale.
- Adverse events; such as drop outs or reports of pain worsening.

Secondary outcome measures (If collected in study)
- Health-related quality of life (HR-QOL)
- Functional ability measured by validated questionnaires/scales or functional testing protocol
- Clinical measures such as joint range of movement, muscle strength
- Reductions in healthcare use, including medication, visits to primary or secondary care
- Self-efficacy for activity such as the Pain Self-Efficacy Questionnaire (PSEQ)
- Outcomes such as satisfaction or overall improvement including global response assessment (GRA)

Time point of assessment
- Short term <2 weeks from end of treatment
- Medium term ≥2 weeks to ≤3 months from end of treatment
- Long term > 3 months from end of treatment

Comparisons
- manual therapy interventions, either stand-alone or in combination, where difference between groups is TPMT
- placebo
- No treatment or another intervention

Data collection and analysis

Selection of studies

Two review authors (XX, XX) determined eligibility by the title and abstract of studies identified by the search. Studies were not anonymised. Studies that clearly did not satisfy inclusion criteria were eliminated, and full copies of the remaining trials were obtained. The two review authors read these studies independently and reached agreement by discussion on inclusion; reasons for exclusion were recorded (see Fig 1).

Data extraction and management

Two review authors (XX, XX) independently extracted data using a standard form which was piloted prior to use. Agreement was confirmed by a third author (XX) before entry into RevMan 5 software[a], a software package recommended by the Cochrane Collaboration for systematic reviewing. The following information was extracted:

- pain condition/s and number of participants treated
- method of delivery of the intervention and details of the clinician applying it
- frequency and duration of treatment
- study design (inactive or active control)
- study duration and follow-up assessment points
- analgesic outcome measures and results
- withdrawals and adverse events (any adverse event, serious adverse events)
- location (country) and study environment
- any declarations of interest.

For missing information from the included studies, the lead author (XX) contacted the study authors by e-mail to request it. If no response was received two further attempts were made. Where studies had more than two arms (two interventions or two controls), these were combined where they were sufficiently similar; disputed decisions were referred to a third reviewer (XX). For crossover studies, the first phase only was analysed.

Data analysis

Data were combined using RevMan 5.3[a] to calculate standardized mean differences (SMD) where data were continuous, and odds ratios (OR) where data were dichotomous (per intervention, timepoint and outcome). All calculations used random effects models because of heterogeneity in the data. The I^2 statistic was used to indicate between-study heterogeneity [24], with values from 0% (no heterogeneity) to 100%. We planned to use subgroup analysis by pain site to investigate sources of heterogeneity but were unable to do so due to insufficient study numbers by pain site. Where there were insufficient data for meta-analysis, we undertook narrative synthesis of the evidence.

Assessment of risk of bias in included studies

Two review authors (XX, XX) independently assessed risk of bias for each study, using Cochrane criteria [25], with any disagreements resolved by discussion. A third reviewer (XX) was consulted for any disagreements.

Results:

The search process is shown in the PRISMA diagram in Figure 1 [26]. The original search for the review was run in May 2016 and updated in May 2017. We were unable to retrieve one record for full-text review [27] despite attempting to contact the authors and publishers, attempting to purchase online and inter library loan request (UK national and international). Data extraction and risk of bias assessment were performed by two independent reviewers (SB, RML). Any differences were checked by a third reviewer (XX). No further studies were found in bibliographies and reference lists of included RCTs.

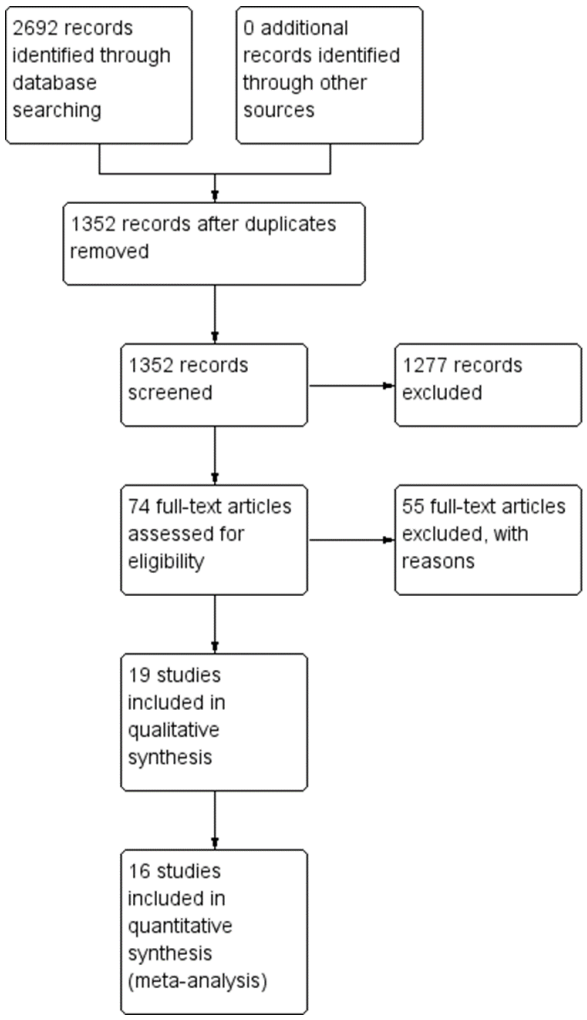
Four relevant ongoing trials were identified from 362 in the search of clinical trials databases. We e-mailed the contact author for each to request data; we received a response from one author but no data. We also searched the reference lists of included studies and websites of researchers active in the area and e-mailed the authors but did not identify further research to include.

Included studies

19 published peer reviewed studies met the inclusion criteria. All were in English and carried out in clinical environments. TPMT techniques were described in terms consistent with the definition: *manual therapy* (including pressure or compression) in 12 studies and *myofascial release* techniques in 7 studies. Studies included 1,027 patients at baseline and 994 at end of treatment, a mean completion rate of 96.7%.

Three studies [28,29,30] had three arms. From Kalamir et al. (2010) [29] we selected one intervention arm and one control arm for our analysis. We were unable to include data from Kalamir et al. (2012) [30] in our analysis. From Campa-Moran et al. [28], we combined the two control arms. Three studies used cross-over design methods [31,32,33] for which we analysed the first phase only.

Figure 1 PRISMA diagram for search results



Excluded studies

Excluded studies (Appendix iii) were largely on acute pain (27), healthy participants (4), were earlier versions of eligible studies (2), or not RCTs (7). 15 studies did not meet our criteria for TMPT that requires some form of ischaemic compression, including other manual therapy (massage, manipulations, deep friction massage or a combination), cranio-sacral therapy, and dry needling to an area remote from the painful region.

Table 1: Summary of Included Studies

Author (year)	N (I:C)	Gender (M:F)	Body region	TrP Clinical Criteria used	Type of Manual Therapy Used	Rx per week, No of weeks of Rx, Outcomes last taken at:	Outcome Measures Primary in bold (if stated)	Prof.	Control
Ajimsha (2014)[34]	34:32	17:48	Foot	No	MFR	3,4 wks, Rx end	**FFI, PPT**	PT	Sham ultrasound
Arguisuelas (2017)[35]	27:27	21:33	Low back	No	MFR	2, 2 wks, 3 Mts	**MPQ, Pain VAS,** RMDQ	PT	Sham myofascial release
Bron (2011)[36]	37:35	28:44	Shoulder	No	MC, Stretch	1, 12 wks, 3 Mts	**DASH**	PT	Waiting list
Campa-Moran (2016)[28]	12:24	7:29	Neck	Yes	OMT	2, 1 wk, Rx End	NDI	PT	Dry needling
DeMeulemeester (2017)[37]	‡22:20	0:42	Neck	No	MC	1, 4 wks, 3 Mts	**NDI, Pain NRS**	PT	Dry needling
Fitzgerald (2012)[38]	39:42	0:81	Pelvis	Partial	MPT	1, 12 wks, Rx End	**GRA,** Adverse events, FSFI	PT	Massage
Fitzgerald (2013)[39]	23:24	23:24	Pelvis	Partial	MPT	1, 12 wks, Rx End	**GRA, Adverse events,** FSFI	PT	Massage
Hains, a (2010)[31]	37:18	21:34	Wrist	Partial	MC	3, 5 wks, Rx End	**CTSQ**	Chiro	TPMT other body part
Hains, b (2010)[32]	41:18	26:33	Shoulder	No	MC	3, 5 wks, Rx End	**SPADI**	Chiro	TPMT other body part
Hains, c (2010)[33]	‡27:11	10:28	Knee	No	MC	3, 5 wks, 3 Mts	**Pain VAS, PGT**	Chiro	TPMT other body part
Harlapur (2010)[40]	30:30	35:25	Foot	No	MFR	Daily, 2 wks, Rx End	**Pain VAS, FFI**	PT	Positional release, US
Kalamir (2010)[29]	20:10	13:17	Facial	Partial	MC, Stretch	2, 5 wks, 6 Mts	**GCPS**	Chiro	Waiting list
Kalamir (2012)[30]	‡62:31	41:50	Facial	Partial	MC, Stretch	2, 5 wks, Rx End	**GCPS**	Chiro	Waiting list
Kalamir (2013)[41]	‡23:23	17:29	Facial	Partial	MC, Stretch	2, 5 wks, Rx End	**Pain NRS**	Chiro	Education
Khuman (2013)[42]	15:15	17:13	Elbow	No	MFR	3, 4 wks, Rx End	PRTEE	PT	Conventional PT
Llamas-Ramos (2015)[43]	‡47:47	32:62	Neck	Partial	MC	1, 2 wks, Rx End	**Pain NRS, NPQ**	PT	Dry needling
Renan Ordine (2010)[16]	‡30:30	15:45	Foot	No	MC, Stretch	4, 4 wks, Rx End	**SF36**	PT	Stretching Protocol
Sharma (2010)[44]	15:15	Unclear	Neck	Yes	MC, Stretch	1, 1 wk, Rx End	NPQ	PT	Relaxation, US, massage
Zoorob (2014)[45]	17:17	0:34	Pelvis	No	MFR	1, 6 wks, 3 Mts	**Pain NRS,** FSFI	PT	Injections

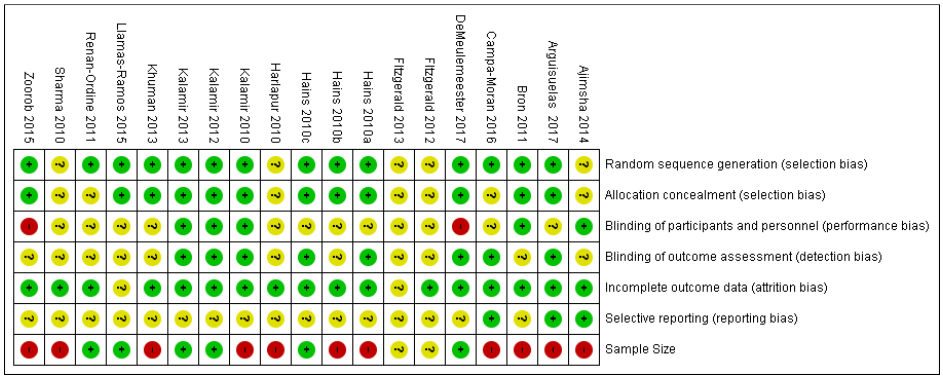
‡ indicates sample size power calculation reported and achieved, based on primary outcome

C = control, Chiro = chiropractor, CLBP = Chronic Low Back Pain CTSQ = Carpal Tunnel Syndrome Questionnaire, DASH = Disability Arm Shoulder Hand, FFI = Functional Foot Index, FSFI = Female Sexual Function Index, Fx = Function, FU = Follow up, I= Intervention, GCPS = Graded Chronic Pain Scale GRA = Global Response Assessment, MC = Manual Compression, MFR = Myofascial Release, MPT = Myofascial Physical Therapy, MTrP = Myofascial Trigger Point, NDI= Neck Disability Index, NPQ = Northwick Park Questionnaire, NRS = Numerical Rating Scale, OM = outcome measure, OMT = Orthopedic Manual Therapy, PGT = Patellar Grind Test, PPT = Pressure Pain Threshold, PRTEE = Patient Rated Tennis Elbow Evaluation, PT = physiotherapy, Prof.=profession, RMDQ = Roland Morris Disability Questionnaire, Rx = treatment, SPADI = Shoulder Pain and Disability Index, VAS = Visual Analogue Scale, Wk = Week

Risk of bias in included studies

Risk of bias was assessed using the RevMan tool[a] (*Figure 2*).

Figure 2 Risk of Bias



Overall, the risk of bias in included studies appeared high for sample size, equivocal for selective reporting and low to moderate for all other categories. Only 8 studies undertook a sample size estimate for pain as the primary outcome measure [16,30,33,37,38,39,41,43], and the sample size was achieved in 6 studies [16,30,33,37,41,43].

Effects of interventions

Primary Outcomes

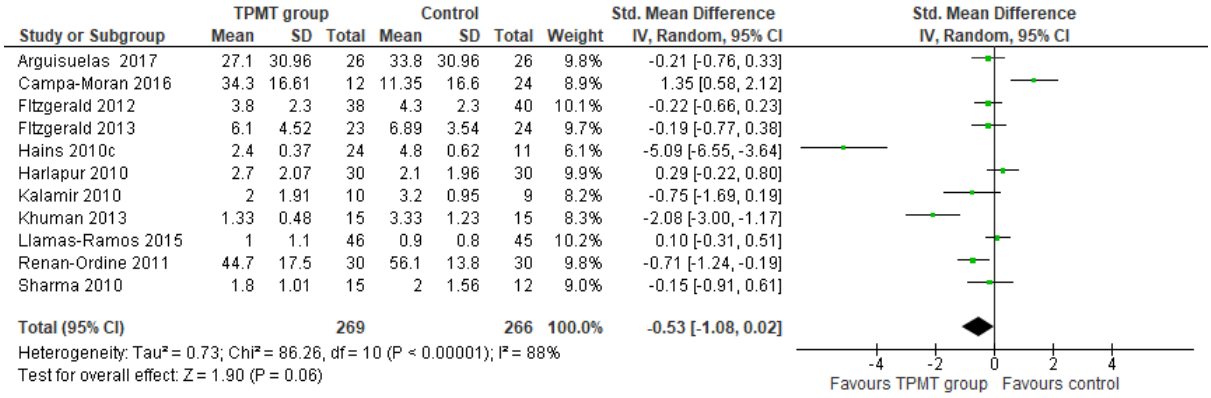
Pain relief

Eleven studies (548 participants) reported mean reduction in pain scores immediately after treatment (*Figure 3*). The standardised mean difference was -0.53 (95% CI -1.08 to 0.02), indicating no significant effect. Heterogeneity (I^2) was very high at 88%. We performed a sensitivity analysis by including only studies that captured pain scores and scored low risk of bias for sample size [16,33,43] (Figure 2) and this did not substantially change the results (SMD -1.70 [95% CI -3.48 to 0.07]). We used the overall SMD to calculate absolute effects on pain reduction, using one study which did not score high for risk of bias in any category [16], and the change in score fell just short of 30% improvement which is at the lower end of moderate as defined in our protocol [22].

Only one study [29] provided data for longer term follow-up at 6 months (19/20 participants) and showed significant pain reduction: standardized mean difference -2.00 (95% CI -3.40 to -0.60). This study had two TPMT arms, one of which contained an education

component (short lectures and exercise) in addition to the TPMT, sufficiently specific as a form of treatment to confound the effect of TPMT, so this arm was excluded from analysis as per protocol following team discussion and referral to the pre-published protocol [22].

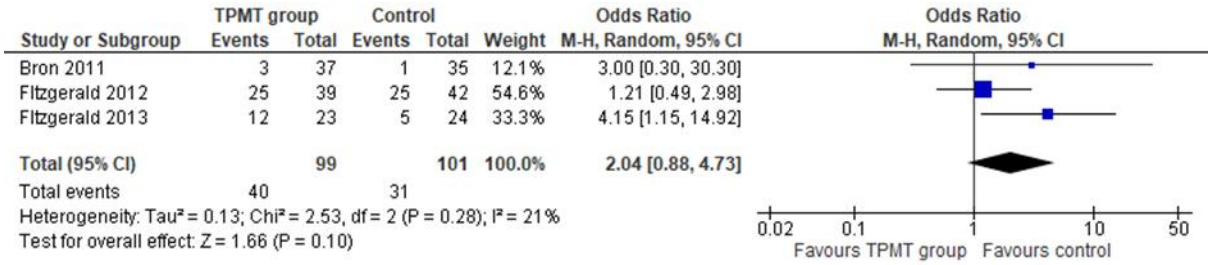
Figure 3 Pain, short term effects



Adverse Events

Only three studies (two pelvic pain and one neck pain) recorded adverse events [36,38,39], including post treatment increased pain, infection, gastrointestinal disturbance and constitutional symptoms (*Figure 4*). All others reported that there were no adverse events but no evidence of asking participants was presented. Odds ratio of excess adverse events in the treatment group was 2.04 (95% CI 0.88 to 4.73) indicating no significant effect.

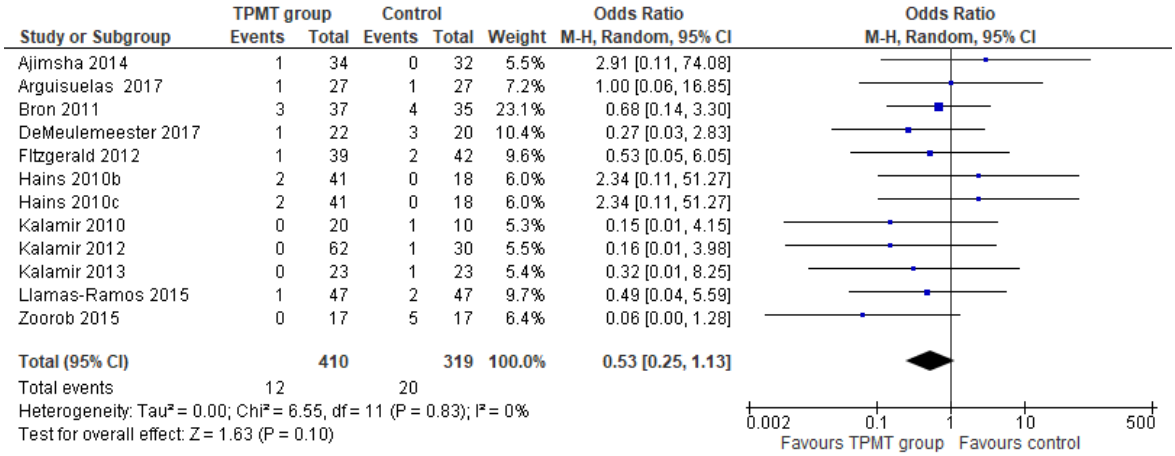
Figure 4 Adverse Events



Withdrawals

Seven studies (318 participants) reported no withdrawals, and 12 (729 participants) reported low numbers of withdrawals (32 participants, 3%) (*Figure 5*). Odds ratio was 0.53 (95% CI 0.25 to 1.13) indicating no significant difference between treatment and control groups.

Figure 5 Withdrawals

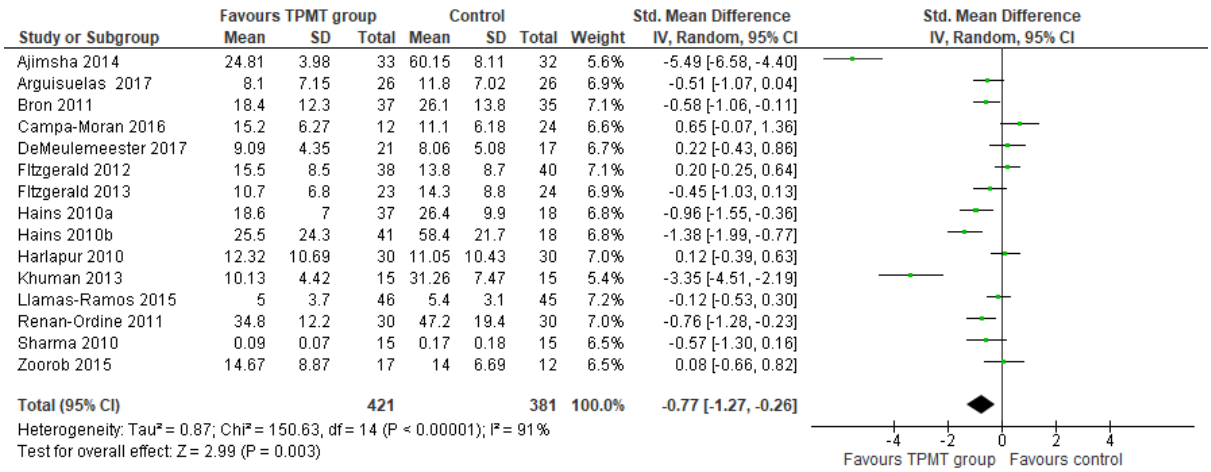


Secondary Outcomes

Function

Fifteen studies (802 participants) reported a range of functional outcomes, combined for this analysis (*Figure 6*), with very high heterogeneity (I^2 = 91%). Outcome measures used are identified in Table 1. The SMD in function was -0.77 (95% CI -1.27 to -0.26), indicating significantly improved function (z = 2.99, p = 0.003). We performed a sensitivity analysis by excluding studies with fewer than 20 participants per arm. Only slight differences in SMD and confidence intervals were found, with the finding still significant in favour of treatment over control for improved function.

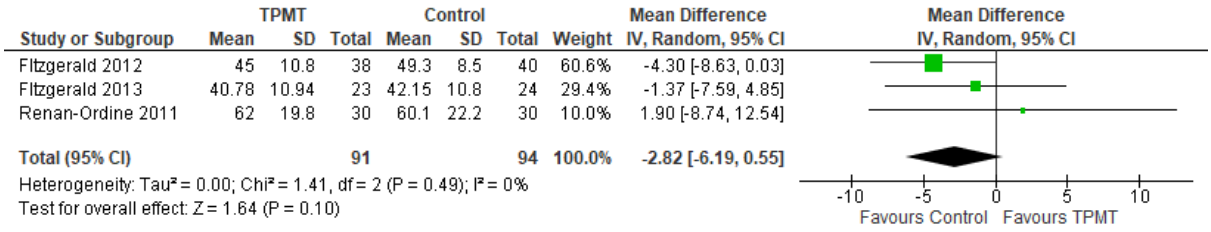
Figure 6 Functional Outcome



Health-related quality of life

Three studies collected HRQoL outcome measures. Two used SF-12 responses [38,39] and one used SF-36 responses [16]. For analysis we chose the mental health domain because we were aiming for minimal overlap with physical function. Results are presented in *Figure 7.* There was no significant benefit of treatment over control in health-related quality of life.

Figure 7 Health-Related Quality of Life Outcome



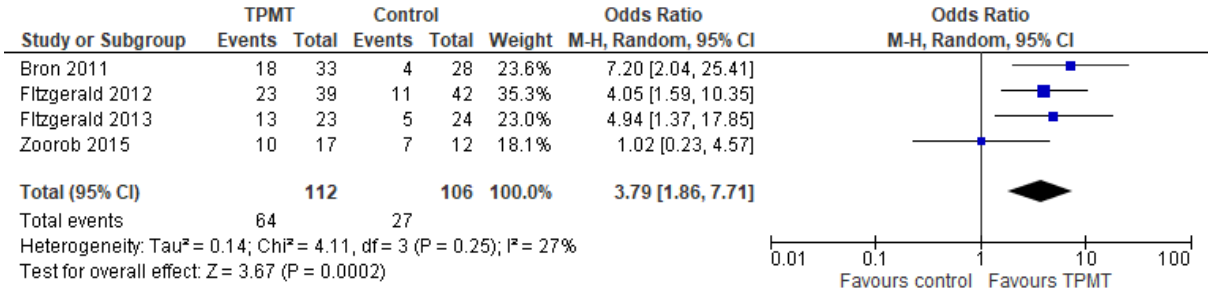
Clinician-reported outcomes

Clinician-reported measures were varied, dependent on condition and body region, and included pressure pain thresholds (PPT) [16, 28, 34, 37, 43] range of movement of the related joint(s) [28, 29,30,36, 41, 43, 44], grip strength [42], and patellar grind test [33]. Most studies reported significant improvement in their chosen clinician-reported outcome measure [16, 28, 29, 30, 33, 34, 37, 41, 42, 43, but the heterogeneous nature of the conditions and outcome measures meant it was not possible to pool data for analysis.

Patient Global Assessment

Six studies (293 participants) collected data related to this outcome [31, 32, 36, 38, 39, 45]. Over all six studies, 68% of participants improved in the intervention groups and 37% in the control groups. Four studies presented the percentage of participants who reported improvement, whilst two reported mean improvement [31, 32] which prevented these two studies being included in the analysis (Figure 8). The odds ratio of the studies included in the meta-analysis was 3.79 (95% CI 1.86 to 7.71), indicating a significant difference in favour of TPMT.

Figure 8 Patient Global Assessment



No data were reported for the outcomes of health care use and self-efficacy.

GRADE Assessment

The GRADE scores [23] for all primary outcomes, apart from withdrawals, was low, meaning our confidence in the effect estimate is limited and the true effect may be substantially different. The low scores were largely attributable to high risk of bias of the small sample sizes. The GRADE score for withdrawals was moderate, meaning we are moderately confident that the true effect is likely to be close to the calculated estimate of effect, but with a possibility that it is substantially different.

For secondary outcomes, again the GRADE scores were low apart from HRQoL which was moderate. The low scores were again largely due to risk of bias related to small sample sizes.

Discussion

This systematic review aimed to determine the effectiveness of TPMT for treating chronic, non-cancer pain in adults. Chronic pain was the rationale for the choice of TPMT as a treatment, but our review of the literature confirmed previously identified uncertainty regarding identification of trigger points [11]. Only two studies [28, 44] described clear clinical criteria for diagnosis. Seven studies [29, 30, 31, 38,39, 41, 43] reported tenderness on palpation as the clinical criterion and 10 studies did not report use of diagnostic criteria (Table 1).

Only two studies [38, 39] followed IMMPACT recommendations for core outcome measures for chronic pain clinical trials [46]. Many different treatment protocols were used, with a large variety of outcome tools with variable time-points for data collection.

Our analysis found no statistically significant benefit of TPMT for pain in the short term for people with chronic non-cancer pain. One study [29] reported pain reduction at six months but was underpowered with low certainty GRADE score (Appendix ii), so results should be treated with caution. Since participants in our included studies had chronic pain, it is disappointing that all but one study [29], did not follow up beyond the end of treatment (table 1). Given this review's finding of a lack of short-term benefit of TPMT for pain reduction, we would not anticipate that pain reduction would emerge at follow-up.

Analysis of functional change showed improved function with a medium to large effect size, but heterogeneity was very high, with TPMT applied to varied conditions and/or parts of the body. The lack of long-term follow-up measures to assess maintenance of functional improvement meant that lasting functional change was not assessed. Despite these overall rather mixed benefits, global patient assessment of TPMT benefits was positive in three of the four studies which reported on this outcome [36,38,39]. Such global assessments can reflect a number of factors beyond benefit from treatment, in particular, a positive assessment of therapist time and attention. It is hard to interpret these changes considering the failure of the main aim of treatment to relieve or reduce pain.

Sixteen studies stated that there were no adverse events but data collection methods were not reported. Of the three studies that reported adverse events, two [38, 39] applied TPMT to pelvic soft tissues, including intra-vaginal tissues. Treatment of the pelvic floor, using internal manual therapy techniques, may be a source of increased anxiety for participants that could contribute to increased pain, which may explain the high rate of adverse events in the active intervention arm; 64% and 52% respectively [38, 39]. In the third study reporting adverse events, TPMT was applied to shoulder pain [36] with the development of frozen shoulder or cervical radiculopathy (n=3 in intervention group and n=1 in control group), although causation cannot be determined.

The withdrawal rate overall was low, suggesting that adverse effects, assessed or not, were not widespread, and enabling better generalisation from the results of those who completed treatment.

Three studies [16,38,39] reported quality of life outcomes, and none reported health care use. Given these outcomes are often given as a rationale for pain treatment we would encourage future studies to consider these outcomes.

Agreements and disagreements with other studies or reviews

A recent systematic review of myofascial release in the treatment of chronic musculoskeletal pain [47] found that current evidence of myofascial release therapy is not sufficient to warrant this treatment in chronic musculoskeletal pain. Our review differs in that Laimi [47] specifically excluded TPMT, arguing that the theory behind TPMT treatment is different to that of myofascial release, even though some overlap in treatment methods may be apparent clinically. However, our conclusions regarding manual therapies for MPS are aligned; current evidence on TPMT is not sufficient to warrant this treatment in chronic musculoskeletal pain, despite the improvement in function and patient global assessment.

Overall our review identified a range of studies, with generally low numbers of participants, 11 of 19 studies with inadequate power, and a wide variety of conditions treated. Only one study examined TPMT for chronic low back pain. We found no evidence of consistent pain reduction from TPMT in the short term. Results from one small trial [29] reported a positive effect on facial pain relief at six months post-TPMT but the risk of bias for this study was high due to small sample size [29]. Overall significant short-term improvement in function was found from six of 15 studies [16, 31, 32, 34, 36, 42], as well as a positive global response in three of four studies [36, 38, 39]. Health related quality of life, measured in three studies [16, 38,39] showed no significant benefit of treatment over control. Insufficient data were available for longer term evaluation or for evaluation of effects of other clinically important outcomes. We support the use of a range of outcome measures, capturing different domains of pain impact, to improve overall measurement of patient response, in accordance with the IMMPACT recommendations [46].

The level of methodological bias in studies was high for sample size, with 11 underpowered studies, and moderate to low in other bias categories. The quality of the evidence for pain, adverse events, functional measures and patient global assessment using the GRADE approach was "low" because the included studies mostly scored high risk of bias for sample size and had high heterogeneity (Appendix ii). We therefore have low confidence in these results. Withdrawals and health related quality of life scored “moderate” for quality of evidence.

We are not aware of any biases in the review process, since our scope was large and not limited to English language, and we have reasonable confidence that TPMT trials were not missed. It is highly unlikely that the trial that could not be retrieved [27] would produce substantive changes in results.

Implications for practice

Chronic pain is a complex condition requiring a multimodal approach to its management, so it is unlikely that treatments such as TPMT, delivered in isolation, can address the complexity of the condition. We acknowledge that contemporary treatment for chronic pain typically involves combinations of a range of treatments along with education and activity. We do, however, support the view that low value health care practices should be questioned [48], and based on the results of this review we do not recommend the use of TPMT as a stand-alone treatment for chronic non-cancer pain.

Implications for research

We recommend adherence to the IMMPACT recommendations [46] for research in chronic pain, capturing a range of domains that are affected by chronic pain, and adoption by authors of standardized terminology to report their interventions and measurements. Chronic non-cancer pain is complex and requires complex interventions. Research needs to be rigorous to detect clinical efficacy with certainty. All studies included in this review were published in the last decade and represent the current quality of RCTs in this field. Based upon the low precision of the results, it would be standard to state that the field would benefit from several well-powered studies with attention to some of the methodological concerns identified here. There are, however, methodological and conceptual reasons not

to do so. Methodologically there is a known high risk of Type I error in small trials meaning treatment effects tend to be reported as more beneficial in small than in large trials [49] and our review identified no significant benefit for the primary outcome of pain reduction. Conceptually there is lack of clarity regarding the pathophysiology and determination of trigger points, and the inadequacy of unimodal interventions for a problem as complex as chronic non-cancer pain.

Authors' conclusions

This review identified no benefit in terms of pain relief in the short term, and one small study with low certainty showing a longer-term effect. Included studies were small and mostly underpowered, with risk of Type 1 error. While patient global assessment was positive, and self-rated function improved (albeit with low certainty), these are insufficient grounds to recommend a treatment whose major aim of pain relief is not realised. The lack of treatment effect for pain relief from TPMT found in our review may reflect the low sample sizes and numbers of studies overall, the high heterogeneity of studies leading to difficulty in identifying a treatment effect in specific conditions, or poor methodological quality or reporting of the studies identified. The possibility that TPMT may not have a clear therapeutic effect when tested in randomised controlled trials cannot be discounted.

Suppliers

a) Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

References

1. Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. Pain. 2015;156(6):1003-1007. doi:10.1097/j.pain.0000000000000160.
2. Bennett R. Myofascial pain syndromes and their evaluation. Best Practice & Research Clinical Rheumatology 2007;21(3):427-45.
3. Borg-Stein J, Simons DG. Focused review: myofascial pain [Focused review: myofascial pain]. Archives of Physical Medicine and Rehabilitation 2002;83(3 Supplement 1):S40-90.
4. Cummings M, Baldry P. Regional myofascial pain: diagnosis and management. Best Practice & Research Clinical Rheumatology 2007;21(2):367-87.
5. Han SC, Harrison P. Myofascial pain syndrome and trigger-point management. Regional Anesthesia 1997;22(1):89-101.
6. Sun MY, Hsieh CL, Cheng YY, Hung HC, Li TC, Yen SM, et al. The therapeutic effects of acupuncture on patients with chronic neck myofascial pain syndrome: a single-blind randomized controlled trial. American Journal of Chinese Medicine 2010;38(5):849-59.
7. Chen Q, Wang HJ, Gay RE, Thompson JM, Manduca A, An KN, Ehman RE, Basford JR. Quantification of Myofascial Taut Bands. Arch Phys Med Rehabil. 2016 Jan;97(1):67-73. doi: 10.1016/j.apmr.2015.09.019.
8. Shah JP, Thaker N, Heimur J, Aredo JV, Sikdar S, Gerber LH. Myofascial Trigger Points Then and Now: A Historical and Scientific Perspective. *PM & R : the journal of injury, function, and rehabilitation*. 2015;7(7):746-761. doi:10.1016/j.pmrj.2015.01.024.
9. Basford JR, An KN. New techniques for the quantification of fibromyalgia and myofascial pain. Curr Pain Headache Rep. 2009 Oct;13(5):376-8.
10. Fernández-de-las-Peñas C, Dommerholt J. Myofascial Trigger Points: Peripheral or Central Phenomenon? Current Rheumatology Reports 2013;16:395.
11. Quintner JL, Bove GM, Cohen ML. A critical evaluation of the trigger point phenomenon. Rheumatology (Oxford). 2015;54(3):392–9.
12. Tough E.A, White A.R, Richards S, Campbell J. Variability of criteria used to diagnose myofascial trigger point pain syndrome - evidence from a review of the literature. The Clinical Journal of Pain 2007;23(3):278-86.
13. Wolfe F, Simons DG, Fricton J, Bennett RM, Goldenberg DL, Gerwin R, et al. The fibromyalgia and myofascial pain syndromes: a preliminary study of tender points and trigger points in persons with fibromyalgia, myofascial pain syndrome and no disease. The Journal of Rheumatology 1992;19(6):944-51.
14. Lucas N, Macaskill P, Irwig L, Moran R, Bogduk N. Reliability of physical examination for diagnosis of myofascial trigger points. A systematic review of the literature. Clin J Pain. 2009;25:80–9.
15. Borg-Stein J. Treatment of fibromyalgia, myofascial pain, and related disorders. Physical Medicine and Rehabilitation Clinics of North America 2006;17(2):491-510.
16. Renan-Ordine R, Alburquerque-Sendín F, de Souza DP, Cleland JA, Fernández-de-Las-Peñas C. Effectiveness of myofascial trigger point manual therapy combined with a self-

stretching protocol for the management of plantar heel pain: a randomized controlled trial. Orthopaedic & Sports Physical Therapy 2011;41(2):43-50.
17. Skootsky SA, Jaeger B, Oye RK. Prevalence of myofascial pain in general internal medicine practice. Western Journal of Medicine 1989;151(2):157-60.
18. Tough EA, White AR, Cummings TM, Richards SH, Campbell JL. Acupuncture and dry needling in the management of myofascial trigger point pain: a systematic review and meta-analysis of randomised controlled trials. European Journal of Pain 2009;13(1):3-10.
19. Simons DG, Travell JG, Simons LS. Myofascial pain and dysfunction: the trigger point manual. 2. Vol. 1, Baltimore: Williams & Wilkins, 1999.
20. Travell JG, Simons DG. , Myofascial pain and dysfunction: the trigger point manual , 1983BaltimoreWilliams and Wilkins
21. D'Ambrogio KJ, Roth GB. Positional Release Therapy: Assessment & Treatment of Musculoskeletal Dysfunction. 1. St Louis: Mosby, 1997.
22. Denneny D, Petersen K, McLoughlin R, Brook S, Hassan S, Williams ACDC. Trigger point manual therapy for the treatment of chronic non-cancer pain in adults. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD011763. DOI: 10.1002/14651858.CD011763.
23. Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Guyatt GH. Chapter 11: Presenting results and 'Summary of findings' tables. In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.
24. Higgins, J. P. T., Thompson, S. G. and Spiegelhalter, D. J. (2009), A re-evaluation of random-effects meta-analysis. Journal of the Royal Statistical Society: Series A (Statistics in Society), 172: 137–159. doi:10.1111/j.1467-985X.2008.00552.
25. Higgins [b] JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.. The Cochrane Collaboration.
26. Higgins [a] JPT, Deeks JJ (editors). Chapter 7: Selecting studies and collecting data. In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.
27. Mathew J T. Myofascial pain syndrome: a comparison of two non-invasive treatment techniques. Physiotherapy and Occupational Therapy Journal 2008 Jul-Sep;1(1):19-31 2008.
28. **Campa-Moran**, I., E. Rey-Gudin, J. FernAinverted-!ndez-Carnero, A. Paris-Alemany, A. Gil-Martinez, L. S. Lerma, A. Prieto-Baquero, J. Alonso-Perez & R. la Touche. Comparison of dry needling versus orthopedic manual therapy in patients with myofascial chronic neck pain: a single-blind, randomized pilot study. Pain Research and Treatment 2015;2015:15 pages.
29. **Kalamir** A., Pollard H. , Vitiello A., Bonello R.. Intra-oral myofascial therapy for chronic myogenous temporomandibular disorders: A randomized, controlled pilot study. Journal of manual & manipulative therapy 2010;18:139-146.

30. **Kalamir** A.**,** Bonello R. , Graham P. , Vitiello A. L., Pollard H.. Intraoral myofascial therapy for chronic myogenous temporomandibular disorder: a randomized controlled trial. Journal of manipulative and physiological therapeutics 2012;35:26-37.
31. **Hains [a] G**, Descarreaux M, Lamy A-M, Hains F. A randomized controlled (intervention) trial of ischemic compression therapy for chronic carpal tunnel syndrome. Journal of the Canadian Chiropractic Association 2010;54(3):155-63.
32. **Hains [b] G**, M. Descarreaux, Hains F.. Chronic shoulder pain of myofascial origin: a randomized clinical trial using ischemic compression therapy. Journal of manipulative and physiological therapeutics 2010;33:362-369.
33. **Hains [c] G**, Hains F. Patellofemoral pain syndrome managed by ischemic compression to the trigger points located in the peri-patellar and retro-patellar areas: A randomized clinical trial. Clinical Chiropractic 2010;13(3):201-209.
34. **Ajimsha** M.S., Binsu D.,Chithra S.. Effectiveness of myofascial release in the management of plantar heel pain: a randomized controlled trial. Foot 2014;9(14):66-71.
35. **Arguisuelas**, M., J. Lison, D. Sanchez-Zuriaga, I. Martinez-Hurtado & J. Domenech-Fernandez. Effects of Myofascial Release in Non-specific Chronic Low Back Pain: A Randomized Clinical Trial. Spine 2016;42(9):627-34.
36. **Bron** C., de Gast A., Dommerholt J. , Stegenga B., Wensing M., Oostendorp R. A. B.. Treatment of myofascial trigger points in patients with chronic shoulder pain: a randomized, controlled trial. BMC Medicine 2011;9(14).
37. **De Meulemeester**, K. E., B. Castelein, I. Coppieters, T. Barbe, A. Cools & B. Cagnie. Comparing Trigger Point Dry Needling and Manual Pressure Technique for the Management of Myofascial Neck/Shoulder Pain: A Randomized Clinical Trial. Journal of Manipulative & Physiological Therapeutics 2016;40(1):11-20.
38. **Fitzgerald**, M. P., Payne C. K. , Lukacz E. S., Yang C. C., Peters K. M., Chai T. C., Nickel J. C. , Hanno P. M., Kreder K. J. , Burks D. A., Mayer R. , Kotarinos R. , Fortman C. , Allen T. M. , Fraser L., Mason-Cover M. , Furey C. , Odabachian L. , Sanfield A. , Chu J. , Huestis K. , Tata G. E., Dugan N. , Sheth H. , Bewyer K. , Anaeme A. , Newton K., Featherstone W. , Halle-Podell R., Cen L. , Landis J. R. , Propert K. J. , Foster H. E. , Kusek J. W., Nyberg L. M.. Randomized multicenter clinical trial of myofascial physical therapy in women with interstitial cystitis/painful bladder syndrome and pelvic floor tenderness. Journal of Urology 2012;187:2113-2118.
39. **Fitzgerald**, M. P., Anderson R. U. , Potts J. , Payne C. K. , Peters K. M. , Clemens J. Q. , Kotarinos R. , Fraser L., Cosby A. , Fortman C., Neville C. , Badillo S. , Odabachian L. , Sanfield A. , O'Dougherty B. , Halle-Podell R., Cen, S. Chuai L. , Landis J. R. , Mickelberg K. , Barrell T. , Kusek J. W., Nyberg L. M.. Randomized multicenter feasibility trial of myofascial physical therapy for the treatment of urological chronic pelvic pain syndromes. Journal of Urology 2013;189:S75-85.
40. **Harlapur**, A. M., Kage V. B. ,Chandu B. Comparison of myofascial release and positional release therapy in plantar fasciitis -- a clinical trial. Indian Journal of Physiotherapy and Occupational Therapy 2010;4(4):8-11.
41. **Kalamir** A., Graham P. L. , Vitiello A. L., Bonello R., Pollard H.. Intra-oral myofascial therapy versus education and self-care in the treatment of chronic, myogenous temporomandibular disorder: A randomised, clinical trial. Chiropractic and manual therapies 2013;21(1).

42. **Khuman** P. R., Trivedi P. , Devi S. , Sathyavani D. , Nambi G., Shah K.. Myofascial release technique in chronic lateral epicondylitis: a randomized controlled study. International journal of health sciences and research 2013;3(7):45-52.
43. **Llamas-Ramos** R.. Comparison of the Short-Term Outcomes Between Trigger Point Dry Needling and Trigger Point Manual Therapy for the Management of Chronic Mechanical Neck Pain: A Randomized Clinical Trial. Journal of orthopaedic and sports physical therapy 2015;45(11):852-861.
44. **Sharma**, A., Angusamy R. , Kalra S., Singh S.. Efficacy of post-isometric relaxation versus integrated neuromuscular ischaemic technique in the treatment of upper trapezius trigger points. Indian journal of physiotherapy & occupational therapy 2010;4(3):1-5.
45. **Zoorob**, D., South M. , Karram M. ,Sroga J. , Maxwell R. , Shah A., Whiteside J.. A pilot randomized trial of levator injections versus physical therapy for treatment of pelvic floor myalgia and sexual pain. International urogynecology journal 2015;26(6):845-852.
46. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain. 2005;113:9–19.
47. Laimi K, Mäkilä A, Bärlund E, Katajapuu N, Oksanen A, Seikkula V, Karppinen J, Saltychev M. Effectiveness of myofascial release in treatment of chronic musculoskeletal pain: a systematic review. Clinical Rehabilitation 2017.
48. Levinson W, Kallewaard M, Bhatia RS, et al 'Choosing Wisely': a growing international campaign BMJ Qual Saf Published Online First: 31 December 2014. doi: 10.1136/bmjqs-2014-003821
49. Nuesch E, Trelle S, Reichenbach S, Rutjes AW, Tschannen B, Altman DG, et al. Small study effects in meta-analyses of osteoarthritis trials: meta-epidemiological study. BMJ. 2010;341:c3515.

1

Appendix i.

Medline Search Strategy

1. Trigger Points/
2. exp Myofascial Pain Syndromes/
3. (trigger point* or trigger site* or muscle knot*).tw.
4. (myofascial adj pain).tw.
5. or/1-4
6. exp Musculoskeletal Manipulations/
7. manual therap*.tw.
8. manipulative therap*.tw.
9. (musculoskeletal adj manipulation*).tw.
10. massage.tw.
11. acupressure.tw.
12. shiatzu.tw.
13. shiatsu.tw.
14. chih ya.tw.
15. zhi ya.tw.
16. kinesiology.tw.
17. manipulation.tw.
18. osteopath*.tw.
19. chiropract*.tw.
20. bodywork.tw.
21. rolfing.tw.
22. reflexolog*.tw.
23. (zone adj therap*).tw.
24. or/6-23
25. 5 and 24
26. exp Pain/
27. pain*.tw.
28. 26 or 27
29. 25 and 28

2

Appendix ii

Summary of findings with GRADE Scores

Summary of findings:

TPMT compared to placebo, control, dry needling or other forms of MT for Pain reduction

Patient or population: Pain reduction

Setting: Chronic Non Cancer Pain

Intervention: TPMT

Comparison: placebo, control, dry needling or other forms of MT

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Certainty	What happens
				Difference		
Short Term Effects (within 2 weeks of end of treatment) № of participants: 548 (11 RCTs)	-	-	-	SMD **0.52 SD lower** (1.13 lower to 0.1 higher)	⨁⨁◯◯ LOW [a,b]	
Long Term Effects (> 3 months after end of treatment) № of participants: 19 (1 RCT)	-	The mean long Term Effects (> 3 months after end of treatment) was **0**	-	MD **2.8 lower** (3.78 lower to 1.82 lower)	⨁⨁◯◯ LOW [c]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **SMD:** Standardised mean difference; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. For sample size; 6 of 11 studies scored high for RoB, 2 scored moderate RoB and only 3 were low

b. High heterogeneity (91%)

c. Low sample size of included study

Summary of findings:

TPMT compared to placebo, control, Dry needling and Manual therapy for Adverse Events & Withdrawals

Patient or population: Adverse Events & Withdrawals

Setting: Chronic Non Cancer Pain

Intervention: TPMT

Comparison: placebo, control, Dry needling and Manual therapy

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Certainty	What happens
				Difference		
Adverse Events № of participants: 200 (3 RCTs)	**OR 2.04** (0.88 to 4.73)	30.7%	**47.5%** (28.0 to 67.7)	**16.8% more** (2.7 fewer to 37 more)	⨁⨁◯◯ LOW [a]	
Withdrawals № of participants: 1047 (19 RCTs)	**OR 0.53** (0.25 to 1.13)	4.2%	**2.3%** (1.1 to 4.7)	**1.9% fewer** (3.1 fewer to 0.5 more)	⨁⨁⨁◯ MODERATE [b]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Moderate (2 studies) to high (1 study, Bron 2011) RoB for sample size. Otherwise Fitzgerald 2012 and 2013 scored unclear for a range of RoB categories.

b. For sample size; 6 of 11 studies scored high for RoB, 2 scored moderate RoB and only 3 were low

Summary of findings:

TPMT compared to placebo, control, dry needling or manual therapy for Functional Change

Patient or population: Functional Change

Setting: Chronic Non Cancer Pain

Intervention: TPMT

Comparison: placebo, control, dry needling or manual therapy

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Certainty	What happens
				Difference		
Function Questionnaire № of participants: 802 (15 RCTs)	-	-	-	SMD **0.81 lower** (1.49 lower to 0.14 lower)	⨁⨁◯◯ LOW [a,b]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **SMD:** Standardised mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. For sample size; 10 of 15 studies scored high for RoB, 2 scored moderate RoB and only 3 were low

b. Very high heterogeneity (92%)

Summary of findings:

TPMT compared to placebo, control, dry needling or Manual Therapy for Health Related Quality of Life

Patient or population: Health Related Quality of Life

Setting: Chronic Non Cancer Pain

Intervention: TPMT

Comparison: placebo, control, dry needling or Manual Therapy

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Certainty	What happens
				Difference		
HRQOL № of participants: 185 (3 RCTs)	-	The mean HRQOL was **0**	-	MD **2.82 lower** (6.19 lower to 0.55 higher)	⨁⨁⨁◯ MODERATE [a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Two of the three studies were unclear for sample size risk of bias. All 3 scored unclear in most RoB categories

Summary of findings:

TPMT compared to placebo, sham, dry needling or manual therapy for Patient Global Assessment

Patient or population: Patient Global Assessment

Setting: Chronic non-cancer pain

Intervention: TPMT

Comparison: placebo, sham, dry needling or manual therapy

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Certainty	What happens
				Difference		
Perceived Improvement № of participants: 218 (4 RCTs)	**OR 3.79** (1.86 to 7.71)	25.5%	**56.4%** (38.9 to 72.5)	**31.0% more** (13.4 more to 47 more)	⨁⨁◯◯ LOW [a]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. All four studies score moderate to high risk of bias for sample size and moderate to high in a range of other RoB domains

Appendix iii

Excluded studies

1. Aguilera F J, MartÃ-n D P, Masanet R A, Botella A C, Soler L B, Morell F B. Immediate effect of ultrasound and ischemic compression techniques for the treatment of trapezius latent myofascial trigger points in healthy subjects: a randomized controlled study. 2009;32(7):515-20.
2. Anonymous. February 2015 erratum.[Erratum for J Orthop Sports Phys Ther. 2014 Nov;44(11):852-61; PMID: 25269764]. Journal of Orthopaedic & Sports Physical Therapy 2015;45(2):147.
3. Arguisuelas Md, Lison Jf, Sanchez-Zuriaga D, Martinez-Hurtado I, Domenech-Fernandez J. Effects of Myofascial Release in Non-specific Chronic Low Back Pain: A Randomized Clinical Trial. 2016;(no pagination).
4. Arguisuelas-Martinez Md, Domenech J, Sanchez-Zuriaga D, Lison-Parraga Jf. Effects of myofascial release in non-specific chronic low back pain: A randomized clinical trial. 2016;25:S395-s396.
5. Arroyo-Morales M, Olea N, Martinez M, Hidalgo-Lozano A, Ruiz-Rodriguez L. Psychophysiological effects of massage-myofascial release after exercise: a randomized sham-control study. Journal of Alternative & Complementary Medicine 2008 Dec;14(10):1223-1229 2008.
6. Behrangrad S, Kamali F. Comparison of ischemic compression and lumbopelvic manipulation as trigger point therapy for patellofemoral pain syndrome in young adults: A double-blind randomized clinical trial. Journal of Bodywork and Movement Therapies. 2016;20.
7. Bialoszewski D, Bebelski M, Lewandowska M, Slupik A. Utility of craniosacral therapy in treatment of patients with non-specific low back pain. Preliminary report. Ortopedia Traumatologia Rehabilitacja 2014;16(6):605-15.
8. Blikstad A, Gemmell H. Immediate effect of activator trigger point therapy and myofascial band therapy on non-specific neck pain in patients with upper trapezius trigger points compared to sham ultrasound: a randomised controlled trial. 2008;11(1):23-9.
9. Bookwala T, Dabholkar T Y, Pandit U, Thakur A, Karajgi A, Yardi S. Comparison of efficacy of active release technique with ultrasound and strain-counterstrain technique with Ultrasound on upper Trapezius trigger points. 2015;6(3):264-70.
10. Boonruab Jurairat, Niempoog Sunyarn, Pattaraarchachai Junya, Palanuvej Chanida, Ruangrungsi Nijsiri. Effectiveness of the court-type traditional Thai massage versus topical diclofenac in treating patients with myofascial pain syndrome in the upper trapezius. Indian Journal of Traditional Knowledge 2016;15(1):30-4.
11. Buttagat V, Narktro T, Onsrira K, Pobsamai C. Short-term effects of traditional Thai massage on electromyogram, muscle tension and pain among patients with upper back pain associated with myofascial trigger points. Complementary Therapies in Medicine 2016;28:8-12.
12. Campa-Moran I, Rey-Gudin E, FernAinverted-!ndez-Carnero J, Paris-Alemany A, Gil-Martinez A, Lerma L S, et al. Comparison of dry needling versus orthopedic manual therapy in patients with myofascial chronic neck pain: a single-blind, randomized pilot study. Pain Research and Treatment 2015 Nov 10;(327307):Epub 2015.
13. Castro-Sanchez A M, Mataran-Penarrocha G A, Arroyo-Morales M, Saavedra-Hernandez M, Fernandez-Sola C, Moreno-Lorenzo C. Effects of myofascial release techniques on pain, physical function, and postural stability in patients with fibromyalgia: a randomized controlled trial [with consumer summary]. Clinical Rehabilitation 2011 Sep;25(9):800-813 2011.

14. Chao Y W, Lin J, Yang J L, Wang W T. Kinesio taping and manual pressure release: Short-term effects in subjects with myofasical trigger point. Journal of Hand Therapy 2016;29(1):23-9.
15. Crawford Cindy, Boyd Courtney, Paat Charmagne F, Price Ashley, Xenakis Lea, Yang EunMee, et al. The Impact of Massage Therapy on Function in Pain Populations-A Systematic Review and Meta-Analysis of Randomized Controlled Trials: Part I, Patients Experiencing Pain in the General Population. Pain Medicine 2016;17(7):1353-75.
16. da Costa Santos Rebeka Borba, Souza Carneiro MaÃ-ra Izzadora, de Oliveira DÃ©borah Marques, do RÃªgo Maciel Adriana Baltar, do Monte-Silva KÃ¡tia Karina, Rodrigues AraÃºjo Maria das GraÃ§as. Impact of dry needling and ischemic pressure in the myofascial syndrome: controlled clinical trial. Fisioterapia em Movimento 2014;27(4):515-522 8p.
17. De-La-Llave-Rincon Ai, Loa-Barbero B, Palacios-Cena M, Salom-Moreno J, Ortega-Santiago R, Ambite-Quesada S, et al. Manual therapy combined with dry needling for the management of patients with patellofemoral pain syndrome. 2017;25:e82.
18. Dibai-Filho Almir Vieira, De Oliveira Alessandra Kelly, Girasol Carlos Eduardo, Cancio Dias Fabiana Rodrigues, De Jesus Guirro Rinaldo Roberto. Additional Effect of Static Ultrasound and Diadynamic Currents on Myofascial Trigger Points in a Manual Therapy Program for Patients With Chronic Neck Pain. A Randomized Clinical Trial. American Journal of Physical Medicine & Rehabilitation 2017;96(4):243-52.
19. FernÃ¡ndez-Lao C, Cantarero-Villanueva I, DÃ-az-RodrÃ-guez L, FernÃ¡ndez-de-las-PeÃ±as C, SÃ¡nchez-Salado C, Arroyo-Morales M. The influence of patient attitude toward massage on pressure pain sensitivity and immune system after application of myofascial release in breast cancer survivors: a randomized, controlled crossover study. 2012;35(2):94-100.
20. Ferreira V T K, Guirro E C O, Rangon F B, Apolinario A, Rezende M S. Efficiency of ischemic compression and kinesiotherapy in the treatment of myofascial trigger points inbreast cancer survivors: A clinical pilot study. 2015;101:eS493-4.
21. Garcia R, Tormos L, Vilanova P, Morales R, Perez A, Segura E. Efectividad de la puncion seca de un punto gatillo miofascial versus manipulacion de codo sobre el dolor y fuerza maxima de prension de la mano (Effectiveness of a myofascial trigger point dry needling versus elbow manipulation on pain and maximum hand grip strength) [Spanish]. Fisioterapia 2011 Nov-Dec;33(6):248-255 2011.
22. Gemmell H, Allen A. Relative immediate effect of ischaemic compression and activator trigger point, therapy on active upper trapezius trigger points: A randomised trial. Clinical Chiropractic 2008;11(4):175-81..
23. Gemmell H, Miller P, Nordstrom H. Immediate effect of ischaemic compression and trigger point pressure release on neck pain and upper trapezius trigger points: a randomised controlled trial. 2008;11(1):30-6.
24. Grieve R, Clark J, Pearson E, Bullock S, Boyer C, Jarrett A. The immediate effect of soleus trigger point pressure release on restricted ankle joint dorsiflexion: A pilot randomised controlled trial. 2011;15(1):42-9.
25. Grieve R, Cranston A, Henderson A, John R, Malone G, Mayall C. The immediate effect of triceps surae myofascial trigger point therapy on restricted active ankle joint dorsiflexion in recreational runners: a crossover randomised controlled trial. 2013;17(4):453-61.
26. Grieve R, Palmer S. Myofascial trigger point therapy for plantar fasciitis: a feasibility study. 2017;25:e94.
27. Hains Guy, Boucher Pierre B, Lamy Anne-Marie. Ischemic compression and joint mobilisation for the treatment of nonspecific myofascial foot pain: findings from two quasi-experimental before-and-after studies. Journal of the Canadian Chiropractic Association 2015;59(1):72-83.

28. Hsieh C Y, Adams A H, Tobis J, Hong C Z, Danielson C, Platt K, et al. Effectiveness of four conservative treatments for subacute low back pain: a randomized clinical trial. 2002;27(11):1142-8.
29. Irnich D, Behrens N, Molzen H, KÃ¶nig A, Gleditsch J, Krauss M, et al. Randomised trial of acupuncture compared with conventional massage and "sham" laser acupuncture for treatment of chronic neck pain. 2001;322(7302):1574-8.
30. Jung-Ho Lee, Eun-Yeong Han. A Comparison of the Effects of PNF, ESWT, and TPI on Pain and Function of Patients with Myofascial Pain Syndrome. Journal of Physical Therapy Science 2013;25(3):341-344.
31. Kage V, Bindra R. Effect of active release technique v/s myofascial release on subjects with plantar fasciitis: a randomized clinical trial. 2016;101:eS702.
32. Kain J, Martorello L, Swanson E, Sego S. Comparison of an indirect tri-planar myofascial release (MFR) technique and a hot pack for increasing range of motion. 2011;15(1):63-7.
33. Kannan P. Management of myofascial pain of upper trapezius: a three group comparison study. Global Journal of Health Science 2012 Sep;4(5):46-52 2012.
34. Keenan J R. Unclear results for the use of botulinum toxin therapy for TMD pain. Evidence-Based Dentistry 2015;16(4):122.
35. Kisiel C, Lindh C. Smartlindring med fysikalisk terapi och manuell akupunktur vid myofasciella nack- och skuldersmartor. 1996;12.
36. Kojidi Marzieh Mohammadi, Okhovatian Farshad, Rahimi Abbas, Baghban Alireza Akbaezade, Azimi Hadi. Comparison Between the Effects of Passive and Active Soft Tissue Therapies on Latent Trigger Points of Upper Trapezius Muscle in Women: Single-Blind, Randomized Clinical Trial. Journal of Chiropractic Medicine 2016;15(4):235-42.
37. Kovcs Fm, Abraira V, Pozo F, Klenbaum Dg, Beltran J, Mateo I, et al. Local and remote sustained trigger point therapy for exacerbations of chronic low back pain: a randomized, double-blind, controlled, multicenter trial. Spine 1997;22(7):786-97..
38. Kuhar S, Subhash K, Chitra J. Effectiveness of myofascial release in treatment of plantar fasciitis: a RCT. Indian Journal of Physiotherapy and Occupational Therapy 2007 Jul-Sep;1(3):3-9 2007.
39. Lugo L H, Garcia H I, Rogers H L, Plata J A. Treatment of myofascial pain syndrome with lidocaine injection and physical therapy, alone or in combination: a single blind, randomized, controlled clinical trial. BMC Musculoskeletal Disorders 2016 Feb 24;17(101):Epub 2016.
40. Matthieu G, Rafael Z P, Edouard-Olivier R. Muscular ischemic compression vs. cervical spine manipulation techniques: Effects on pressure pain threshold in the trapezius muscle. International Journal of Osteopathic Medicine 2013;16(1):e21-2.
41. Mendez-Rebolledo G, Gatica-Rojas V, Mardones-Pavez V, Ibarra-Silva O. Efectividad del cross tape y compresion isquemica en puntos gatillo miofasciales latentes en musculos epicondileos laterales: ensayo clinico aleatorizado (Effectiveness of the cross tape and ischemic compression on latent myofascial trigger points in lateral epicondylar muscles: a randomized clinical trial) [Spanish]. Fisioterapia 2015 May-Jun;37(3):128-134 2015.
42. O'Reilly A, Pollard H. TMJ pain and chiropractic adjustment: a pilot study. Chiropractic Journal of Australia 1996;26(4):126-129 1996.
43. Okhovatian Farshad, Mehdikhani Royah, Naimi Sedigheh sadat. Comparison between the immediate effect of manual pressure release and strain/counterstrain techniques on latent trigger point of upper trapezius muscle. Clinical Chiropractic 2012;15(2):55-61 7p.
44. Oliveira-Campelo N M, Melo C A, Alburquerque-SendÃ-n F, Machado J P. Short- and medium-term effects of manual therapy on cervical active range of motion and pressure pain sensitivity in latent myofascial pain of the upper trapezius muscle: a randomized controlled trial. 2013;36(5):300-9.

45. Pratelli E, Pintucci M, Cultrera P, Baldini E, Stecco A, Petrocelli A, et al. Conservative treatment of carpal tunnel syndrome: comparison between laser therapy and Fascial Manipulation(Â®). 2016;19(1):113-8.
46. Rajarajeswaran P. Effects of spray and stretch technique and post isometric relaxation technique in acute active central trigger point of upper trapezius. Indian Journal of Physiotherapy and Occupational Therapy 2010 Oct-Dec;4(4):121-124.
47. Rodriguez-Blanco C, Cocera-Morata F M, Heredia-Rizo A M, Ricard F, Almazan-Campos G, Oliva-Pascual-Vaca A. Immediate effects of combining local techniques in the craniomandibular area and hamstring muscle stretching in subjects with temporomandibular disorders: a randomized controlled study. Journal of Alternative & Complementary Medicine 2015 Aug;21(8):451-459.
48. Salom-Moreno J, De-Diego-Garcia J, Palacios-Cena M, Ortega-Santiago R, De-La-Llave-Rincon Ai, Ambite-Quesada S, et al. Immediate effects of manual therapy targeting the cervical or orofacial region in neck symptoms in patients with myofascial temporomandibular pain. 2017;25:e69-70.
49. Sarrafzadeh J, Ahmadi A, Yassin M. The effects of pressure release, phonophoresis of hydrocortisone, and ultrasound on upper trapezius latent myofascial trigger point. Archives of Physical Medicine & Rehabilitation 2012;93(1):72-7.
50. Sata Jay. A Comparative Study Between Muscle Energy Technique and Myofascial Release Therapy on Myofascial Trigger Points in Upper Fibres of Trapezius. Indian Journal of Physiotherapy & Occupational Therapy 2012;6(3):144-148 5p.
51. Sohns S, Schnieder K, Licht G, Piekartz H. Manual trigger point therapy of shoulder pain: randomized controlled study of effectiveness. 2017;30(6):549-59.
52. Takamoto K, Bito I, Urakawa S, Sakai S, Kigawa M, Ono T, et al. Effects of compression at myofascial trigger points in patients with acute low back pain: A randomized controlled trial. European Journal of Pain 2015;19(8):1186-96.
53. Truyols-DomÃ- Nguez S, Salom-Moreno J, Abian-Vicen J, Cleland J A, FernÃ¡ndez-de-Las-PeÃ±as C. Efficacy of thrust and nonthrust manipulation and exercise with or without the addition of myofascial therapy for the management of acute inversion ankle sprain: a randomized clinical trial. 2013;43(5):300-9.
54. Webb T R, Rajendran D. Myofascial techniques: What are their effects on joint range of motion and pain? â€“Â A systematic review and meta-analysis of randomised controlled trials. Journal of Bodywork and Movement Therapies 2016;20(3):682-99.
55. Yeganeh Lari A, Okhovatian F, Naimi Ss, Baghban A. The effect of the combination of dry needling and MET on latent trigger point upper trapezius in females. Manual Therapy 2016;21:204-9.