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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

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 software⁸, 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 5.3⁸ 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.
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

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

‡ 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 (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**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TPMT group Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
<th>IV, Random, 95% CI</th>
<th>Std. Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arguis &amp; Nolas 2017</td>
<td>271</td>
<td>30.06</td>
<td>32</td>
<td>38.9</td>
<td>30.98</td>
<td>26</td>
<td>9.8%</td>
<td>-0.21 [0.20, 0.33]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Campo-Morán 2016</td>
<td>34.3</td>
<td>16.61</td>
<td>12</td>
<td>11.35</td>
<td>15.6</td>
<td>24</td>
<td>8.6%</td>
<td>1.35 [0.58, 2.12]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fitzgerald 2012</td>
<td>3.8</td>
<td>2.3</td>
<td>25</td>
<td>4.3</td>
<td>2.3</td>
<td>24</td>
<td>10.1%</td>
<td>-0.22 [0.66, 0.23]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fitzgerald 2013</td>
<td>0.1</td>
<td>0.52</td>
<td>23</td>
<td>23.0</td>
<td>3.54</td>
<td>24</td>
<td>9.7%</td>
<td>-0.19 [0.27, 0.36]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haines 2011 c</td>
<td>2.4</td>
<td>0.37</td>
<td>24</td>
<td>4.0</td>
<td>0.62</td>
<td>11</td>
<td>8.1%</td>
<td>-5.09 [3.55, -9.94]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haripour 2010</td>
<td>2.7</td>
<td>2.97</td>
<td>30</td>
<td>2.1</td>
<td>1.96</td>
<td>30</td>
<td>9.6%</td>
<td>0.26 [0.22, 0.91]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Karim 2010</td>
<td>2.1</td>
<td>1.91</td>
<td>10</td>
<td>3.2</td>
<td>0.95</td>
<td>9</td>
<td>8.2%</td>
<td>-0.76 [4.5, 0.19]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Krouse 2012</td>
<td>1.93</td>
<td>0.60</td>
<td>15</td>
<td>2.23</td>
<td>1.23</td>
<td>15</td>
<td>8.5%</td>
<td>2.99 [3.52, -1.17]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liarmas-Ramos 2015</td>
<td>1.1</td>
<td>1.1</td>
<td>46</td>
<td>0.9</td>
<td>0.8</td>
<td>45</td>
<td>10.2%</td>
<td>0.10 [0.31, 0.51]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosario-Ordine 2011</td>
<td>44.7</td>
<td>17.5</td>
<td>30</td>
<td>56.1</td>
<td>13.8</td>
<td>30</td>
<td>9.8%</td>
<td>-0.71 [-1.24, -0.19]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sharma 2010</td>
<td>1.8</td>
<td>1.0</td>
<td>15</td>
<td>2</td>
<td>1.56</td>
<td>12</td>
<td>8.0%</td>
<td>-0.18 [0.64, 0.61]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 269 [266, 100.0%] = 0.53 [1.08, 0.02]

**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**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TPMT group Events</th>
<th>Control Total</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bron 2011</td>
<td>3</td>
<td>31</td>
<td>1.04</td>
<td>0.88</td>
<td>4.73</td>
</tr>
<tr>
<td>Fitzgerald 2012</td>
<td>25</td>
<td>26</td>
<td>0.24</td>
<td>0.08</td>
<td>0.68</td>
</tr>
<tr>
<td>Fitzgerald 2013</td>
<td>12</td>
<td>24</td>
<td>3.17</td>
<td>0.12</td>
<td>1.49</td>
</tr>
</tbody>
</table>

Total (95% CI): 99 [100.0%] = 2.04 [0.88, 4.73]

**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

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitzgerald 2012</td>
<td>45</td>
<td>10.8</td>
<td>30</td>
<td>48.8</td>
<td>8.5</td>
<td>40</td>
<td>60.00%</td>
<td>-4.30 [-0.83, 0.03]</td>
<td></td>
</tr>
<tr>
<td>Fitzgerald 2013</td>
<td>40.78</td>
<td>10.94</td>
<td>23</td>
<td>42.15</td>
<td>10.8</td>
<td>24</td>
<td>29.4%</td>
<td>-1.37 [-5.59, 2.85]</td>
<td></td>
</tr>
<tr>
<td>Reman-Criddle 2011</td>
<td>52</td>
<td>15.9</td>
<td>30</td>
<td>60.1</td>
<td>22.2</td>
<td>30</td>
<td>10.00%</td>
<td>-1.90 [-9.74, 12.54]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>91</td>
<td>100.00%</td>
<td></td>
<td>94</td>
<td>100.00%</td>
<td></td>
<td>2.82 [-6.19, 0.55]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Ch² = 1.41, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 1.64 (P = 0.10)

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.
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


References

16. Renan-Ordine R, Alburquerque-Sendin F, de Souza DP, Cleland JA, Fernández-de-Las-Peñas C. Effectiveness of myofascial trigger point manual therapy combined with a self-


Appendix i.

Medline Search Strategy

1. Trigger Points/
2. exp Myofascial Pain Syndromes/
3. (trigger point* or trigger site* or muscle knot*).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
**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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short Term Effects (within 2 weeks of end of treatment)</td>
<td>-</td>
<td>-</td>
<td>SMD 0.52 SD lower (1.13 lower to 0.1 higher)</td>
<td>⬤豳◯◯ LOW ab</td>
<td></td>
</tr>
<tr>
<td>No of participants: 548 (11 RCTs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long Term Effects (&gt; 3 months after end of treatment)</td>
<td>-</td>
<td>The mean long Term Effects (&gt; 3 months after end of treatment) was 0</td>
<td>MD 2.8 lower (3.78 lower to 1.82 lower)</td>
<td>⬤豳◯◯ LOW c</td>
<td></td>
</tr>
<tr>
<td>No of participants: 19 (1 RCT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*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

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

*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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Function Questionnaire</td>
<td>-</td>
<td>SMD 0.81 lower (1.49 lower to 0.14 lower)</td>
<td>LOW</td>
<td>-</td>
</tr>
</tbody>
</table>

| Nr of participants (studies) | - | - | - | - |

**Number of participants:** 802 (15 RCTs)

*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 the 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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRQOL</td>
<td>-</td>
<td>-</td>
<td>MD 2.82 lower (6.19 lower to 0.55 higher)</td>
<td>☒ ☒ ☒ ✔️ MODERATE</td>
</tr>
</tbody>
</table>

*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 the effect

**Explanations**

- 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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perceived Improvement</td>
<td>OR 3.79 (1.86 to 7.71)</td>
<td>25.5% 56.4% (38.9 to 72.5)</td>
<td>31.0% more (13.4 more to 47 more)</td>
<td>LOW *</td>
</tr>
</tbody>
</table>

*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 the effect.

**Explanations**

- 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 ii

Excluded studies


