Cochrane Library

Cochrane Database of Systematic Reviews

Trigger point manual therapy for the treatment of chronic non-cancer pain in adults (Protocol)

Denneny D, Petersen K, McLoughlin R, Brook S, Hassan S, Williams ACDC

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.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Protocol]

Trigger point manual therapy for the treatment of chronic non-cancer pain in adults

Diarmuid Denneny[1], Katrine Petersen[1], Rebecca McLoughlin[1], Suzanne Brook[1], Salma Hassan[1], 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

Contact address: Diarmuid Denneny, Pain Management, UCLH NHS Foundation Trust, London, UK. diarmuid.denneny@uclh.nhs.uk.

Editorial group: Cochrane Pain, Palliative and Supportive Care Group.
Publication status and date: New, published in Issue 6, 2015.

Citation: 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.

ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To determine the effectiveness of trigger point manual therapy for treating chronic non-cancer pain in adults.

BACKGROUND

Description of the condition

Chronic pain has long been defined as pain that persists beyond the healing time needed to recover from an injury (Patterson 2003), and often for longer than six months (Elkins 2007; Keefe 1982). In contrast with acute pain, chronic pain may communicate very little about an associated or underlying disease process (Patterson 2003; Chapman 1999). The International Association for the Study of Pain (IASP) defines chronic pain as 'pain without apparent biological value that has persisted beyond the normal tissue healing time (usually taken to be 3 months)' (Harstall 2003). For the purposes of our review, we will use the IASP definition of chronic pain; that is, pain that has persisted beyond three months following an initial injury.

Myofascial pain (MP) is a form of pain that is thought to arise from myofascial trigger points (TrPs). Myofascia consists of muscle and the highly innervated connective tissue that surrounds it. TrPs are commonly thought of as taut bands within muscle that are usually painful to palpation, reproduce the patient's symptoms, and cause referred pain (Borg-Stein 2002). The four most commonly used clinical criteria to define TrPs according to Tough 2007 are i) a tender spot in a taut band of skeletal muscle, ii) patient pain recognition, iii) predicted pain referral pattern and iv) local twitch response. MP can be acute and chronic in presentation. It is a commonly diagnosed disorder that is thought to be caused by muscle injury, overuse or repetitive strain (Bennett 2007). Incidence reporting varies from 30% to 93% in clinics of different specialities and pain management centres (Cummings 2007; Fishbain 1986; Fricton 1985; Han 1997; Skootsky 1989).

There is controversy in the literature regarding the existence, clinical significance and underlying mechanisms behind TrPs. Traditionally the focus has been on peripheral mechanisms underlying the condition. It has been postulated that abnormal neurophysiology and a perturbed biochemical milieu are relevant to TrPs

(Bennett 2007). There is some evidence that TrPs may be associated with increased release of acetylcholine by the nerve terminal of an abnormal motor endplate (Mense 2003, Simons 2002). Increased release of acetylcholine can result in sustained depolarisation of the postjunctional membrane of the muscle fibre and produce sustained sarcomere shortening and contracture. It is thought that this may greatly increase local energy consumption and reduce local circulation that produces local ischemia and hypoxia. Mechanical, chemical, or other noxious stimuli or injury may mediate the abnormal release of acetylcholine (Liley 1956). When compared to normal muscle, some studies suggest that the active TrPs have an acidic pH environment and elevated levels of several biologically relevant molecules such as tumour necrosis factor-alpha (TNFα), interleukin-1b, calcitonin-gene-related polypeptide (CGRP), substance P, bradykinin, serotonin and norepinephrine (Shah 2005). It is hypothesised that these active factors might also stimulate the local autonomic nervous system fibres to release more acetylcholine, completing a 'positive feedback loop' (Mense 2001; Simons 1999).

More recently research is moving towards central mechanisms behind the condition (Fernández-de-las-Peñas 2013). Referred pain, the most characteristic sign of TrPs, is thought by some to be a central phenomenon initiated and activated by peripheral sensitisation, whereby the peripheral nociceptive input from the muscle can sensitise dorsal horn neurons that were previously silent (Fernández-de-las-Peñas 2013). TrPs are seen by some as a peripheral source of nociception that can act as ongoing nociceptive stimuli contributing to pain propagation and widespread pain (Fernández-de-las-Peñas 2013). The precise pathophysiological basis of MP remains unclear and a definitive explanation has yet to be agreed.

There is controversy in the literature regarding the assessment of TrPs (Fernández-de-las-Peñas 2013; Tough 2007; Wolfe 1992). TrPs are predominantly identified and diagnosed by palpation although the reliability of this is questioned in the literature (Lucas 2009 Wolfe 1992). It is unclear whether professional training or expertise improves ability to palpate or diagnose TrPs (Wolfe 1992). Patients may experience pain, and may also experience difficulties due to the pain including inability to work, mood changes, and reduced quality of life (Borg-Stein 2002). In most cases, the discomfort usually resolves in a few weeks without medical intervention. When the pain persists or worsens and becomes chronic, it is referred to as a myofascial pain syndrome (MPS) (Bennett 2007; Borg-Stein 2002).

Many pharmacologic and nonpharmacologic treatments are used in the management of TrPs associated with MP. Drugs such as analgesics (e.g. tramadol), non-steroidal anti-inflammatory drugs, tricyclic antidepressants (e.g. amitriptyline), alpha-2 adrenergic agonists (such as tizanidine), and anticonvulsant drugs are commonly used. Recently, botulinum toxin has also been used for the treatment of MP (Bennett 2007; Borg-Stein 2002; Borg-Stein 2006; Fleckenstein 2010; Leite 2009; Soares 2012). However, the effectiveness of medication can often be unsatisfactory and side effects are common. More targeted therapies include trigger point manual therapy (TPMT), acupuncture, dry needling, local injection, low-power laser, muscle-stretching technique, and massage (Borg-Stein 2002; Borg-Stein 2006; Renan-Ordine 2011; Sun 2010; Tough 2009).

In a systematic review of acupuncture and dry needling for the management of TrP pain (Tough 2009) the authors concluded that there was limited evidence that deep needling directly into TrPs has an overall treatment effect when compared with standardised care. They also suggested that there was no logical basis for choosing the optimal intervention for MP until different interventions were compared directly. Currently there are no systematic reviews comparing the effects of manual therapy in the form of TPMT with dry needling, acupuncture or other forms of TrP treatment. The current review aims to redress this and will focus on TPMT.

Description of the intervention

For the purposes of this review we will define TPMT as treatment that involves the manual application of pressure, usually sustained digital pressure, but may include the use of devices (for example the *Jacknobber* ® or *Knobble* ®) to apply pressure to the TrPs. We will not consider devices that penetrate the skin such as acupuncture needles as a form of TPMT but we may include them in this review as possible comparisons with TPMT. The therapist may place the muscle containing the trigger point into positions of longitudinal tension or stretch whilst performing the TPMT. The optimal duration of applied pressure, patient positioning and frequency of treatments is at present not clearly reported or defined in the literature. We will not include treatments with more general effects that are not specifically addressing the TrP, including transverse friction massage, muscle energy techniques, mobilisation, massage, manipulations, and spray and stretch.

How the intervention might work

The proposed mechanisms of the proposed effect of TPMT, or any form of treatment to TrPs, is poorly understood at present. Explanations tend to focus on a peripherally maintained model of pain. Ischaemic compression is the most cited theory used to explain the effect of TPMT. It is thought that the application of pressure to a TrP produces ischaemia that ablates the TrP (Lavelle 2007; Simons 1999). Theories relating to the effect on the central nervous system have been postulated previously, for example D'Ambrogio 1997 described adjustments to pain threshold in the spinal cord following TPMT. There is growing interest in the central mechanisms behind TrPs and their treatment (Fernández-de-las-Peñas 2013).

Why it is important to do this review

No 'gold standard' of management has been suggested for chronic non-cancer pain, including MP. The benefits of TPMT remain controversial (Tough 2009). It has been suggested that treatment of TrPs may not be appropriate for chronic pain conditions, being more suitable for conditions such as whiplash associated disorder or 'sustained postural strain' (Tough 2009). A systematic review of the evidence from randomised clinical trials (RCTs) for the effectiveness of TPMT may assist patients with their choice and expectations of treatments, help clinicians in their treatment choices, and inform future clinical guidelines that may be of use to policymakers and those who commission health care.

OBJECTIVES

To determine the effectiveness of trigger point manual therapy for treating chronic non-cancer pain in adults.

METHODS

Criteria for considering studies for this review

Types of studies

We will include RCTs (including those of parallel, cluster-randomised and cross-over design) published in any language. We will translate studies published in a language other than English. To reduce risk of bias we will exclude studies in which participants were not randomised to intervention groups . We will include studies regardless of publication status.

Types of participants

We will include all studies of adults, 18 years of age or over, with chronic non-cancer pain presentations. We will exclude studies of headaches and progressive neurological conditions. We anticipate predominantly musculoskeletal, back pain, pelvic pain and facial pain patient groups although we will not limit to these groups if appropriate.

For the purposes of this review we define chronic pain as pain of greater than three months' duration. Where studies include patients with pain of both longer and shorter than three months' duration, and it is possible to distinguish the results from both groups, then we will include the data from the chronic pain group.

Types of interventions

We will include all comparisons of manual therapy interventions, as described in the Description of the intervention above, employed in either a stand-alone fashion or in combination where the only difference between the active group and the comparison group is TPMT, compared with placebo, no treatment or another intervention, or of varying interventions compared with each other, which are aimed at treating pain or disability, or both, associated with TrPs.

Due to anticipated heterogeneity of modes of delivery and of therapists delivering, we will accept any reported delivery of the intervention but we anticipate predominantly qualified manual therapists including physiotherapists, osteopaths and chiropractors. We will not apply restrictions on the duration of the intervention or the frequency with which it is delivered because optimal treatment dose is not clearly defined in the literature. We will include multimodal interventions where TPMT is separately analysed.

We will include studies that include sham interventions as controls , however given the difficulty of delivering sham TPR treatment, control conditions can also include

- no treatment or waiting list control,
- any active treatments such as standard manual therapy, standard physiotherapy, stretch, acupuncture, rehabilitative and psychological interventions,
- drug therapies, including TrP injections.

Types of outcome measures

Primary outcomes

1. Changes in pain severity/intensity as measured using a visual analogue scale (VAS), numerical rating scale (NRS), verbal rating scale or Likert scale. For the purposes of this review we will define moderate change as between 30% and 49% change on NRS, and substantial change will be considered to be 50% or greater improvement from baseline (Dworkin 2008).
2. Adverse events such as drop outs or reports of pain worsening.

We will present and analyse primary outcomes as change on a continuous scale or in a dichotomised format as the proportion of participants in each group who attained a predetermined threshold of improvement. For example, we will judge cut-points from which to interpret the likely clinical importance of (pooled) effect sizes according to provisional criteria proposed in the IMMPACT consensus statement (Dworkin 2008).

Secondary outcomes

1. Health-related quality of life (HR-QOL).
2. Changes in functional ability as measured by validated questionnaires/scales such as the Brief Pain Inventory (BPI)

interference scale (minimum 1 point change) or functional testing protocol.

3. Physiotherapy measures such as range of movement, strength.

4. Reductions in healthcare use, including medication, visits to primary or secondary care.

5. Self-efficacy for activity such as the Pain Self Efficacy Questionnaire (PSEQ)

6. Outcomes such as satisfaction or overall improvement

We will present and analyse secondary outcomes as change on a continuous scale or in a dichotomised format. For example, equivalent measures of treatment effect with respect to patient's global impression of change (PGIC) have been defined as 'much' improved (moderate benefit) and 'very much' improved (substantial benefit) (Dworkin 2008).

Search methods for identification of studies

Electronic searches

We will search the following databases:

- Cochrane Central Register of Controlled Trials (CENTRAL, latest issue);
- Ovid MEDLINE (1946 to present);
- Ovid EMBASE (1974 to present);
- EBSCO CINAHL (1982 to present);
- Ovid PsycINFO (1806 to present);
- Ovid AMED (1985 to present);
- LILACS (1986 to present);
- PEDro (1929 to present);
- Web of Science (ISI) (1970 to present);
- SciVerse SCOPUS (1823 to present);
- Database of Abstracts of Reviews of Effects (DARE), *The Cochrane Library* (1994 to present);
- Health Technology Assessments (1994 to present);

We will use the search strategy shown in Appendix 1 to search MEDLINE,amend where necessary, to search the other databases listed. We will apply no language or date restrictions.

Searching other resources

We will review the bibliographies and reference lists of any RCTs and review articles identified, contact the authors of unpublished work, search the websites of researchers active in the area, and search www.clinicaltrials.gov and apps.who.int/trialsearch/ to identify additional published or unpublished data.

Data collection and analysis

Selection of studies

Two review authors (DD and KP) will determine eligibility by reading the title and abstract of studies identified by the search. Studies that clearly do not satisfy inclusion criteria will be eliminated, and we will obtain full copies of the remaining studies. Two review authors (DD and KP) will read these studies independently and reach agreement by discussion. A third author (SB) will be consulted in case of disagreement. We will not anonymise the studies in any way before assessment. We will include a PRISMA study flow diagram in the full review (Liberati 2009) to document the screening process, as recommended in the Cochrane Handbook (Higgins 2011a).

Data extraction and management

Two review authors (SB and SH) will independently extract data using a standard form which we will pilot. We will check for agreement before entry into RevMan 5 (RevMan 2014). We will include information about:

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

Assessment of risk of bias in included studies

Two review authors (RML and SH) will independently assess risk of bias for each study, using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b) and adapted from those used by the Cochrane Pregnancy and Childbirth Group, with any disagreements resolved by discussion. If this is not possible then we will consult a third reviewer (DD). We will assess the following for each study.

- Random sequence generation (checking for possible selection bias). We will assess the method used to generate the allocation sequence as: low risk of bias (any truly random process, e.g. random number table; computer random number generator); unclear risk of bias (method used to generate sequence not clearly stated), high risk of bias (studies using a non-random process, e.g. odd or even date of birth; hospital or clinic record number. We will exclude studies at high risk of bias.

- Allocation concealment (checking for possible selection bias). The method used to conceal allocation to interventions before assignment determines whether intervention allocation could have been foreseen in advance of or during recruitment, or changed after assignment. We will assess the methods as: low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes); unclear risk of bias (method not clearly stated); high risk of bias (studies that do not conceal allocation e.g. open list). We will exclude studies at high risk of bias.
- Blinding of outcome assessment (checking for possible detection bias). Due to the nature of the intervention being reviewed it is extremely unlikely that there will be double-blinded trials. Where studies have included blinding we will assess the methods used to blind study participants and outcome assessors from knowledge of which intervention a participant received. We will assess the methods as: low risk of bias (study states that it was blinded and describes the method used to achieve blinding); unclear risk of bias (study states that it was blinded but does not provide an adequate description of how this was achieved). High risk of bias (We will judge unblinded studies as high risk of bias unless they demonstrate (for uncertain or low risk of bias) equivalence of patient expectation of benefit and equivalence of therapist allegiance and skills across conditions. We will note this in the 'Summary of findings' table).
- Incomplete outcome data (checking for possible attrition bias due to the amount, nature, and handling of incomplete outcome data). We will assess the methods used to deal with incomplete data as: low risk of bias (< 10% of participants did not complete the study or used 'baseline observation carried forward' analysis, or both); unclear risk of bias (method not clearly stated); high risk of bias (used 'last observation carried forward' analysis' or 'completer' analysis).
- Size of study (checking for possible biases confounded by small size). We will assess studies as being at low risk of bias (≥ 200 participants per treatment arm); unclear risk of bias (50 to 199 participants per treatment arm); high risk of bias (< 50 participants per treatment arm).

Measures of treatment effect

We will present treatment effect sizes using appropriate metrics. We will calculate risk ratio (RR) with 95% confidence intervals (CIs) for dichotomised outcome measures.We will calculate the number needed to treat for an additional beneficial outcome (NNTB) as an absolute measure of treatment effect where possible.

We will express the size of treatment effect on pain intensity, as measured with a VAS or NRS, using the mean difference (MD) (where all studies utilised the same measurement scale) or the standardised mean difference (SMD) (where studies used different scales). In order to aid interpretation of the pooled effect size we will back-transform the SMD to a 0 to 100 mm VAS format on the basis of the mean standard deviation from trials using a 0 to 100 mm VAS where possible.

Unit of analysis issues

If there is more than one treatment arm, we will combine them where they represent sufficiently similar treatment; otherwise two review authors, SH and RML will independently decide which best represents the treatment under scrutiny. They will refer disagreements to a third reviewer (DD).

Where cross-over design trials are included we will analyse the first phase only.

In the case of cluster RCTs we plan to meta-analyse the effect estimates and their standard errors from analysis using the generic inverse-variance method in RevMan 2014 as recommended by the Cochrane Handbook, section 9.4.3 (Deeks 2011). Where data allow we plan to adjust for the effects of clustering using an estimate of the intracluster (or intraclass) correlation coefficient (ICC) as per Cochrane Handbook recommendations in section 16.3.4 (Higgins 2011c) .

Dealing with missing data

Where information is missing from the included studies, we will contact the study authors to provide additional information.

Assessment of heterogeneity

Clinical heterogeneity will be dealt with by attempting to combine studies that examine similar conditions (e.g. pelvic pain, chronic low back pain) or therapists (e.g. physiotherapists, chiropractors). We will assess heterogeneity using the Chi^2 test to investigate the statistical significance of such heterogeneity, and the I^2 statistic to estimate the amount of heterogeneity (Higgins 2003). Where significant heterogeneity is present (we will use a P value of 0.1 as the cut off value to determine significant heterogeneity), we will explore subgroup analyses using pre-planned criteria as outlined below in Subgroup analysis and investigation of heterogeneity.

Assessment of reporting biases

We will consider the possible influence of publication/small study biases on review findings. Where possible, for studies that have utilised dichotomised outcomes, we will test for the possible influence of publication bias on each outcome by estimating the number of participants in studies with zero effect required to change the NNTB to an unacceptably high level (defined as an NNTB of 10), as outlined by Moore 2008.

Data synthesis

Assuming significant clinical heterogeneity, we will use a random-effects model for meta-analysis.

Where possible, we will group extracted data according to duration of effect. We will define short-term effects as those measured at less than two weeks from the end of treatment; medium-term effects as those that are recorded in the period between two weeks to three months from the end of treatment; and long-term effects as those measured at more than three months post-treatment.

Where inadequate data are found we will perform narrative synthesis of the evidence using the GRADE system, as described in Chapter 12 of the Cochrane Handbook for Systematic Reviews of Interventions (Schünemann 2011).

Subgroup analysis and investigation of heterogeneity

1. If there are sufficient trials, we plan to analyse those with baseline pain <30/100 and ≥30/100 and Y studies separately, because clinical utility depends on effects not being restricted to relatively mild pain intensity.
2. We plan subgroup analysis, where there are sufficient numbers of studies, according to practitioner, such as physiotherapists, osteopaths, chiropractors, physicians.
3. We plan subgroup analysis of studies according to type of pain if there are sufficient for meaningful groupings such as pelvic pain, low back pain, widespread pain, facial pain

Sensitivity analysis

Where possible, we plan sensitivity analyses to assess the effect of the different methodological decisions made throughout the review process by removal of cluster RCTs to leave individually randomised trials.

We will conduct sensitivity analyses on risk of bias where sufficient data are available (investigating the influence of excluding studies classified at high risk of bias).

ACKNOWLEDGEMENTS

We would like to thank Joanne Abbott, the Trials Search Co-ordinator with the Cochrane Pain Palliative and Supportive Care Group, for her assistance with designing the search strategy.

We would also like to thank Anna Hobson, Managing Editor, and Yvonne Roy, Assistant Managing Editor, with the Cochrane Pain, Palliative and Supportive Care Group for their assistance, advice and support.

Cochrane Review Group funding acknowledgement: The National Institute for Health Research (NIHR) is the largest single funder of the Cochrane PaPaS Group. Disclaimer: The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, National Health Service (NHS) or the Department of Health.

REFERENCES

Additional references

Bennett 2007
Bennett R. Myofascial pain syndromes and their evaluation. *Best Practice & Research Clinical Rheumatology* 2007;**21**(3): 427–45.

Borg-Stein 2002
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.

Borg-Stein 2006
Borg-Stein J. Treatment of fibromyalgia, myofascial pain, and related disorders. *Physical Medicine and Rehabilitation Clinics of North America* 2006;**17**(2):491–510.

Chapman 1999
Chapman CR, Nakamura Y, Flores LY. Chronic pain and consciousness: a constructivist perspective. In: Gatchel RJ, Turk DC editor(s). *Factors in Pain: Critical Perspectives*. New York: Guilford Press, 1999:35–55.

Cummings 2007
Cummings M, Baldry P. Regional myofascial pain: diagnosis and management. *Best Practice & Research Clinical Rheumatology* 2007;**21**(2):367–87.

D'Ambrogio 1997
D'Ambrogio KJ, Roth GB. *Positional Release Therapy: Assessment & Treatment of Musculoskeletal Dysfunction*. 1. St Louis: Mosby, 1997.

Deeks 2011
Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org..

Dworkin 2008
Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *Journal of Pain* 2008;**9**(2): 105–21.

Elkins 2007
Elkins G, Jensen MP, Patterson DR. Hypnotherapy for the management of chronic pain. *International Journal of Clinical and Experimental Hypnosis* 2007;**55**:275–87.

Fernández-de-las-Peñas 2013
Fernández-de-las-Peñas C, Dommerholt J. Myofascial Trigger Points: Peripheral or Central Phenomenon?. *Current Rheumatology Reports* 2013;**16**:395.

Fishbain 1986
Fishbain DA, Goldberg M, Meagher BR, Steele R, Rosomoff H. Male and female chronic pain patients categorized by DSM-III psychiatric diagnostic criteria. *Pain* 1986;**26**(2): 181–97.

Fleckenstein 2010
Fleckenstein J, Zaps D, Rüger LJ, Lehmeyer L, Freiberg F, Lang PM, et al. Discrepancy between prevalence and perceived effectiveness of treatment methods in myofascial pain syndrome: results of a cross-sectional, nationwide survey. BMC Musculoskeletal Disorders 2010; Vol. 11, issue 32.

Fricton 1985
Fricton JR, Kroening R, Haley D, Siegert R. Myofascial pain syndrome of the head and neck: a review of clinical characteristics of 164 patients. *Oral Surgery, Oral Medicine, Oral Pathology* 1985;**60**(6):615–23.

Han 1997
Han SC, Harrison P. Myofascial pain syndrome and trigger-point management. *Regional Anesthesia* 1997;**22**(1): 89–101.

Harstall 2003
Harstall C, Ospina M. How prevalent is chronic pain?. *Pain Clinical Updates* 2003;**11**(2):1–4.

Higgins 2003
Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327** (7414):557–60.

Higgins 2011a
Higgins 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.

Higgins 2011b
Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.. The Cochrane Collaboration.

Higgins 2011c
Higgins JPT, Deeks JJ, Altman DG (editors). Chapter 16: Special topics in statistics. 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.

Keefe 1982
Keefe FJ. Behavioral assessment and treatment of chronic pain: current status and future directions. *Journal of Consulting and Clinical Psychology* 1982;**50**:896–911.

Lavelle 2007
Lavelle W, Smith HS. Myofascial trigger points. *Anesthesiology Clinics* 2007;**25**:841–51.

Leite 2009
Leite FM, Atallah AN, El Dib R, Grossmann E, Januzzi E, Andriolo RB, et al. Cyclobenzaprine for the treatment of myofascial pain in adults. *Cochrane Database of Systematic Reviews* 2009, Issue 3. [DOI: 10.1002/ 14651858.CD006830.pub3]

Liberati 2009
Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Annals of Internal Medicine* 2009;**151**(4):W65–94.

Liley 1956
Liley AW. An investigation of spontaneous activity at the neuromuscular junction of the rat. *The Journal of Physiology* 1956;**132**(3):650–66.

Lucas 2009
Lucas N, Macaskill P, Irwig L, Moran R, Bogduk N. Reliability of physical examination for diagnosis of myofascial trigger points. *Clinical Journal of Pain* 2009;**25** (1):80–9.

Mense 2001
Mense S, Simons DG, Russell IJ. *Muscle pain: understanding its nature, diagnosis, and treatment*. Baltimore: Lippincott Williams & Wilkins, 2001.

Mense 2003
Mense S, Simons DG, Hoheisel U, Quenzer B. Lesions of rat skeletal muscle after local block of acetylcholinesterase and neuromuscular stimulation. *Journal of Applied Physiology* 2003;**94**(6):2494–501.

Moore 2008
Moore RA, Barden J, Derry S, McQuay HJ. Managing potential publication bias. In: McQuay HJ, Kalso E, Moore RA editor(s). *Systematic Reviews in Pain Research: Methodology Refined*. Seattle: IASP Press, 2008:15–23.

Patterson 2003
Patterson DR, Jensen MP. Hypnosis and clinical pain. *Psychological Bulletin* 2003;**129**:495–521.

Renan-Ordine 2011
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.

RevMan 2014 [Computer program]
The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. The Cochrane Collaboration, 2014.

Schünemann 2011
Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, Guyatt GH. Chapter 12: Interpreting results and drawing conclusions. 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.

Shah 2005
Shah JP, Phillips TM, Danoff JV, Gerber LH. An in vivo microanalytical technique for measuring the local biochemical milieu of human skeletal muscle. *Journal of Applied Physiology* 2005;**99**(5):1977–84.

Simons 1999
Simons DG, Travell JG, Simons LS. *Myofascial pain and dysfunction: the trigger point manual*. 2. Vol. **1**, Baltimore: Williams & Wilkins, 1999.

Simons 2002
Simons DG, Hong CZ, Simons LS. Endplate potentials are common to midfiber myofacial trigger points. *American Journal of Physical Medicine & Rehabilitation* 2002;**81**(3): 212–22.

Skootsky 1989
Skootsky SA, Jaeger B, Oye RK. Prevalence of myofascial pain in general internal medicine practice. *Western Journal of Medicine* 1989;**151**(2):157–60.

Soares 2012
Soares A, Andriolo RB, Atallah ÁN, da Silva EMK. Botulinum toxin for myofascial pain syndromes in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 4. [DOI: 10.1002/14651858.CD007533.pub3]

Sun 2010
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.

Tough 2007
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.

Tough 2009
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.

Wolfe 1992
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.

* *Indicates the major publication for the study*

APPENDICES

Appendix 1. 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

CONTRIBUTIONS OF AUTHORS

DD directed the project.

DD, AW, KP, SH, RML and SB all contributed to the conceptualising and authoring of the protocol, and will contribute to the development of the full review.

DECLARATIONS OF INTEREST

Diarmuid Denneny: none known

Amanda Williams: none known

Katrine Petersen: none known

Salma Hassan: none known

Suzanne Brook: none known

Rebecca McLoughlin: none known