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Myofascial Pain and Treatment

Is there a dose response relationship between soft tissue manual therapy and clinical outcomes in fibromyalgia?

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ABSTRACT

Background: Current clinical guidelines do not support the use of manual therapy (MT) interventions for Fibromyalgia (FM) patients, despite evidence of positive biochemical, mechanical and psychological effects, and the popularity of hands-on treatments amongst patients. An optimal dose for MT has not been established; this may explain the discrepancies found within the published literature. The aim of this systematic review was to determine whether there is a dose response relationship for MT leading to improvements in core domains of FM symptomology; Pain, Mood, Sleep, Global Measure of Impact (Functional Status & Quality of Life).

Methods: We searched six databases from 1990 to January 2018; studies were evaluated using the PEDro scale. Within-group (ES*d*) and between-group (ES*g*) Effect Sizes were calculated.

Results: We identified and screened 4012 articles, 12 articles were critically appraised. Overall, there is moderate evidence that MT has positive effects on the four clinical outcomes investigated. However, there was no consistent dose response relationship observed across all studies.

Conclusions: A dose of approximately 45 min MT, three to five times per week, for three to five weeks, totalling 11 h 15 min, should be considered a baseline generic protocol for treatment delivery and research trials. Further research is necessary to confirm domain specific, or patient specific optimal doses. Moderator variables such as treatment time, frequency, duration; and MT type also need to be explored to ensure optimal delivery of MT in future research and clinical care provision.

1. Introduction

1.1. Definition and current management

Fibromyalgia (FM) is an enigmatic disease with no clear aetiology, diagnostic markers, or best treatment protocol. Sufferers experience a myriad of symptoms including; widespread pain, fatigue, sleep disturbance, decreased function, affect disruption, and cognitive deficit. (Hauser and Fitzcharles, 2018). Due to its high, and reportedly increasing prevalence, 0.2–6.6% in the general population (Marques et al., 2017); and the impact on Health Related Quality of Life (HRQOL), there is an associated economic burden for society and for the individual (Eijk-Hustings et al., 2016).

Despite FM being considered a problem of central sensitivity and maladapted central processing (Clauw, 2014), it has been suggested that the periphery should not be ignored (Staud, 2011). Afferent input to the central nervous system via touch modalities could provide the stimulus for positive bioplastic adaption in the central nervous system. Additionally, the main symptom which guides patient's health seeking behaviour is muscle pain. Localised treatments such as soft tissue manual therapies are often sought (Wahner-Roedler et al., 2005), and have the potential to reduce ongoing nociceptive afferent input from altered tissue mechanics such as trigger points. No 'cure' has been identified, therefore the aim of treatment is to provide symptomatic relief tailored to the individual. Recent evidence shows only modest improvements in outcomes (Thieme et al., 2017).

1.2. Guidelines and literature

Clinical guidelines have supported active-engagement in self management through a multi-component approach including exercise, pharmacology and Cognitive Behaviour Therapy (CBT) (Hauser et al., 2017). Manual Therapies have not been supported;

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the revised 2015 EULAR (European League Against Rheumatism) guidelines gave a 'weak against' judgement for MT, despite their sub group analysis revealing 'evidence of a positive effect with massage of 5 or more weeks duration' (Macfarlane et al., 2017). Ablin et al. (2013) evaluated recent guidelines with a specific focus on complementary and alternative therapies, their summary statement relating to MT was to discourage the use of 'passive physical treatments e.g. massage "magic pill" '. Physiological evidence however has supported the therapeutic potential for MT (Field, 2010 & 2014, Holey and Dixon, 2014; Liptan, 2010).

Authors have suggested insufficient numbers of high quality studies and heterogeneity found between trials, as reasons for the lack of support for MT (Terry et al., 2012; Terhorst et al., 2011). The variety of interventions, and dosing patterns reported in previous reviews shows a lack of standardisation (Yuan et al., 2015; Kalichman, 2010; Terhorst et al., 2011). Without standardisation of dose, it is possible that even with the 'right intervention' 'the wrong duration will skew research toward a negative outcome' (Walden, 2015). Crawford et al. (2016) has suggested; 'Drug trials undergo systematic phase trials to determine consistent and adequate dosing, massage trials do not carry out such processes and often do not provide rationale for dose related variables'. Sherman et al. (2014) suggested that inconclusive reviews investigating efficacy of massage for chronic neck pain resulted from inadequate doses of the intervention, their 6-arm dosing trial showed significant dose-dependant benefits, indicating the relevance of dosage.

1.3. Therapeutic action of MT

Manual therapies using hands on touch to manipulate bodily tissues, can be directed at soft tissue or joint. Within the soft tissue therapies, massage has received the most exposure in the literature. Other forms of soft tissue MT have also been investigated in relation to treatment for FM; including Myofascial release (MFR), Cranial Sacral Therapy (CST), Fasciotherapy, Connective Tissue Massage (CTM), Manual Lymphatic Drainage Therapy (MLDT). All soft tissue MT's can usually be described by the definition used for massage; 'a systematic and scientific manipulation of the soft tissues of the body with rhythmical pressure and stroking for the purpose of obtaining or maintaining health' (Sritoomma et al., 2014). The therapeutic mechanism is thus described as 'thought to relieve pain through several pathways, including increasing the pain threshold by releasing endorphins and closing the gate of pain at the spinal cord level.' (Sritoomma et al., 2014).

This definition comes from a biomechanical perspective, the accuracy of which has been challenged in recent years. Other authors however, have posited broader concepts, such as considering touch-based therapy as; an 'informed 'desensitizer' of the system' (Zusman, 2002), a tool to intervene in the interoceptive pathway (Courtois et al., 2015); a neuroaffective process which can prepare patients to self regulate physiological activation (LaPierre, 2003). The resulting therapeutic benefits are now attributed to a broader 'complex interplay between neurophysiological effects, placebo, patient expectation, and therapeutic alliance' (Bialosky et al., 2009). Within Lederman (2015) 'Process Approach', MT is redefined as a 'vehicle to deliver touch effects' such as positive sense of sense and well-being' items which are reportedly lacking in many FM patients (Schleicher et al., 2005). However there is no discussion in the literature regarding the length of time necessary for this interplay to reach a positive clinical outcome.

2. Aim

The aim of this systematic review was to assess if the current literature provides any evidence of a dose response relationship between MT and clinically important outcomes. In order to assess the true efficacy of an intervention for FM, multi symptom outcomes need to be reviewed as recommended by the Outcome measures in Rheumatology Clinical Trials (OMERACT) FM working group. Core symptom domains include; pain, sleep, emotional wellbeing and functional status (measured within Global measures of impact; functional impact and quality of life) (Mease et al., 2009).

A dose response relationship is described as a direct association between the level of exposure to an intervention and a desired effect or outcome.

Any evidence regarding dose could inform further clinical trials in ensuring an optimal dose of MT is delivered, this would allow more accurate assessment of the role of MT in the management of FM.

3. Method

3.1. Protocol

The protocol for this review was registered at www.prospero.com (No.CRD42018091401).

3.2. Study eligibility criteria

Eligibility criteria followed the PICO format.

Population: defining the population as adults with a confirmed diagnosis based on the ARC criteria (Wolfe et al., 1990) ensured a more homogenous group of participants across studies. Intervention: presumed differences brought about by the mechanical properties of different MT styles were not the focus of this review, but rather the total dose of MT delivered to the participants, as a potentially biopsychosocial intervention. Therefore the intervention type was kept broad to incorporate any soft tissue MT. Soft tissue therapies delivered via machinery were excluded as the supposed psychological effects of human touch were absent. C-tactile (CT) afferents play a role in affective touch, and have the potential to create neurophysiological and psychological change. Only non-glabrous skin contains CT afferents, therefore MT to glabrous skin only (such as reflexology) was excluded. Control: recognising the limited numbers of studies investigating MT within FM, no limits were imposed on the control group criteria, to ensure sufficient articles for review. Outcomes: it is important to examine multidimensional aspects of FM symptomology to truly investigate therapeutic efficacy, therefore OMERACT domains were used.

3.3. Data sources

A computerized systematic literature search was performed searching; AMED, BNI, CINAHL, Medline, EMBASE, PsycINFO, PubMed, and PEDro (inception through January 2018). Only English texts were reviewed, no date restrictions were applied. Reference lists from studies which met the inclusion criteria, and systematic reviews were manually reviewed.

3.4. Electronic search strategy

A broad systematic approach was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). Relevant literature was identified using the terms 'fibromyalgia' and 'manual therapy' with multiple synonyms (Table 1.).

Table 1
Search strategy.

Population	Intervention
Fibromyalgia	Manual Therapy
FM	Physiotherapy
FMS	Physical therapy
Fibrositis	Touch
Pyschophysiologic disorder	Massage
Chronic multi-symptom* disorder	Manual manipulation
Chronic multi system* disorder	Light touch
Central sensitivity syndrome	Bowen
Myofascial pain	Rolfing
Somataform disorder	Connective tissue massage (CTM)
Functional somatic syndrome	Network spinal analysis (NSA)
Widespread pain disorder	Osteopathy
Bodily distress syndrome	Craniosacral therapy
	Feldenkrais
	Chiropractic
	Fascia*
	Myofascia*
	Myofascial release (MFR)
	Mobilisation
	Soft tissue

3.5. Study selection

All studies were scrutinized through their title and abstract. Potentially eligible texts were retrieved and evaluated; those selected were included for data extraction and synthesis.

3.6. Data collection

Data were extracted using an adapted form (Bettany-Saltikov, 2012).

Due to missing data and the need for clarification on elements of the published data, attempts were made to contact authors of five studies. Some authors were unable to provide original data, others did not respond to requests for information.

3.7. Study appraisal

The first author (SS) assessed methodological quality for each study using the PEDro (Physiotherapy Evidence Database) scale, a number of studies were cross checked by the second author (CK) for inter-rater reliability. The PEDro scale is based on a Delphi list (Verhagen et al., 1998) which uses 11 items to identify the internal validity of a study, and to indicate when a study may have sufficient statistical information to make their results interpretable.

PEDro scale scores range from one to ten points; with $\geq$6 representing a cut-off score for high quality studies (Maher et al., 2003).

3.8. Data analysis

Studies were ordered according to the total dose of MT provided over the trial, from the smallest (least time) to the largest (most time), and grouped according to the outcome measured. Where MT was used as the control, labelling of active and control was reversed in order to synthesise all MT study arms. Studies comparing two forms of MT where the dose of each MT differed, were reported twice, in order that each dose of MT was represented and analysed separately.

Effect size (ES) was calculated as a measure of the effectiveness of treatment, Hedge's *g* for between-group ES and Cohen's *d* for within-group ES (Social Science Statistics, 2019).Where a study used more than one measure to examine the same outcome, the results of the multiple measures were standardised and averaged in order to provide one ES per outcome. Effect sizes were standardised by reversal where necessary, in order that all positive figures demonstrated an improved outcome resulting from MT (e.g., a reduction in pain, or increase in function).

To visualise any dose response pattern across all core domains, within-group ES versus MT dose were displayed on a scattergraph. For studies reporting a range of treatment times (Ekici et al 2009, 2017), the mean dose was used, to avoid extreme values.

A narrative synthesis based on within, and between-group, comparisons was used for those studies where raw data was unavailable.

4. Results

4.1. Study selection

A total of 4012 studies were identified through database searches and other resources; following removal of duplicates and exclusions, a total of 12 studies met the inclusion criteria (Fig. 1).

4.2. Study characteristics

Table 3 summarises the characteristics of the included studies, along with a measure of methodological quality (PEDro scale). Sample sizes ranged from 12 to 92 participants. Six studies stated all participants were female (Ekici et al 2009, 2017; Castro-Sánchez et al., 2014; Sunshine et al., 1996; Liptan et al., 2013; Lund et al., 2006), three studies included samples with over 94% female participants (Yuan et al., 2013; Castro-Sánchez et al., 2011a; Matarán-Peñarrocha et al., 2011), one study had an approximately equal split of male and female participants (Castro-Sánchez et al., 2014), and two studies did not state the gender of participants (Field et al., 2002; Castro-Sánchez et al., 2011c).

Sixteen different clinical measures, and two different methods for assessing pain on palpation (PPT: Pressure Pain Thresholds, the minimum pressure required to induce a pain response & PTP: Painful Tender Point Count, number of painful regions on palpation) were used to assess the outcomes of interest. Four studies (Field et al., 2002; Sunshine et al., 1996; Lund et al., 2006; Castro-Sánchez et al., 2011b) included both clinical outcome measures and biomarker measures.

A range of MT interventions were used in the experimental groups. One study used MT as the control (Ekici et al., 2017), and two studies tested two forms of MT against one another (Ekici et al., 2009; Liptan et al., 2013). Control interventions used active, placebo, and no treatment options.

Methodological quality (PEDro scale) was classified as 'high' (scoring $\geq$ 6) for eleven of twelve studies.

4.3. Synthesis of results

Table 3 displays pre- and post-intervention scores, and within/between-group ES (Cohens *d* & Hedges *g* respectively). Figures were taken from the literature or calculated where possible. Studies were ordered according to the dose of MT delivered, from the smallest (least time) to the largest (most time), to look for evidence of a dose response.

Fig. 2 visualises the overall findings related to the question of evidencing a dose response relationship for all core domains.

4.4. Pain outcomes

Pain has always been the predominant target symptom for FM medicine, as it is the main source of suffering for the individual. No

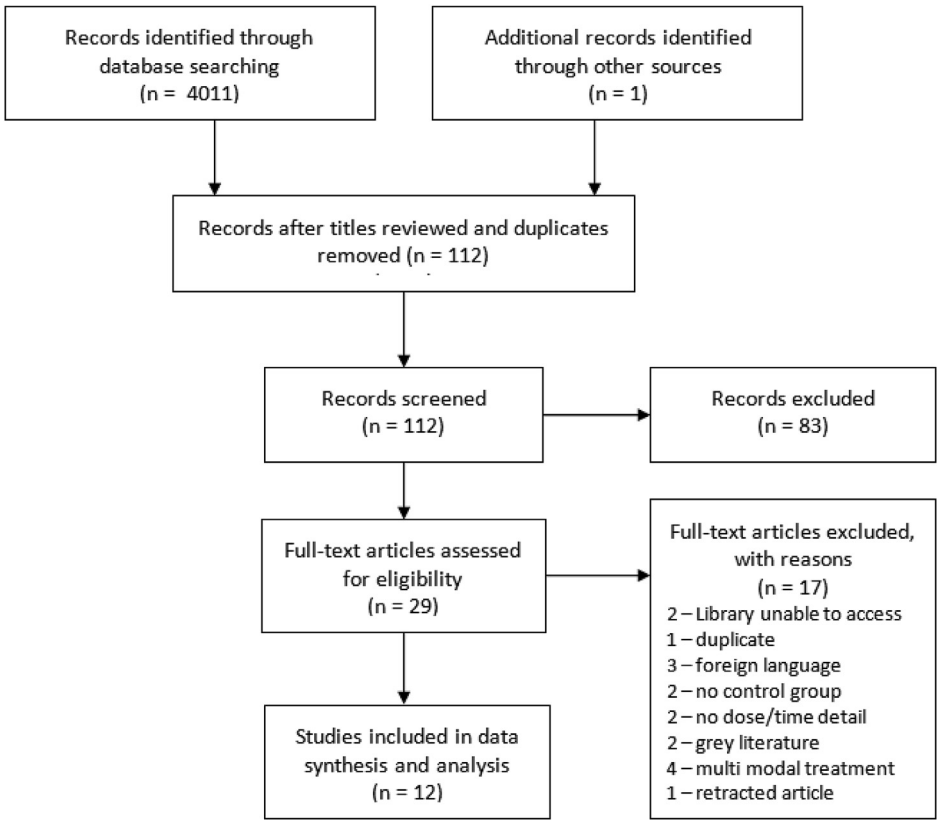

Fig. 1. Documentation of screening methods using PRISMA.

evidence was found of a linear, dose response between MT and pain scores amongst FM participants. Large within-group ESs were found from treatment durations ranging from between one and 4 h (Ekici et al., 2017) up to 13 h 20 min (Yuan et al., 2013).

Yuan et al. (2013) recorded the greatest between-group ES (1.51), however, relative treatment efficacy cannot be guaranteed as the control group was an inactive wait list.

Ekici et al. (2009**) recorded the greatest within-group ES (2.4), for their MLDT treatment group (11 h 15 min MT delivered). This ES was almost double their comparative CTM group (delivering; 1 h 15 min – 7 h 30 min).

Field et al. (2002) and Yuan et al. (2013) are the only two studies to present consistently large ESs for both within, and between-group results, suggesting a range of optimal dosing patterns, as being between 5 h and 13 h 20 min.

4.5. Mood outcomes

Low mood is a valuable therapeutic target for FM sufferers as a core domain of symptomatic treatment (Mease et al., 2009). Additionally, low mood can be a barrier to active engagement in behaviour change. Addressing low mood therefore, supports the overall self-management approach to FM. The data presented here suggests an optimal dose of 5 h MT, this dose being the only one to report a large within-group ES (0.92) (Field et al., 2002). In this study however, the overall between-group ES was small, due to data from two measures (STAI, and POMS) favouring the control group. The third measure used in this study (CES-D) recorded a statistically significant improvement for the massage group only; thereby creating an overall positive between-group ES. With all three mood measures amalgamated, the CES-D score alone was responsible for the positive between-group ES. In studies delivering more than 5 h MT, mood measures reported a number of scores which did not reach clinical or statistical significance. In contrast, the trials providing ≤5 h, recorded moderate within-group ES and statistically significant change.

4.6. Sleep outcomes

There is a strong association between sleep disturbance and FM, whether the association is one of causation or consequence is unknown. Therefore improved sleep is an important therapeutic target for FM sufferers. The results of this review did not identify a linear dose response between dose of MT and improvements to sleep. The largest within-group ESs are seen by two studies conducted by the same authors, however, they delivered the shortest and second to longest duration of treatment within this cluster (Ekici et al., 2017 = 1–4 h, & Ekici et al., 2009** = 11hrs 15). Different types of MT were delivered in these two studies, CTM and MLDT respectively. These studies provided the highest intensity of treatments per week, three and five times per week respectively, comparative to other trials within the cluster. Between-group ESs only reached positive significance in Yuan et al. (2013) study, however, relative treatment efficacy cannot be guaranteed as the control group was an inactive wait list.

4.7. Global Measure of Impact outcomes

Overall measure of disease impact is reflected by measures of multi-dimensional Functional Status and Health related Quality of life (HRQOL). Gold standard approaches to treatment are therefore required to have a positive impact in overall measures of function, and

Table 2
Summary of study characteristics; study type, participant details, 'manual therapy' intervention & delivery dose, control/comparator, quality score (PEDRo).

Study ID; Author(s) & Publication Date	Study Design	Participant Detail; Sample Size, Age, Gender	Interventions; Duration, Number and Frequency of Sessions, Total MT Treatment Time (dose)	Outcome Measures	PEDro Scale
Ekici et al. (2017)	RCT	Sample size: EG (PE) = 21, CG (CTM) = 22. Age: mean 37 yrs (SD 7yrs). Gender; all female	Pilates versus CTM. Pilates; 1 h class 3 x/ week for 4 weeks CTM; 5–20 min 3 x/ week for 4 weeks. Total MT dose: 1–4 h	Pain: PPT algometry and VAS. Sleep: NHP item Mood: STAI. GMI: NHP, FIQ. Other: nil	9
Ekici et al. (2009)* (First entry - CTM data used as experimental group)	RCT	Sample size: Exp = 25, Control = 25 Age range: >25 yrs, average 37.9 yrs. Gender: all female.	CTM versus MLDT CTM; 5min- 20 min session 5 x/week for 3 weeks Total dose CTM: 1hr 15 - 7hrs 30	Pain: PPT algometry and VAS Sleep: items within NHP Mood: nil GMI: FIQ, NHP Other: nil	7
Castro-Sánchez et al. (2014)	RCT	Sample size: EG = 45, CG = 44 Age range: 18 –70 yrs Gender: 54% female, 46% male	Manual therapy versus no treatment 45 min session 1 x/week, for 5 weeks Total MT dose: 3 h 45	Pain: PPT algometry – mean of three trials, over 20 tender points. McGill Pain Questionnaire: PRI, and PPI, VAS + Body chart. Sleep: PSQI Mood: CES-D GMI: FIQ Other: nil	9
Field et al. (2002)	RCT	Sample size: 20 Age range: average 50.9 yrs Gender: ?	Massage versus relaxation Massage: 30 min 2 x/week for 5 weeks Relaxation: 30 min 2 x/week for 5 weeks Total MT dose: 5 h	Pain; VAS, algometry over 18 sites Sleep; sleep log, timex motion recorder overnight Mood; STAI, POMS, CES-D GMI: nil Other; saliva samples for substance P	6
Sunshine et al. (1996)	RCT	Sample size: 30 Age range: 18–80 yrs Gender: all female	Massage versus TENS and sham TENS Massage: 30mins x 2/week for 5 weeks Controls: 30 min x 2/week for 5 weeks Total MT dose: 5 h	Pain: algometry on 18 tender points Sleep; interview Mood: STAI, POMS, CES-D GMI: interview on daily functioning. Other:salivary cortisol.	5
Liptan et al. (2013)	parallel study non randomised	Sample size: 12 Age range: 21–50 yrs Gender: all female	MFR versus SM MFR: 90 min session 1 x/ week for 4 weeks SM: 90 min session 1 x/week for 4 weeks Total MT dose: 6 h	Pain; localised pain measure – modified NMQ Sleep: nil Mood: nil GMI: FIQ R Other: nil	6
Lund et al. (2006)	RCT	Sample size: EG = 10, CG = 9 Age: mean = 50.7yrs (SD 9.7 yrs) Gender all female	Massage versus relaxation 30 min session 2 x/week for 6 weeks Total MT dose: 6 h	Pain: Swedish version of NHP Sleep: nil Mood: CRPS - A, NHP GMI: nil Other: HRV, Bp, 24 h urine samples for CRF-L1	6
Ekici et al. (2009)** (Second entry - MLDT data used as experimental group)	as above	as above	MLDT versus CTM MLDT; 45 min session 5 x/week for 3 weeks. Total dose MLDT: 11 h 15	as above	as above
Yuan et al. (2013)	Controlled pilot trial	Sample size: 40 - (20 per group) Age range: 30 –65 yrs Gender: 33 female, 1 male	Shiatsu versus home education booklet Shaitsu: 50 min 2 x/week for 8 weeks Control: wait listed for 8 weeks Total MT dose: 13 h 20	Pain: VAS, PPT on 18 points Sleep: PSQI Mood: STAI GMI: FIQ Other: nil	6
Castro-Sánchez et al. (2011a)	RCT	Sample size: EG = 30, CG = 29. Age range: 18 –65 yrs Gender: F:M EG = 94%:6% CG = 96%:4%	Massage-myofascial release therapy versus sham magnetotherapy. 90 min session 1 x/week for 20 weeks. Total MT dose: 30 h	Pain: VAS, algometry on 18 tender sites (painful y/ n at 4 kg). Sleep: PSQI. Mood: STAI, BDI GMI: SF-36 Other: nil	8
Castro-Sánchez et al. (2011b)	RCT	Sample size: EG = 46, CG = 46. Age range: 16 –65yrs. Gender: 100% female	CST versus sham magnetotherapy 1 h session 2 x/week for 20 weeks. Total MT dose: 40 h	Pain: pressure algometry on 18 tender sites. Sleep: nil Mood: nil GMI: CGI-S (researcher measured). CGI-I (patient rated) Other: HRV recorded by 24 h Holter monitoring.	9
Castro-Sánchez et al. (2011c)	Single blind clinical trial nested in an experimental study.	Sample size: EG = 45, CG = 41 Age range: 45 –65 yrs Gender: ?	MFR versus sham ultrasound and shortwave. 1 h session 2 x/week for 20 weeks. Total MT dose: 40hrs	Pain: algometry at 18 points. McGill pain questionnaire. Sleep: nil Mood: nil GMI: FIQ, CGI-S & CGI-I both patient rated. Other: postural stability.	9
Matarán-Peñarrocha et al., 2011	Experimental double-blind longitudinal clinical trial	Sample size: EG = 43, CG = 41 Age range: 34 –63 yrs Gender: 81 female, 3 male	CST versus sham Ultrasound CST: 1 h 2 x/week for 25 weeks Control: 30 min 2 x/week Total MT dose: 50hrs	Pain: VAS Sleep: PSQI Mood: BDI & STAI GMI: SF-36 Other: nil	6

OUTCOMES - PPT: Pressure point threshold; VAS: visual analogue scale; GMI: Global Measure of Impact; NHP: Nottingham Health Profile; STAI: State Trait Anxiety index; FIQ & FIQ R: Fibromyalgia Impact Questionnaire (R = revised); PSQI: Pittsburgh Sleep Quality Index; CES-D: Center for Epidemiological Studies Depression Scale; MPQ - PPI: McGill Pain Questionnaire - Present Pain Intensity; MPQ - PRI: McGill Pain Questionnaire - Present Rating Index; POMS: Profile of Mood States; NMQ: Nordic Musculoskeletal Questionnaire; CRPS-A: Comprehensive Psychopathological Rating Scale - Affective; HRV: Heart Rate Variability; BDI: Becks Depression Index; SF-36: Short Form Health Survey - 36; CGI-S: Clinical Global Impression of Severity; CGI-I: Clinical Global Measure of Improvement; CRF-L1: corticotropin releasing factor-like immunoreactivity. INTERVENTIONS - PE: Pilates Exercise; CTM: Connective Tissue Massage; MLDT: Manual Lymphatic Drainage; MFR: Myofascial Release; SM: Swedish Massage; CST: Cranial Sacral Therapy; TENS: Transcutaneous Nerve Stimulation RCT: Randomised Controlled Trial; EG: Experimental group; CG: Control Group; SD: Standard deviation.

HRQOL, to reduce the impact of FM. The results of this review did not identify a linear dose response between dose of MT and improvements to FM impact.

Within-group ESs were reported as large only in studies of ≤13 h 20 (Yuan et al., 2013). The greatest ES was recorded by the MLDT group in the Ekici et al. study (2009**) = (2.18). Between-group results show moderate ESs, although some study results favour the control intervention. Of the three studies delivering 30 h treatment or more, two studies; Castro-Sánchez et al. (2011a) and Matarán-Peñarrocha et al., 2011, report negative ES compared to the comparator. However, both studies appear to have inconsistencies in the reporting of the scores for the SF-36, which may confound the interpretation of their results.

Table 3
Within and between-group effect sizes by outcome domains.

Study	Outcome measure	MT GROUP			CONTROL GROUP			Within-group (MT) Effect Size (d)	Between-group Effect Size (g)	Narrative Comment
		Baseline: mean (SD)	Final: mean (SD)	N	Baseline: mean (SD)	Final: mean (SD)	N			
Pain Outcomes										
Ekici et al. (2017)	PPT R	1.51 (0.46)	2.30 (0.76)	21	1.43 (0.30)	2.75 (0.52)	15	1.38	−0.53	VAS; Both groups experienced significant improvements (P = > .05), both groups also showed improvements in PPT.
	PPT L	1.64 (0.55)	2.47 (0.90)		1.53 (0.34)	3.03 (0.61)				
	VAS	6.62 (2.45)	2.53 (2.16)		8.75 (0.91)	2.15 (0.90)				
Ekici et al. (2009)*	PPT R	1.64 (0.56)	2.41 (0.74)		1.68 (0.57)	2.82 (0.72)	25	1.25	−0.51	Both treatments led to significant improvements (P < .05) in pain, CTM improvements were smaller and with a greater SD than for MLDT. No baseline statistical difference in pain measures were reported between groups.
	PPT L	1.91 (0.94)	2.66 (1.04)		1.66 (0.47)	2.95 (0.78)				
	VAS	6.52 (2.29)	2.59 (2.05)		6.98 (1.91)	1.49 (1.19)				
Castro-Sánchez et al. (2014)	MPQ PPI	2.25	1.7	45	2.4	2.35	44	0.72	–	MT was effective in achieving statistically significant improvements in; pain intensity, TPC, PPT. Sex differences were observed, women responded more than men in impact of FM and pain, men showed a greater decrease in depression and PPT than women, similar improvements were seen in sleep and tender point count. Effect sizes taken directly from article.
	MPQ PRI	40.05	33.8		39.75	39.55				
	VAS	7.7	6.5		8	7.5				
	TPC (20)	15.8	–		15.9	–				
	PPT (kPa)	343.21	440.92		385.7	387.8				
Field et al. (2002)	TPC (18)	15.4 (1.7)	10.5 (6.1)	10	16.1 (2.2)	14.6 (4)	10	0.92	0.84	TPC and VAS reduced significantly (P < .005 and P < .001 respectively), with no significant reduction in control group.
	VAS	6.0 (3.2)	3.7 (2.9)		7.7 (1.6)	6.3 (3)				
Sunshine et al. (1996)	VAS	8.6	5.3	10	8.15	7.25	10	–	–	No SD data available, therefore effect size could not be calculated. The MT group alone reported significant improvements in self reported pain, and pain threshold. Two control groups were compared, active electrotherapy and sham. Results from both groups were combined, and mean values were used for the purpose of analysis.
	PPT (kg)	3.4	4.5		2.85	3.35				
Liptan et al. (2013)	modified NMQ	–	–	6	–	–	6	–	–	No raw data available. Aicken separation test indicated further research is needed to compare MFR and swedish massage, both treatments were well tolerated, and effective, with no significant difference between them. The study suggests that MFR may result in greater reductions in pain. Parallel design attempted to reduce confounding influence of placebo. NMQ; scores improved in both groups.
Lund et al. (2006)	NHP	–	–	10	–	–	6	–	–	No raw data available. Less indications of pain post treatment reported by; 1/10 participants in the MT group and 3/6 in the relaxation group. One month after intervention, 4/10 in the MT group & 2/6 in relaxation group, report less pain.
Ekici et al. (2009) **	PPT R	1.68 (0.57)	2.82 (0.72)	25	1.64 (0.56)	2.41 (0.74)	25	2.4	0.51	Both treatments led to significant improvements (P < .05) in pain. The decrease in VAS resulting from MLDT indicates high clinical significance.
	PPT L	1.66 (0.47)	2.95 (0.78)		1.91 (0.94)	2.66 (1.04)				
	VAS	6.98 (1.91)	1.49 (1.19)		6.52 (2.29)	2.59 (2.05)				
Yuan et al. (2013)	VAS	7.2 (2.3)	5.1 (2.5)	17	6.4 (1.1)	7.1 (1.8)	17	0.83	1.51	MT group: 40.6% change in VAS pre-post; clinically significant relative to control group
	PPT - (kg)	0.8 (0.4)	1.2 (0.6)		0.8 (0.4)	0.6 (0.4)				MT group: 76.4% change in PPT pre-post; clinically significant relative to control group
Castro-Sánchez et al. (2011a)	VAS	–	–	30	–	–	29	–	–	No raw data available. MT group: significant improvement (P < .43) in pain versus baseline & control group. Results illustrations suggest mean decrease of just over 10 mm on VAS post intervention.
	PTP	14.4	7.9		18.4	18.5				No SD available. Reduced numbers of patients reporting painful tender points at all 18 sites in MT group; statistically significant reduction in 8/18 tender points. No change in control group.
Castro-Sánchez et al. (2011b)	PTP	36.1	27.9	46	35.6	35.4	46	–	–	No SD available. Significant decrease in number of patients with tender points at 13/18 tender point sites versus baseline, and control group.
	MPQ VAS	9.13 (0.8)	7.98 (1.03)	45	8.9 (1.3)	8.87 (1.01)	41	0.6	0.64	Significant improvement in mean pain score versus baseline (F = 6.19, P < .026).

Castro-Sánchez et al. (2011c)	MPQ - sensory	19.3 (9.2)	16.5 (8.6)		19.9 (10.6)	20.3 (6.5)				Significant improvement in mean score versus baseline ($F = 3.21$, $P < .041$).
	MPQ - affective	5.6 (3.4)	4.2 (3.4)		4.9 (4.2)	5.3 (4.1)				Significant improvement in mean score versus baseline ($F = 5.29$, $P < .031$).
	MPQ - evaluative	24.9 (12.6)	20.6 (6.3)		25.3 (10.7)	25.9 (5.3)				Signifcant improvement in mean score versus baseline ($F = 5.44$, $P < .032$).
	PTP	32.4	24.8		32.3	32.5				Significant decrease in number of tender points versus baseline in 7 of 18 tender points. No change in control group
Matarán-Peñarrocha et al. (2011)	VAS	9.13	8.18	43	8.9	8.88	41	–	–	No SD available. Significant improvement versus baseline ($P < .035$), and versus control ($P < .041$)
Mood Outcomes										
Ekici et al. (2017)	STAI - state	48.33 (12.56)	41.81 (12.50)	21	47.73 (10.67)	32.33 (7.25)	15	0.51	−0.49	Both groups experienced improvement in pre-post scores for State and Trait anxiety. Pilates improvement was significantly greater ($P = .008$) in State anxiety than CTM.
	STAI - Trait	50.71 (10.63)	46.05 (7.55)		55.07 (10.63)	45.33 (7.95)				
Castro-Sánchez et al. (2014)	CES-D	23.7 (8.3)	18.8	45	25.9 (6.9)	26.15	44	0.69	–	2×2 mixed ANCOVA indicates significant group $\times$ time interactions for mood $P = < 0.001$ with those in the MT group achieving better outcomes than the control. Effect Size taken from article, pressumed to be within group Effect Size, unable to check calculations as no SD available.
Field T et al., 2002	CES-D	18.0 (9.2)	12.3 (9.5)	10	17.7 (8.7)	17.1 (5.3)	10	0.92	0.05	STAI and POMS were measured before and after interventions on the first and last days; immediate and significant improvements were reported in both measures, both time points for both groups, favouring relaxation slightly. Only the CES-D reported a significant ($P < .05$) improvement in the massage group.
	STAI	43.7 (9.5)	31.1 (11.2)		41.9 (8.5)	29.2 (6.7)				
	POMS	10.0 (9.9)	2.8 (4.5)		11.0 (9.2)	1.8 (3.2)				
Sunshine et al. (1996)	STAI	45.4	34.1	10	47.2	35.3	10	–	–	STAI and POMS were measured before and after interventions on the first and last days; immediate and significant improvements were reported in both measures, at both time points for the experimental group. The control groups experienced smaller improvements and in the sham TENS some outcomes worsenend. The improvements in CES-D outcomes did not reach significance. No SD data available, therefore Effect Size could not be calculated.
	POMS	17.3	12		17.25	12.75				
	CES -D	31.9	26.8		31.8	28.6				
Lund et al. (2006)	CRPS-A NHP	–	–		–	–		–	–	No raw data. Non-zero RP value indicates there was a group wide systemic post intervention improvement in CRPS dimensions following massage ($P = .02$), the group change was reduced one month post treatment, and individual variation was increased. NHP showed reduced emotional reactions in 6/10 massage, 3/6 relaxation group, 1 month after intervention 6/10 massage, 1/6 control group reported reduced reactions.
Yuan et al. (2013)	STAI - S	53.9 (8.4)	48 (10)	17	55.5 (11.2)	52.1 (11.3)	17	0.58	0.31	STAI-S: 4.62% decrease pre-post, not clinically or statistically different vs control group
	STAI - T	57.9 (9.4)	53.1 (9.1)		52.9 (11.6)	55.5 (12)				STAI-T: 13.22% decrease pre-post not clincally significant, but statistically different vs control group.
Castro-Sánchez et al. (2011a)	STAI	–	–		–	–		–	–	STAI: No mean/SD data. Significant improvement in trait anxiety reported ($p = < .041$) vs baseline & control. No change in state anxiety.
	BDI	–	–		–	–				BDI: No mean/SD data. No change reported in either group vs baseline.
Matarán-Peñarrocha et al. (2011)	BDI	2.52	2.08	43	2.5	2.52	41	–	–	No sig diff between groups or versus baseline
	STAI - state	23.32	20.53		22.28	24.43				$P < .029$ sig difference in MT versus baseline
	STAI- trait	26.88	25		26.15	26.7				$P < .042$ sig difference in MT versus baseline. Significant difference between group $P < .045$.
Sleep Outcomes										
Ekici et al. (2017)	NHP—S	28.24 (27.49)	5.22 (8.80)	21	37.44 (30.92)	6.95 (8.01)	15	1.13	0.2	Both groups reported an improvement ($P = > .05$) = small between group Effect Size
Ekici et al. (2009)*	NHP item	27.72 (30.72)	4.38 (8.26)	25	35.89 (29.82)	4.44 (8.66)	25	1.04	0.01	Both groups experienced significant ($P < .05$) improvements. Between group final Effect Size shows little difference, favouring CTM. Variance in baseline figures, shows a greater reduction in 2nd (MLDT) group.
Castro-Sánchez et al. (2014)	PSQI (0—21)	16.9 (3.3)	14.55	45	16.9 (4.2)	16.6	44	0.72	–	No SD was available, Effect Sizes were reported in the study. 2×2 mixed ANCOVA indicates significant group $\times$ time interactions for sleep ($P = < 0.001$) with those in the MT group achieving better outcomes than the control. No significant interaction of gender on outcomes.
Field et al. (2002)	sleep hours	5.8 (1.1)	6.4 (1.1)	10	5.6 (1.3)	6.2 (.8)	10	0.44	0	The experimental group recorded a significant reduction in recorded movements and increased hours of sleep versus baseline. The final sleep movements recorded for the experimental group remain higher
	sleep movements									

(*continued on next page*)

Table 3 (*continued*)

Study	Outcome measure	MT GROUP			CONTROL GROUP			Within-group (MT) Effect Size (d)	Between-group Effect Size (g)	Narrative Comment
		Baseline: mean (SD)	Final: mean (SD)	N	Baseline: mean (SD)	Final: mean (SD)	N			
Pain Outcomes										
		101.3 (57.5)	83.3 (52.8)		86.1 (45.5)	74.6 (24.8)				than the control group which affects the Effect Size, however they experienced a larger decrease from baseline.
Sunshine et al. (1996)	self report - number of nights with sleep difficulties	6.1	3.4	10	4.65	4.1	10	–	–	The massage group only reported a significant reduction (P = .005) in nights of sleep disturbance.
Ekici et al. (2009)**	NHP item	35.89 (29.82)	4.44 (8.66)	25	27.72 (30.72)	4.38 (8.26)	25	1.43	−0.01	Both groups experienced significant (P < .05) improvements. Between group final Effect Size shows little difference, with a negative Effect Size with MLDT as Exp group. Variance in baseline figures, shows a greater reduction in 1st (MLDT) group.
Yuan et al. (2013)	PSQI (0–21)	12.0 (4.0)	8.1 (5.2)	17	11.9 (4.7)	12.1 (4.3)	17	0.84	0.84	MT group: 34.4% change in PSQI pre-post; clinically significant relative to control group
Castro-Sánchez et al. (2011a)	PSQI	–	–		–	–		–	–	No means or SD. MT group showed significant improvement vs baseline in sleep latency (p = <.041) and sleep duration (p = <.039), no other items recorded significant findings, no changes recorded in control group.
Matarán-Peñarrocha et al. (2011)	PSQI (0–21)	–	–	43	–	–	41	–	–	No means or SD. MT group had significant improvement in total score P < .043, with significant difference in items for sleep duration and sleep disturbance vs control group.
Global Measure of Impact										
Ekici et al. (2017)	NHP	212.73 (124.5)	80.79 (64.73)	21	294.25 (90.21)	69.03 (38.34)	15	1.39	−0.4	Significant reductions were seen in both groups on both measures (FIQ: P = .001). Within each measure, sub items favoured Pilates or CTM. FIQ items: 'work missed' and 'physical impairment', were the only improvements to not reach significance for CTM group.
	FIQ	50.20 (22.46)	28.68 (14.22)	21	55.12 (10.07)	22.12 (4.58)	15			
Ekici et al. (2009)*	NHP	201.22 (129.16)	76.89 (63.21)	25	198.95 (96.63)	52.93 (31.61)	25	1.21	−0.67	Both treatment groups led to significant improvements in NHP & FIQ.
	FIQ	49.51 (20.99)	28.55 (13.46)		47.81 (15.59)	18.88 (8.30)				
Castro-Sánchez et al. (2014)	FIQ	66.7	56.65	45	67.6	66.75	44	0.87	–	No SD available; Effect Size data taken from article. MT had a significant effect on impact post treatment. Women had greater Effect Size on FIQ than men (W = 1.09, M = 0.64).
Liptan et al. (2013)	FIQ-R	–	–		–	–		–	–	Aickin separation test indicted change score trended in the hypothesised direction (favoured MFR over SM), MFR group (mean = 10.14, SD = 16.2) SM group (mean = 0.33, SD = 4.93). Between group difference was not significant. 5/8 subjects in MFR group reported clinically significant improvement (1/8 of SM group reached significance), 3/8 = >30% reduction in score (14% reduction is rated as clinically significant).
Ekici et al. (2009)**	NHP	198.95 (96.63)	52.93 (31.61)	25	201.22 (129.16)	76.89 (63.21)	25	2.18	0.67	MLDT led to statistically significant improvements in FIQ (p = .010) versus CTM.
	FIQ	47.81 (15.59)	18.88 (8.30)		49.51 (20.99)	28.55 (13.46)				
Yuan et al. (2013)	FIQ	66.7 (18.8)	48.2 (20.4)	17	65.2 (16.1)	61.4 (17.8)	17	0.94	0.69	MT group: 22.30% change pre-post; clinically significant relative to control
Castro-Sánchez et al. (2011a)	SF-36 physical function	5.23 (5.36)	46.72 (6.71)	30	50.24 (8.47)	51.03 (8.24)	29	0.63	−0.36	The results section reports significant improvement versus baseline in; physical function p = < .007, physical role p= < .039, body pain p = < .043, and social function p = <.048, and no changes within control group. However, results Table 4 shows reduced scores for the MT group (lower scores reflect decreased quality of life and more disability). Figures given in the results section state the baseline score for physical function in the experimental group was 5.23, this number appears very different from the other results figures and may be an error; calculated Effect Size figures may therefore be unreliable.
	SF-36 physical role	25.97 (7.32)	22.91 (7.15)		26.36 (6.25)	26.32 (6.29)				
	SF-36 body pain	76.56 (6.31)	73.93 (8.21)		78.93 (11.43)	77.54 (11.63)				
	SF-36 general health	67.82 (5.21)	65.20 (5.43)		68.78 (7.22)	69.85 (6.24)				
	SF-36 vitality	60.85 (6.41)	63.53 (8.17)		59.42 (5.32)	59.99 (9.41)				
	SF-36 social function	64.03 (8.03)	59.55 (4.22)		64.43 (13.22)	64.03 (10.15)				

	SF-36 emot' role	48.98 (8.13)	46.42 (11.32)	46.55 (7.32)	47.74 (9.26)					
	SF-36 mental health	77.45 (12.31)	78.27 (10.22)	81.10 (1.29)	82.02 (11.67)					
Castro-Sánchez et al. (2011c)	FIQ spanish version	64.95 (18.2)	56.10 (17.3)	45 63.94 (16.4)	65.85 (18.5)	41 0.5	0.54		The FIQ total score showed significant improvement vs baseline in the MT group; CG reported no change. The pain item on the FIQ achieved the highest level of significance (F = 6.95, P < .021)	
Matarán-Peñarrocha et al. (2011)	SF-36 physical function	49.43 (6.90)	45.90 (5.87)	43 51.90 (9.92)	50.53 (9.12)	41 −0.4	−0.37		The results section describes significant improvements for the MT group in: physical function, ($p < .024$), physical role ($p < .020$), body pain ($p < .043$), general health ($p < .039$), vitality ($p < .041$), and social function ($p < .029$). However, Results Table 2 shows lower post intervention scores, (lower scores on SF-36 indicate decreased quality of life and more disability). These items also recorded significant differences between the 2 groups, with the control group not achieving significant change versus baseline. Effect Size figures may therefore be unreliable.	
	SF-36 physical role	25.17 (6.88)	22.10 (6.84)	25.86 (7.35)	25.8 (6.98)					
	SF-36 body pain	75.76 (7.2)	73.12 (6.08)	78.43 (12.75)	78 (13.07)					
	SF-36 general health	67.02 (4.25)	64.40 (4.65)	68.28 (6.84)	68.35 (6.39)					
	SF-36 vitality	60.05 (5.23)	62.73 (5.27)	58.90 (6.27)	59.48 (7.73)					
	SF-36 social function	63.23 (7.12)	58.75 (6.74)	63.93 (12.41)	63.50 (11.57)					
	SF-36 emot' role	49.18 (7.65)	45.60 (7.85)	46.35 (5.69)	47.23 (5.66)					
	SF-36 mental health	76.65 (11.23)	77.48 (8.73)	80.60 (9.66)	81.15 (10.42)					

Fig. 2. Within-group effect size versus dose (MT treatment time).

5. Discussion

This systematic review follows on from recent reviews (Li et al., 2014; Yuan et al., 2015; Terhorst et al., 2011; Kalichman, 2010; Terry et al., 2012) looking at efficacy, and uniquely uses the literature to search for any evidence of a dose response relationship for optimal doses of MT. This is an important enquiry as current clinical guidelines offer no support for the use of MT, in contrast to reported patient preference (Wahner-Roedler et al., 2005). Also, current approaches to FM fail to achieve significant and lasting clinical improvements (Thieme et al., 2017) therefore further developments are necessary.

This review has identified four important contributions to the study of the role of MT within the care of patients with FM, by looking at the question of dose.

Firstly; this review has identified a paucity of contemporary research in this area of MT and FM. The review did not identify a large evidence base, nor any new literature within the field since previous systematic reviews. The criticism of MT as 'unworthy and passive' (Randell, 1992), and therefore not consistent with the approach of active self management, has changed clinical practise as governed by guidelines. Neglecting to continue with significant, contemporary research into this area, has prevented detailed assessment of MT's potential clinical utility.

Secondly; this review has suggested a lack of systematic dosing of MT as a potential consideration for the current lack of supportive evidence from recent systematic reviews and guidelines. The range of treatment protocols used within the studies reviewed varied greatly. Previous systematic reviews looking only for evidence of treatment efficacy have aggregated the effects from several studies; however the lack of precision of included studies due to different doses could distort the interpretation or 'skew the results' as suggested by Walden (2015), thus masking the potential efficacy of correctly dosed MT.

Of the twelve articles reviewed, five were produced by the same research team (Castro-Sánchez et al., 2014, 2011a; 2011b, 2011c; Matarán-Peñarrocha et al., 2011), two were conducted by Ekici et al., and two were conducted by the Touch Research Institute (Field et al., 2002; Sunshine et al., 1996). Patterns seen within ESs were clustered according to authors, despite differing treatment doses used. This could suggest other moderators, such as trial methodology and MT type, are also meaningful in the final results analysis. All studies were penalised on quality assessment (PEDro scale) due to lack of blinding of participants and therapists. However, this is to be expected due to the nature of MT interventions, where neither participant nor therapist can be blinded. Allocation was not reported as concealed in six of the included studies; of these, three studies; Ekici et al., (2009), Field et al., (2002) and Yuan

et al., (2013), frequently report greater ESs than other trials under each outcome. It is therefore feasible that this weakness in randomisation could have contributed to exaggerated results. No other trends were seen correlating the quality of the study with ESs.

Thirdly; MT has been shown to be effective through measures of ES. This review did not provide sufficient data to identify, or refute the concept of a linear dose response relationship. However the use of ES figures for four of the main clinically important domains, supports MT as an effective therapy.

Within the cluster of studies measuring pain, five out of seven achieved large within-group ESs. Of the two studies with only moderate ESs, Castro-Sánchez et al. (2011c) provided a significantly larger dose of MT, thereby suggesting this extended protocol did not enhance outcomes. Castro-Sánchez et al. (2014) scored only a moderate ES, despite MT being compared to no treatment. However this trial differed from every other trial in the review as fifty percent of its participants were male; a tentative suggestion could be made that gender differences influenced the study results, and should therefore be considered in deciding on optimal dose and treatment expectations.

Effect sizes for measures of mood present a more linear response. Increasing ESs are seen as treatment doses rise from 1 h to 5 h, and then drop to moderate ES, with the longest protocol of 13 h 20 min. However, in their discussion, Lund et al. (2006), suggest their results identified individual responses to treatment confirmed by measure of Relative Rank Variance (RV). Different subgroups of people, with different affect symptoms were thought to respond differently. This lends further support to the concept identified through pain measure analysis, that individual variations must be considered in planning doses for optimal outcomes.

Effect sizes for measures of sleep do not present a consistent dose response pattern, however the highest ES was detected with Ekici et al.'s study (2009**). This study delivered MT five times per week, and both MT treatment arms achieved ESs greater than one. The only other study to achieve an ES of greater than one was Ekici et al. (2017) which delivered MT three times per week. All other studies did not reach an ES of one, and had less frequent MT sessions per week. A tentative suggestion could therefore be made; if the focus of treatment is to improve sleep, the frequency parameter may be critical, thus increasing the frequency may lead to improved outcomes.

Looking at the domain of overall FM impact, this review has identified a trend for the lesser dosage studies ($\leq$13 h 20 min) achieving larger ESs. As was found with the other clinical domains, the more intense dosage patterns provided the greater ESs, with the optimal dose being 45 min, five times per week for three weeks (Ekici et al., 2009**). As the dose becomes extended over a longer period, 20–25 weeks, for the final three studies in this cluster, ES drops. These studies provided longer individual sessions, and a greater total amount of MT compared with the more successful studies, however they failed to increase outcomes. They were delivered once or twice weekly which mirrors two of the studies found in the highly effective cluster, and therefore this weekly frequency cannot be claimed to be suboptimal. Myofascial Release (MFR) and Cranio Sacral Therapy (CST) were the interventions delivered in these, less effective trials, therefore it could be suggested that the decrease in efficacy relates to the chosen intervention rather than the dosage pattern. With the exceptions of Ekici et al. (2009) and Liptan et al. (2013), no other trials have compared different forms of MT, and therefore this suggestion cannot be further explored within the current literature. The trends seen within this review identify Ekici et al. (2009**) as generating higher than average ESs across the domains, thereby suggesting MLDTs comparative effectiveness against other MT interventions.

Considering the more immediate and short term results from MT across pain, sleep, and mood, there would be an expected improvement in quality of life as an individual's perspective becomes more positive. This outcome would be best captured through qualitative studies, which was outside the scope of this review. This review suggests the biopsychosocial integration of MTs effects leading to a decreased impact of disease. However, as a stand-alone intervention, the impact starts to reduce over time. Gold standard approaches for FM are currently multidisciplinary, due to the multidimensional nature of the illness process. Therefore the role for correctly dosed MT interventions may be to prepare appropriate patients bio-pyscho-socially, as part of an integrated approach, and should not be assessed as single intervention, for long term change.

By combining the results and discussion points from each domain, it is possible to tentatively suggest a baseline dose of 45 min MT, three to five times per week, for three to five weeks, totalling 11.15 h, as a generic protocol for treatment planning with further refinement of a personalised dose (Díaz-Rodríguez et al., 2016), dependant on gender and affect. Finally, outcomes oriented dose parameters, either as a single intervention for a single domain, or as an integrated part of a multidisciplinary self management program, may need to be set. This protocol moves beyond the earlier recommendation by Li et al. (2014) meta analysis concluding that MT of $\geq$5 weeks achieved beneficial effects for FM patients.

This recommended protocol raises challenges for health care provision, such as financial and staffing implications which would need to be considered. In a climate where multidisciplinary staffing is already reported as insufficient in many pain services throughout the UK (Price et al., 2018); increased levels of staffing and potentially an extended skill mix would be required. Increased patient contact time would require additional funding, at a time when the sustainability of healthcare is already under scrutiny. Currently, self-management programs are able to provide cost efficiencies due to large numbers of patients being seen simultaneously. Costs would therefore be seen to increase in the short term with the addition of this protocol. However, these costs could be met by longer term decreases in healthcare utilisation amongst FM patients, as a result of improved clinical outcomes.

Whilst the evidence suggests potential predicators for good responders to treatment; these identifiers would need to be established in order to work with low 'numbers needed to treat' (NNT), to guarantee cost, and clinical effectiveness.

The biggest implication of all could be seen by some, as a move back towards medicalisation of FM, and the 'passive recipient of medicine' model of healthcare. The NHS 5 Year Forward View (2014) puts forwards the issue of sustainability for the NHS. Long term conditions, rather than illnesses susceptible to a 'one-off cure', are suggested as areas where prevention, and supported self-management, should be the approach of choice.

Identifying when and where a treatment intervention would fit within the over arching self-management approach, would require clear rationales, patient specific guidelines, and outcome measures; to ensure efficacy, and cost effectiveness.

The fourth contribution made by this review is to describe the reasons used for dose selection, and the consideration for dosage parameters that are found in the current literature.

The reviewed articles each described the mechanical effects proposed to be the active ingredient within MT. Central effects; cortisol reduction, immune and neuroendocrine enhancement, increased serotonin, psychological shifts, stimulation of endogenous opioids, and peripheral effects; increased circulation, decreased muscle tension, increased oxygenation of tissues, reduction of fibrous adhesions, were proposed. Only three studies attempted a discussion related to the rationale for the dosage of MT used. Castro-Sánchez et al. (2011c) described testing an increased

dose as a development on previously conducted research. In their discussion they stated that by increasing from once, to twice-weekly treatments, there were improvements in pain, sensory and affective dimensions. Ekici et al. (2009) described how each dose/session of connective tissue massage was determined by patient experience, and observed vascular skin changes during the treatment. This form of person centred, subjective approach to dose did not provide greater results against the comparator treatment, and therefore did not support tailoring dose in this way. Liptan et al. (2013) described testing a 'low dose' based on the therapist's clinical experience, and to enhance patient acceptability; all studies showed high levels of patient acceptability for MT through low drop out figures, and therefore this rationale for a low dose appears unsupported. The limited explanation of the rationale behind MT dosages, indicates that this concept is not routinely considered when trialling MT interventions.

Moyer et al. (2004) meta-analysis for massage therapy research, comments on the limited evidence for 'body-as-machine' rationales (pain gate stimulation, circulatory effects) for the application of MT, and suggested the notion of MT as a comparable intervention to psychotherapy. Using a somatic psychotherapeutic paradigm for understanding the therapeutic action of MT, led to the suggestion that perspectives gained from psychotherapeutic research should be applied to future MT trials. Psychotherapy literature also lacks a clear protocol of optimal dose, however there is a general consensus that 13–18 sessions are required to help 50% of patients (Hansen et al., 2006).

Kalichman, in his 2010 review, recommended future studies should not only look at physiological and psychological effects but also the evidence for how these effects come about. Four of the included studies (Field et al., 2002; Sunshine et al., 1996; Lund et al., 2006; Castro-Sánchez et al., 2011b) included both clinical outcome measures and physiological mechanisms measures.

Insufficient numbers of studies analysed the same biomarkers, therefore the question of optimal dose could not be explored through physiological markers within this review.

Other literature has commented on possible optimal doses when considering MT; Brattberg (1999) stated the analgesic effect of Connective Tissue Massage (CTM) appeared gradually with the first 15 treatments. Of those successful studies within the pain domain, the only one (Castro-Sánchez et al., 2014) to drop below a large ES, delivered only five treatments, the others in the cluster delivered 10–16, consistent with Brattberg's suggestion. Sailer et al. (2016) showed functional connectivity of brain regions changed throughout a 40 min session of slow stroking, with increasing activation in brain reward centres during the first 20 min. These numbers reflect the timings found in the most effective trials within this review from Ekici et al. (2017) being the shortest only just reaching 20 min, and Yuan et al. (2013) at 50 min. This could indicate changes in functional brain connectivity, as an important component of therapeutic change, and therefore a longer dose of treatment would be unnecessary. Rapaport et al. (2012) showed that in healthy individuals the dosage and frequency of light touch, and in particular massage, increased its efficacy, with twice a week treatments having a far longer lasting and more effective biologic activity than once weekly. Kalichman (2010) also noted in his review that all successful studies used a MT intervention once to twice per week. This review added to the evidence of increased frequency creating improved outcomes. The two studies showing the greatest ESs across domains provided the most frequent treatments per week; Ekici et al. (2009 & 2017) providing five and three sessions per week respectively.

Moving away from the biomechanical explanatory model for MT, research has provided the notion of MT as an 'interoceptive generator' driving neuroaffective processes of physiological self regulation (Courtois et al., 2015; Calsius et al., 2016; LaPierre, 2003). This perspective positions MT as an appropriate therapeutic tool for the proposed lack of neurodevelopmental self soothing systems, thought to be a risk factor for development of FM (Low and Schweinhardt, 2011). In order to assess outcomes or change along these lines of enquiry, qualitative data would provide a more valuable resource. No qualitative or mixed methods studies were included in the review. Dupuis (2015) however, reported that following one session of fasciatherapy, FM patients stated their symptom relief was 'very important in improving the relationship they had with their body, and reassessing their lifestyle'. Mooney (2015), reported changes in attitude and awareness that enabled FM patients to feel less helpless and more capable of choosing optimal personal treatment plans, following an established protocol of Medical Massage (12 sessions of 40–60 min).

These qualitative changes in patients' perceptions and readiness for change could indicate a powerful therapeutic outcome of MT, but again, the question of dose was not discussed in these studies. A change in perception, body awareness, and readiness for change, suggests MT could be a useful adjunct to multi-modal approaches, however no studies were found in this review exploring MT as an adjunct to usual care. Celenay et al. (2017) did demonstrate a MT intervention of 5–20 min twice per week for six weeks, as an adjunct to exercise therapy. Their results showed significantly increased beneficial effects on pain, sleep and fatigue outcomes with the addition of MT.

5.1. Limitations

Combining of different styles of MT, and having a wide inclusion for control groups is a limitation in this study. Tighter restrictions would have created more focus on the dose being the only variable; however tighter restrictions of the original search would have resulted in insufficient numbers of articles to analyse. The response to MT is likely to occur on many bio-psychosocial levels, and therefore the variety of styles of intervention may be of lesser importance when answering a question of dose.

Due to heterogeneity of outcomes used, and lack of raw data, data analysis was not possible for all the included studies, therefore limiting the data available for observing trends of any dose response relationship.

6. Conclusion

This review did not identify a linear dose response relationship using the current literature, however it presents the current evidence base in such a way as to highlight the moderate and large ESs associated with a variety of MTs. It provides a tentative formulae for MT delivery; 45 min, three to five times per week, lasting three to five weeks, and an overall dose of approximately 11.15 h; with the clear mandate to further define a stratified approach to MT use, under certain conditions and for certain patients.

An unintentional result of this review was to identify a paradigm shift in the explanatory model for MT away from biomechanical, and towards neuroaffective physio-psychologic (Field, 2014). This calls for a more holistic way of assessing effect, thereby indicating the need for mixed methods research approach.

Viewing MT from this new perspective, could redefine MT as an intervention which is not in conflict with the self-management approach, but could be used as an adjunct. By facilitating a physiopsychological change, FM patients may be enabled to participate more fully in active approaches to self-management. MT would therefore need to be assessed as an adjunct to normal care, rather than as a stand-alone intervention.

By analysing the data in this way, the overall suggestion is one of treatment utility under many clinical outcomes, with the need to refine dosing parameters dependant on individual patient characteristics such as gender and affect, and potentially to become outcome specific.

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Author agreement

I certify that all authors have seen and approved the final version of this manuscript being submitted. The article is the authors'.

Declaration of competing interest

None.

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References

Ablin, J., Fitzcharles, M., Buskila, D., Shir, Y., Sommer, C., Häuser, W., 2013. Treatment of fibromyalgia syndrome: recommendations of recent evidence-based interdisciplinary guidelines with special emphasis on complementary and alternative therapies. Evid. Based Compl. Altern. Med. https://doi.org/10.1155/2013/485272. Article ID 485272, 7 pages.

Bettany-Saltikov, 2012. How to Do a Systematic Literature Review in Nursing: a Step-by-step Guide: A Step-by-step Guide. Open University Press, Berkshire.

Bialosky, J.E., Bishop, M.D., Price, D.D., Robinson, M.E., George, S.Z., 2009. The mechanisms of manual therapy in the treatment of musculoskeletal pain: a comprehensive model. Man. Ther. 14 (5), 531–538. https://doi.org/10.1016/j.math.2008.09.001.

Brattberg, G., 1999. Connective tissue massage in the treatment of fibromyalgia. Eur. J. Pain 3, 235–244. https://doi.org/10.1016/S10903801(99)90050-2.

Calsius, J., De Bie, J., Hertogen, R., Meesen, R., 2016. Touching the lived body in patients with medicaally uneplained symptoms. How an integration of hands-on bodywork and body awareness in psychotherapy may help peopple with aleithymia. Front. Pyschol. 7, 1–11. https://doi.org/10.3389/fpsyg.2016.00253. Hypothesis and theory article 253.

Castro-Sánchez, A.M., Matarán-Peñarrocha, G.A., Granero-Molina, J., Aguilera-Manrique, G., Quesada-Rubio, J.M., Moreno-Lorenzo, C., 2011a. Benefits of Massage-Myofascial Release Therapy on Pain, Anxiety, Quality of Sleep, Depression, and Quality of Life in Patients with Fibromyalgia. Evidence Based Complementary and Alternative Medicine. eCAM:2011 ID: 561753. https://doi.org/10.1155/2011/561753A, 9 pages.

Castro-Sánchez, A.M., Matarán-Peñarrocha, G.A., Sánchez-Labraca, N., Quesada-Rubio, J.M., Granero-Molina, J., Moreno Lorenzo, C., 2011b. A randomized controlled trial investigating the effects of craniosacral therapy on pain and heart rate variability in fibromyalgia patients. Clin. Rehabil. 25 (1), 25–35. https://doi.org/10.1177/0269215510375909.

Castro-Sánchez, A.M., Matarán-Peñarrocha, G.A., Arroyo-Morales, M., Saavedra-Hernández, M., Fernández-Sola, C., Moreno-Lorenzo, C., 2011c. Effects of myofascial release techniques on pain, physical function, and postural stability in patients with fibromyalgia: a randomized controlled trial. Clin. Rehabil. 25 (9), 800–813. https://doi.org/10.1177/0269215511399476, 2011.

Castro-Sánchez, A.M., Aguilar-Ferrándiz, M.E., Matarán-Peñarrocha, G.A., Sánchez-Joya Mdel, M., Arroyo-Morales, M., Fernández-de-las-Peñas, C., 2014. Short-term effects of a manual therapy protocol on pain, physical function, quality of sleep, depressive symptoms, and pressure sensitivity in women and men with fibromyalgia syndrome: a randomized controlled trial. Clin. J. Pain 30 (7), 589–597. https://doi.org/10.1097/AJP.0000000000000008.

Celenay, S., Kulunkoglu, B.A., Yasa, M.E., Cansu Sahbaz Pirincci, C.S., Yildirim, N.U., Kucuksahin, O., Ugurlu, F.G., Selami Akkus, S., 2017. A comparison of the effects of exercises plus connective tissue massage to exercises alone in women with fibromyalgia syndrome: a randomized controlled trial. Rheumatol. Int. 37 https://doi.org/10.1007/s00296-017-3805-3, 1799–180.

Clauw, D.J., 2014. Fibromyalgia: a clinical review. JAMA, J. Am. Med. Assoc. 311, 1547–1555. https://doi.org/10.1001/jama.2014.3266.

Courtois, I., Cools, F., Calsius, J., 2015. Effectiveness of body awareness interventions in fibromyalgia and chronic fatigue syndrome: a systematic review and meta-analysis. J. Bodyw. Mov. Ther. 19, 35–56. https://doi.org/10.1016/j.jbmt.2014.04.003.

Crawford, C., Boyd, C., Paat, C.F., Price, A., Xenakis, L., Yang, E., Zhang, W., the Evidence for Massage Therapy (Emt) Working Group, 2016. 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 Med. 17, 1353–1375. https://doi.org/10.1093/pm/pnw099.

Díaz-Rodríguez, L., Fernández-Pérez, A.M., Galiano-Castillo, N., Cantarero-Villanueva, I., Fernández-Lao, C., Martin-Martin, L.M., Arroya-Morales, M., 2016. Do patient profiles influence the effects of massage? A controlled clinical trial. Biol. Res. Nurs. 18 (5), 489–497. https://doi.org/10.1177/1099800416643182.

Dupuis, C., 2015. An exploratory study on the effects of DBM fasciatherapy on a population suffering from fibromyalgia. Physiotherapy 101 (Suppl. 1), e336–e337. https://doi.org/10.1016/j.physio.2015.03.542.

Ekici, G., Bakar, Y., Akbayrak, T., Yuksel, I., 2009. Comparison of manual lymph drainage therapy and connective tissue massage in women with fibromyalgia: a randomized controlled trial. J. Manip. Physiol. Therapeut. 32 (2), 127–133. https://doi.org/10.1016/j.jmpt.2008.12.001.

Ekici, G., Unal, E., Akbayrak, T., Vardar-Yagli, N., Yakut, Y., Karabulut, E., 2017. Effects of active/passive interventions on pain, anxiety, and quality of life in women with fibromyalgia: randomized controlled pilot trial. Women Health 57 (1), 88–107. https://doi.org/10.1080/03630242.2016.1153017.

Eijk-Hustings, Y., Kroese, M., Creemers, A., Landewé, R., Boonen, A., 2016. Resource utilisation and direct costs in patients with recently diagnosed fibromyalgia who are offered one of three different interventions in a randomised pragmatic trial. Clin. Rheumatol. 35, 1307–1315. https://doi.org/10.1007/s10067-015-3067-y.

Field, T., Diego, M., Cullen, C., Hernande-Reif, M., Sunshine, W., Douglas, S., 2002. Fibromyalgia pain and substance P decrease and sleep improves after massage therapy. J. Clin. Rheumatol. 8 (2), 72–76. https://doi.org/10.1097/00124743-200204000-00002.

Field, T., 2010. Touch for socioemotional and physical wellbeing: a review. Dev. Rev. 30 (4), 367–383. https://doi.org/10.1016/j.dr.2011.01.001.

Field, T., 2014. Massage therapy research review. Compl. Ther. Clin. Pract. 20 (4), 224–229. https://doi.org/10.1016/j.ctcp.2014.07.002.

Hansen, N., Lambert, M., Forman, E., 2006. The psychotherapy dose-response effect and its implications for treatment delivery services. Clin. Pyschol. Sci. Pract. 9 (3), 329–343. https://doi.org/10.1093/clipsy.9.

Holey, L.A., Dixon, J., 2014. Connective tissue manipulation: a review of theory and clinical evidence. J. Bodyw. Mov. Ther. 18 (1), 112–118. https://doi.org/10.1016/j.jbmt.2013.08.003.

Hauser, W., Ablin, J., Fitzcharles, M., 2017. Management of fibromyalgia: key messages from recent evidence-based guidelines. Pol. Arch. Intern. Med. 127 (1), 47–56. https://doi.org/10.20452/pamw.3877.

Hauser, W., Fitzcharles, M., 2018. Facts and myths pertaining to fibromyalgia. Dialogues Clin. Neurosci. 20, 53–62. https://doi.org/10.1038/jid.2015.269.

Kalichman, L., 2010. Massage therapy for fibromyalgia symptoms. Rheumatol. Int. 30 (9), 1151–1157. https://doi.org/10.1007/s00296-010-1409-2.

LaPierre, A., 2003. From felt-sense to felt-self: neuroaffective touch and the relational matrix. Psychol. Psychoanal. 23 (4), 43–46.

Li, Y.H., Wang, F.Y., Feng, C.Q., Yang, X.F., Sun, Y.H., 2014. Massage therapy for fibromyalgia: a systematic review and meta-analysis of randomized controlled trials. PloS One 9 (2), e89304. https://doi.org/10.1371/journal.pone.0089304.

Lederman, E., 2015. A process approach in manual and physical therapies: beyond the structural model. CPDO Online J. 1–18.

Liptan, G.L., 2010. Fascia: a missing link in our understanding of the pathology of fibromyalgia. J. Bodyw. Mov. Ther. 14 (1), 3–12. https://doi.org/10.1016/j.jbmt.2009.08.003.

Liptan, G., Mist, S., Wright, C., Arzt, A., Jones, K.D., 2013. A pilot study of myofascial release therapy compared to Swedish massage in fibromyalgia. J. Bodyw. Mov. Ther. 17 (3), 365–370. https://doi.org/10.1016/j.jbmt.2012.11.010.

Low, L., Schweinhardt, P., 2011. Early Life Adversity as a Risk Factor for Fibromyalgia in Later Life. Pain Research and Treatment. Article ID 140832, pp. 1–15. https://doi.org/10.1155/2012/140832.

Lund, I., Lundeberg, T., Carleson, J., Sönnerfors, H., Uhrlin, B., Svensson, E., 2006. Corticotropin releasing factor in urine–a possible biochemical marker of fibromyalgia. Responses to massage and guided relaxation. Neurosci. Lett. 403 (1–2), 166–171. https://doi.org/10.1016/j.neulet.2006.04.038, 2006 Jul 31.

Macfarlane, G.J., Kronisch, C., Dean, L.E., Atzeni, F., Häuser, W., Fluß, E., Choy, E., Kosek, E., Amris, K., Branco, J., Dincer, F., Leino-Arjas, P., Longley, K., McCarthy, G.M., Makri, S., Perrot, S., Sarzi-Puttini, P., Taylor, A., Jones, G.T., 2017. EULAR revised recommendations for the management of fibromyalgia. Ann. Rheum. Dis. 76, 318–328. https://doi.org/10.1136/annrheumdis-2016-209724.

Maher, C.G., Sherrington, C., Herbert, R.D., Moseley, A.M., Elkins, M., 2003. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys. Ther. 83 (8), 713–721.

Marques, A.P., Santo, A.S.D.E., Berssaneti, A.A., Matsutani, L.A., Yuan, S.L.K., 2017. Prevalence of fibromyalgia: literature review update. Rev. Bras. Reumatol. Engl. Ed. 57 (4), 356–363. https://doi.org/10.1016/j.rbre.2017.01.005.

Matarán-Peñarrocha, G.A., Castro-Sánchez, A.M., García, G.C., Moreno Lorenzo, C., Carreño, T.P., Onieva Zafra, M.D.O., 2011. Influence of craniosacral therapy on anxiety, depression and quality of life in patients with fibromyalgia. Evid. base

Compl. Alternative Med. https://doi.org/10.1093/ecam/nep125. Article ID 178769, 9 pages.
Mease, P., Arnold, L.M., Choy, E.H., Clauw, D.J., Crofford, L.J., Glass, J.M., Martin, S.A., Morea, J., Simon, L., Strand, C.V., Williams, D.A., Omeract Fibromyalgia Working Group, 2009. Fibromyalgia syndrome module at OMERACT 9: domain construct. J. Rheumatol. 36 (10), 2318–2329. https://doi.org/10.3899/jrheum.090367.
Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., Prisma Group, 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 6 (7), e1000097 https://doi.org/10.1371/journal.pmed.1000097, 2009.
Mooney, K., 2015. Exploring the role of peripheral mechanisms: an evaluation of a theory-based approach to reducing symptoms of Fibromyalgia. (Order No. 3711757). Doctor of Philosophy (Ph.D.). In: Psychology Thesis. Saybrook University San Francisco, California. Available from ProQuest Dissertations & Theses Global. (1707928857).
Moyer, C., Rounds, J., Hannum, J.W., 2004. A meta-analysis of massage therapy research. Psychol. Bull. 130 (1), 3–18. https://doi.org/10.1037/0033-2909.130.1.3.
Price, C., C de C Williams, A., Smith, B., Bottle, A., 2018. The national pain audit for specialist pain services in England and wales 2010–2014. Br. J. Pain. https://doi.org/10.1177/2049463718814277.
Randell, P., 1992. The crisis of clnical theory suppporting osteopathic practice: a critique and new proposal. Br. Orthopt. J. 9, 5–7.
Rapaport, M.H., Schettler, P., Bresee, C., 2012. A preliminary study of the effects of repeated massage on hypothalamic–pituitary–adrenal and immune function in healthy individuals: a study of mechanisms of action and dosage. J. Alternative Compl. Med. 18 (8), 789–797. https://doi.org/10.1089/acm.2011.0071.
Sailer, U., Triscoli, C., Häggblad, G., Hamilton, P., Olausson, H., Croy, I., 2016. Temporal dynamics of brain activation during 40 minutes of pleasant touch. Neuroimage 139, 360–367. https://doi.org/10.1016/j.neuroimage.2016.06.031, 2016.
Schleicher, H., Alonso, C., Shirtcliff, E.A., Muller, D., Loevinger, B.L., Christopher, L., Coea, C.L., 2005. In the face of pain: the relationship between psychological well-being and disability in women with fibromyalgia. Psychother. Psychosom. 74, 231–239. https://doi.org/10.1159/000085147.
Sherman, K.J., Cook, A.J., Wellman, R.D., Hawkes, R.J., Kahn, J.R., Deyo, R.A., Cherkin, D.C., 2014. Five-week outcomes from a dosing trial of therapeutic massage for chronic neck pain. Ann. Fam. Med. 12 (2), 112–120. https://doi.org/10.1370/afm.1602.
Social Science Statistics, 2019. Effect Size Calculator. (2019, January). Retrieved from. https://www.socscistatistics.com/effectsize/.
Sritoomma, N., Moyle, W., Cooke, M., O'Dwyer, S., 2014. The effectiveness of Swedish massage with aromatic ginger oil in treating chronic low back pain in older adults: a randomized controlled trial. Compl. Ther. Med. 22 (1), 26–33. https://doi.org/10.1016/j.ctim.2013.11.002.
Staud, R., 2011. Peripheral pain mechanisms in chronic widespread pain. Best Pract. Res. Clin. Rheumatol. 25 (2), 155–164. https://doi.org/10.1016/j.berh.2010.01.010.
Sunshine, W., Field, T.M., Quintino, O., Fierro, K., Kuhn, C., Burman, I., Schanberg, S., 1996. Fibromyalgia benefits from massage therapy and transcutaneous electrical stimulation. J. Clin. Rheumatol. 2 (1), 18–22.
Terhorst, L., Schneider, M.J., Kim, K.H., Goozdich, L.M., Stilley, C.S., 2011. Complementary and alternative medicine in the treatment of pain in fibromyalgia: a systematic review of randomized controlled trials. J. Manip. Physiol. Therapeut. 34 (7), 483–496. https://doi.org/10.1016/j.jmpt.2011.05.006.
Terry, R., Perry, R., Ernzt, E., 2012. An overview of systematic reviews of complementary and alternative medicine for fibromyalgia. Clin. Rheumatol. 31 (1), 55–66. https://doi.org/10.1007/s10067-011-1783-5.
The Nhs 5 year forward View, 2014. NHS England, Care Quality Commission, Health Education England, Monitor, Public Health England. Trust Development Authority, London: NHS England. Available at: www.england.nhs.uk/ourwork/futurenhs/. (Accessed 15 June 2019).
Thieme, K., Mathys, M., Turk, D., 2017. Evidenced-based guidelines on the treatment of fibromyalgia patients: are they consistent and if not, why not? Have effective psychological treatments been overlooked? J. Pain 18 (7), 747–756. https://doi.org/10.1016/j.jpain.2016.12.006.
Verhagen, A.P., de Vet, H.C., de Bie, R.A., Kessels, A.G., Boers, M., Bouter, L.M., Knipschild, P.G., 1998. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. J. Clin. Epidemiol. 51, 1235–1241.
Wahner-Roedler, D.L., Vincent, A., Mandrekar, J.N., Thompson, J.M., Oh, T.H., Loehrer, L.L., Elkin, P.L., Bauer, B.A., 2005. Use of complementary and alternative medical therapies by patients referred to a fibromyalgia treatment program at a tertiary care center. Mayo Clin. Proc. 80, 55–60. https://doi.org/10.4065/80.1.55.
Walden, M., 2015. Designing effective corrective exercise programs: the importance of dosage. J. Bodyw. Mov. Ther. 19 (2), 352–356. https://doi.org/10.1016/j.jbmt.2015.02.006.
Wolfe, F., Smythe, H.A., Yunus, M.B., Bennett, R.M., Bombardier, C., Goldenberg, D.L., Tugwell, P., Campbell, S.M., Abeles, M., Clark, P., et al., 1990. The American college of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheumatol. 33 (2), 160–172.
Yuan, S.L., Berssaneti, A.A., Marques, A.P., 2013. Effects of shiatsu in the management of fibromyalgia symptoms: a controlled pilot study. J. Manip. Physiol. Therapeut. 36 (7), 436–443. https://doi.org/10.1016/j.jmpt.2013.05.019.
Yuan, S.L., Matsutani, L.A., Marques, A.P., 2015. Effectiveness of different styles of massage therapy in fibromyalgia: a systematic review and meta-analysis. Man. Ther. 20, 257–264.
Zusman, M., 2002. Review article Forebrain-mediated sensitization of central pain pathways: 'non-specific' pain and a new image for MT. Man. Ther. 7 (2), 80–88.