Accepted Manuscript

Laser Acupuncture for Treating Musculoskeletal Pain: A Systematic Review with Meta-analysis

Dina Law, Suzanne McDonough, Chris Bleakley, G David Baxter, Steve Tumilty

PII: S2005-2901(14)00114-9

DOI: 10.1016/j.jams.2014.06.015

Reference: JAMS 179

To appear in: *Journal of Acupuncture and Meridian Studies*

Received Date: 13 January 2014

Revised Date: 18 June 2014

Accepted Date: 25 June 2014

Please cite this article as: Law D, McDonough S, Bleakley C, Baxter GD, Tumilty S, Laser Acupuncture for Treating Musculoskeletal Pain: A Systematic Review with Meta-analysis, *Journal of Acupuncture and Meridian Studies* (2014), doi: 10.1016/j.jams.2014.06.015.

Laser Acupuncture for Treating Musculoskeletal Pain: A Systematic Review with Meta-analysis

Authors:

Dina Law[1], Suzanne McDonough[2], Chris Bleakley[2], G David Baxter[1], Steve Tumilty[1]

Affiliations:

[1]Centre for Health, Activity and Rehabilitation Research, School of Physiotherapy, University of Otago, New Zealand

[2]Centre for Health, Activity and Rehabilitation Technologies, University of Ulster, Northern Ireland

Corresponding author. Dina Law, Centre for Health, Activity and Rehabilitation Research, School of Physiotherapy,University of Otago, PO Box 56, Dunedin 9054, New Zealand

E-Mail: dinalawnp@gmail.com

Abstract

Laser acupuncture has been studied extensively over several decades to establish evidence-based clinical practice. This systematic review aims to evaluate the effects of laser acupuncture on pain and functional outcomes when it is used to treat musculoskeletal disorders and to update existing evidence with data from recent randomized controlled trials (RCTs). A computer-based literature search of the databases MEDLINE, AMED, EMBASE, CINAHL, SPORTSDiscus, Cochrane Library, PubMed, Current Contents Connect, Web of Science, and SCOPUS was used to identify RCTs comparing laser acupuncture to control interventions. A meta-analysis was performed by calculating the standardized mean differences and 95% confidence intervals to evaluate the effect of laser acupuncture on pain and functional outcomes. Included studies were assessed for their methodological quality and appropriateness of laser parameters. Forty-nine RCTs met the inclusion criteria. Two-thirds (31/49) of these reported positive effects, were of high methodological quality, and had adequately reported the dosage. Negative or inconclusive studies commonly failed to demonstrate these features. For all diagnostic subgroups, positive effects for both pain and functional outcomes were more consistently seen at longer follow-up times after treatment rather than immediately after treatment. Evidence of moderate quality supports the effectiveness of using laser acupuncture to manage musculoskeletal pain when an appropriate treatment dosage is applied; however, the positive effects are only seen at longer follow-up times after the cessation of treatment, not immediately after.

KEYWORDS

acupuncture therapy;

low-level laser therapy;

pain;

review

1 Introduction

Musculoskeletal disorders represent a significant cost to the healthcare system [1]. A recent report estimated 1.7 billion individuals globally are affected by various kinds of musculoskeletal problems, and highlighted the considerable impact of chronic pain and disabilities upon individuals [2]. Coupled with the increasing risk factors such as obesity, sedentary lifestyles, and aging populations in modern world [3, 4], increasing prevalence of musculoskeletal disorders is foreseeable, exacerbating the healthcare burden.

Recent research confirms that treatments such as physical therapy, acupuncture, and massage remain popular with pain sufferers. A survey conducted in 16 European countries showed that 70% of participants who suffered from musculoskeletal pain sought other forms of treatment apart from medication [5]. Of these, acupuncture is one of the most common types of alternative treatment for patients looking for long-term pain management [6], which provides a relatively safe option with minimal side effects. Growing demand for - and provision of - acupuncture services have been seen

in different countries [5, 7, 8] resulting an interest in, and rapid development of, acupuncture research in order to establish a more solid evidence-based practice [9].

Such research development extends to other forms of acupuncture apart from the traditional needling method. The use of low-level laser to stimulate acupuncture points is suggested to be a safer technique due to its non-invasive nature, and its acceptability for people with needle phobia [10]. Laser acupuncture is considered to be an effective alternative to traditional needling, is useful in patients who are needle phobic or for use at acupuncture points where complicated application of the needle is appropriate [10, 11].

Ever since laser acupuncture studies in the 1970s [12, 13], researchers have focused on the underlying mechanism of laser acupuncture to build the scientific basis for clinical practice. Controversy remains concerning the mechanisms of laser acupuncture, which being free from any mechanical stimulation, do not share similar pain modulation pathways as traditional needling acupuncture [10]. Rather than producing 'needling sensation', the acupuncture point irradiated by the laser needs to receive sufficient energy to elicit the physiological effect at the cellular level, based upon the wider principle of "photobiomodulation" [14-16]. A key point to determine the effectiveness of laser acupuncture is the dosage applied: this issue has been stressed in several recent papers [16, 17]. The development of dosage guidelines for laser acupuncture is confounded by the lack of a clear understanding of the mechanisms underpinning such treatment, as dosage dependency is normally explored during the stage of *in vitro* and animal studies [10]. At present, The World Association for Laser Therapy (WALT) Guidelines for LLLT published in 2010 only

provide recommendations for general laser treatment on different conditions, no specific guidelines have been developed for laser acupuncture [18, 19]. Hence, selection of laser parameters and dosage are often subjective or based on clinical experience. Studies may apply an inappropriate dosage or inadequately report the parameters hence the results of these studies would be difficult to replicate or provide data to formulate a most efficacious dose. [20-22].

More recent evidence supports the physiological effects of laser acupuncture, including anti-inflammatory [23] and anti-nociceptive effects [24]. Such studies highlight the potential effect of laser acupuncture under well-controlled conditions; however, whether or not these results can be extrapolated to the clinical setting remains unclear. It is critically important to understand the relevance of laser irradiation parameters, together with the appropriate selection of acupoints, to the effectiveness of laser acupuncture for musculoskeletal conditions.

Despite the growth of evidence in the field of laser acupuncture, its effectiveness for musculoskeletal condition remains unclear because of inconclusive results from different studies [14, 20, 22]. This expansion may suggest a shift in the evidence base, therefore it is timely to review the results from recent studies to confirm the current evidence base for laser acupuncture. A systematic review with meta-analysis was therefore conducted to update the previous review in this area [17] with the following aims:

- To assess the clinical effectiveness of laser acupuncture for pain and functional outcomes for musculoskeletal conditions;
- To explore the relationship of parameter choice to outcomes;

- To establish the level of evidence of the effectiveness of laser acupuncture with an update of current literature.

2 Methods

2.1 Protocol and registration

This systematic review was conducted and reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline [25]; a pre-registered protocol was not used.

2.2 Selection criteria

Studies included for this review had to meet the following criteria.

2.2.1 Types of studies

Randomized controlled trials (RCT) and controlled clinical trials (CCT) published in peer-reviewed journals. Studies published from database inception to 1st March 2013 were included, in order not to miss any records, and to update the findings of our previous systematic review [17] by including more current publications. Due to resource limitations, this review excluded non-English language publications.

2.2.2 Types of participants

Human participants with musculoskeletal diseases or injuries, and presenting with pain were included. Systemic illness and headache were not included. There were no restrictions based on age, gender, or physical activity status.

2.2.3 Types of intervention

Studies evaluating laser acupuncture as the primary intervention were included. Such intervention needed to include active low level laser therapy to Traditional Chinese Medicine acupuncture points, trigger points, or tender points. Studies with a primary intervention using needling, other forms of stimulation on acupuncture points, or applying laser therapy on non-acupuncture points, were not considered. Studies were included which compared laser acupuncture with one of the following as a control intervention: placebo or sham laser, no treatment, or other treatments, such as medication, exercise therapy, or other electrotherapy modalities.

2.2.4 Types of outcome measures

Studies were included which assessed pain or function using at least one of the following as primary outcomes: pain level (visual analogue scale), a global assessment of participants' improvement (subjective improvement, proportion of objective measures improvement, overall improvement), or a functional outcome measure (validated questionnaire or functional scale specific to the presenting condition).

2.2.5 Length of follow-up

There was no restriction applied to the length of follow-up.

2.3 Search strategy

Studies were identified by an electronic search on the following databases: MEDLINE (1946 to 1st March 2013), AMED (1985 to 1st March 2013), EMBASE (1947 to 1st March 2013), CINAHL (1981 to 1st March 2013), SPORTSDiscus (1960 to 1st March 2013), Cochrane Library, PubMed (1950 to 1st March 2013), Current Contents Connect (1998 to 1st March 2013), Web of Science (1900 to 1st March 2013) and SCOPUS (1960 to 1st March 2013). The same search strategy was used in subject-based databases as shown in appendix A. In addition, Google Scholar (1st January 2013 to 1st March 2013), Physiotherapy Evidence Database (PEDro; 1966 to 1 March 2013), and two key journals (*Lasers in Surgery and Medicine*; 2005 to 1st March 2013 and *Photomedicine and Laser Surgery*; 2005 to 1st March 2013) were searched manually to cover recent studies which may have not been included in other databases. Two independent reviewers ran the search independently on 1 March 2013.

2.4 Selection of studies

Two independent reviewers assessed the eligibility of all studies independently by screening the titles and abstracts with the above selection criteria. Full-text articles were retrieved if there was any uncertainty. When there was disagreement between the two reviewers, the study was reassessed using the selection criteria as a basis for consideration for its eligibility until consensus was achieved. Relevant studies were retrieved as full-text articles, either from the databases or study authors, for final assessment of inclusion or exclusion. Reference lists of retrieved articles were checked for any missing relevant articles.

2.5 Assessment of methodological quality

All included studies were assessed for methodological quality using the PEDro scale [26]. Two reviewers performed the assessment independently in a standardized manner; they were not blinded to details of the studies. Disagreements between reviewers were resolved by consensus and a third reviewer was consulted if disagreements persisted. Methodological qualities of the included studies were rated with a total of 10 rated items of the PEDro scale. All included studies were also assessed for their level of risk of bias by two independent reviewers. The risk of bias assessment helps to identify any major methodological flaws from different domains of the included studies [27]. Further subgroup analyses related to bias assessment were planned where appropriate.

2.6 Data extraction

Two independent reviewers extracted data from included studies. Disagreements were resolved by discussion; if no agreement could be reached, a third reviewer was available for cross-referral.

Data were extracted from each included trial on:

- Study population;
- Details of interventions;
- Types of outcome measures;
- Laser acupuncture dosage (including parameters recommended by the World Association for Laser Therapy (WALT) [28] or calculation of missing data if possible).

2.7 Outcome measures

Data from included studies were pooled for further meta-analysis where appropriate. If available, means and standard deviations for outcome measures were extracted or calculated using published relevant data with Review Manager (RevMan) software, version 5.2 [29]. Unpublished data were not sought from authors because of time limitations. Data were categorized and analyzed as follows:

- Pain score – using visual analogue scale (VAS) and expressing raw score on a 0 to 10 scale. Change in scores (difference between various time points in a study) were also considered but grouped separately.
- Pressure pain threshold – algometric measurement expressed in kg/cm^2.
- Functional score – using validated functional scales, measuring grip strength, or comparing the difference in functional scores before and after the intervention.

2.8 Statistical analysis

Dichotomous outcomes were expressed as relative risks, and continuous outcomes were expressed as standardized mean difference (SMD); both were presented with 95% confident interval (CI) [27]. A negative SMD was defined to indicate favorable effects of laser acupuncture to the control intervention and vice versa. The magnitude of overall effect size was classified as small (0.2 to 0.5), moderate (0.5 to 0.8) and large (>0.8) according the value of SMD using the Cohen's categories [30]. Qualitative analysis was performed if studies failed to provide data to be pooled for analysis. Studies were assessed for heterogeneity using the chi-square test to decide

whether a random or fixed effect model was used; chi-square test with a p value ≥ 0.05 indicates a significant heterogeneity [27]. I^2 value quantifies the degree of heterogeneity from moderate (I^2 > 30%), substantial (I^2 > 50%) to considerable (I^2 > 75%) [27].

2.9 Subgroup and sensitivity analyses

Subgroup analyses were conducted to evaluate the overall effects as follows:

- Diagnosis;
- Control intervention;
- Follow-up period – measures taken immediately at the end of the intervention (short-term effect) or from 6 to 26 weeks-post randomization (long-term effect);
- Site of laser acupuncture application – acupuncture point, trigger point or tender point.

Sensitivity analyses were conducted for testing the robustness of the pooled effect size. Effects were examined according to risk of bias to ensure analysis was not biased from any study with high methodological flaws.

2.10 Risk of bias across studies

The risk of publication bias was assessed by analyzing the symmetry of the funnel plots generated by RevMan. Lower risk of bias presented with more symmetrical funnel plots while higher risk of bias presented with more asymmetry [31].

2.11 Quality of evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to judge and categorize the quality of evidence for the primary outcomes [32]. This reflects the extent of confidence of the estimated effects by considering the study design and other confounding factors that may affect the judgment. The quality grades used were:

High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

3 Results

3.1 Study selection

Figure 1 depicts the process of study selection with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. The search was conducted on 1st March 2013 and retrieved a total of 2093 potential relevant records. After adjusting for duplicates, 1432 records remained. One additional study was retrieved from Google Scholar. A total of 49 studies were eligible and included for current review.

3.2 Study characteristics

Table 1 summarizes the characteristics of all 49 included studies. All studies were RCTs published in English. A total of 2360 participants were involved aged 18 years or above. All trials were conducted in either a primary or secondary healthcare setting. Participants received 3 to 15 treatment sessions over a period of 1 to 12 weeks. Laser acupuncture was performed by physiotherapists or other trained healthcare professions in most of the trials; however half of the studies failed to report this clearly.

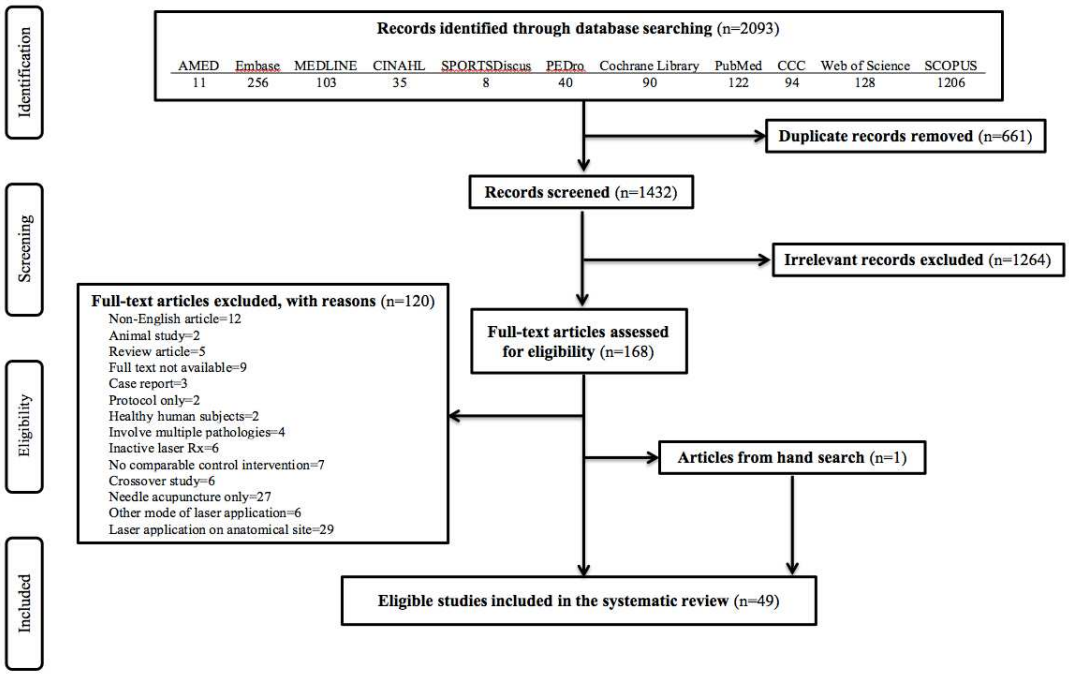


Figure 1. PRISMA flow diagram

*Table 1. Characteristics of the included studies**

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*
Ferreira LA [33]	2013	Temporomandibular joint disorder	40	Laser acupuncture (20) vs. placebo (20)	Monthly until intervention completed
Kannan P [34]	2012	Myofascial pain	45	Ultrasound (15) vs. laser (15) vs. ischemic compression (15)	End of intervention
Lin ML [35]	2012	Low back pain	60	Laser acupuncture (21) vs. placebo (21)	After each session
Sattayut S [36]	2012	Temporomandibular joint disorder	30	Low energy density laser (10) vs. high energy density laser (10) vs. placebo (10)	After each session
Skorupska E [37]	2012	Lateral epicondylitis	80	LLLT (40) vs. ultrasound (40) (trigger point application vs. anatomical site application; 20 in each subgroup)	End of intervention; 12-month
Lee JH [38]	2011	Myofascial trigger point pain	24	Laser (12) vs. placebo (12)	End of intervention
Rayegani SM [39]	2011	Myofascial pain	49	Laser (17) vs. ultrasound (16) vs. placebo laser (16)	6-week
Emanet SK [40]	2010	Lateral epicondylitis	47	Laser acupuncture (24) vs. placebo (23)	End of intervention; 12-week after intervention
Glazov G [41]	2010	Low back pain	100	Laser acupuncture (45) vs. placebo (45)	After each session; 6-week after intervention; 6-month after intervention
Katsoulis J [42]	2010	Tendomyopathy	11	Laser (7) vs. placebo (4)	3-month after intervention
Oz S [43]	2010	Myofascial pain	40	Laser (20) vs. occlusal splint (20)	End of intervention
Zhao L [44]	2010	Knee osteoarthritis	40	Laser on acupuncture point (19) vs. Laser on sham point (17)	2-week; 4-week

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*
Carrasco TG [45]	2009	Myofascial pain	60	Laser (30) vs. placebo (30) – 3 parameter groups;10 in each group	After 4 sessions; after 8 Rx; 15-day after intervention; 1-month after intervention
Glazov G [46]	2009	Low back pain	100	Laser acupuncture (45) vs. placebo (45)	After each session; 6-week after intervention; 6-month after intervention
Shen X [47]	2009	Knee osteoarthritis	40	Laser acupuncture (20) vs. placebo (20)	2-week; 4-week
Shirani AM [48]	2009	Myofascial pain	16	Laser acupuncture (8) vs. placebo (8)	After first session; 1-week; the day with complete pain relief
Shen X [49]	2008	Knee osteoarthritis	48	Laser acupuncture (24) vs. placebo (24)	2-week; 4-week
Dundar U [50]	2007	Myofascial pain	64	Laser acupuncture (32) vs. placebo (32)	4-week
Lam L [51]	2007	Lateral epicondylitis	39	Laser acupuncture (21) vs. placebo (18)	After 5 sessions; end of intervention; 3-month after intervention
Matsutani LA [52]	2007	Fibromyalgia	20	Laser (10) vs. no laser (10)	End of intervention
Mazzetto MO [53]	2007	Temporomandibular joint disorder	48	Laser (24) vs. placebo (24)	After 4 sessions; after 8 sessions; 30-day after intervention

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*
Yurtkuran M [54]	2007	Knee osteoarthritis	55	Laser (27) vs. placebo (25)	2-week; 12-week
Aigner N [55]	2006	Whiplash injury	50	Laser acupuncture (23) vs. placebo (22)	After each session; end of intervention; 8-12 months after injury
Armagan O [56]	2006	Fibromyalgia	32	LLLT (16) vs. placebo (16)	End of intervention; 6-month after intervention
Chow RT [57]	2006	Chronic neck pain	90	Laser (45) vs. placebo (45)	7-week; 12-week
Kiralp MZ [58]	2006	Myofascial pain	43	Laser (23) vs. trigger point injection (20)	End of intervention; 6-month after intervention
Altan L [59]	2005	Myofascial pain	53	Laser (23) vs. placebo (25)	2-week; 12-week after intervention
Tam G [60]	2005	Periarthritis of shoulder	60	Corticosteroid injection (20) vs. LLLT (21) vs. wait-and-see policy (18)	3-week; 6-week; 12-week; 26-week; 52-week
Ceylan Y [61]	2004	Myofascial pain	46	Laser (19) vs. placebo (20)	End of intervention
Chow RT [62]	2004	Chronic neck pain	20	Laser (10) vs. placebo (10)	7-week; 12-week
Gur A [63]	2004	Myofascial pain	60	Laser (30) vs. placebo (30)	2-week; 3-week; 12-week
Ilbuldu E [64]	2004	Trigger point pain	60	Placebo laser (20) vs. dry needling (20) vs. laser (20)	End of intervention; 6-month

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*
Al-Shenqiti A [65]	2003	Rotator cuff tendinitis	55	Laser (26) vs. placebo (29)	End of intervention; 3-month
Hakguder A [66]	2003	Myofascial pain	62	Laser (31) vs. no laser (31)	End of intervention; 3-week after intervention
Gur A [67]	2002	Fibromyalgia	40	Laser (20) vs. placebo (20)	End of intervention
Wong W [68]	2001	Carpal tunnel syndrome	12	Laser (12) vs. placebo (12)	End of intervention
Chen SM [69]	1997	Myofascial pain	21	Placebo (5) vs. continuous laser (7) vs. pulsed laser (9)	End of intervention
Conti PCR [70]	1997	Temporomandibular joint disorder	20	Laser (10) vs. placebo (10)	After each session
Laaskso EL [71]	1997	Myofascial trigger point pain	41	Red laser (15) vs. Infrared (IR) laser (16) vs. placebo (10)	Before each session; after each session
Logdberg-Andersson M [72]	1997	Tendinitis & myofascial pain	176	Laser (92) vs. placebo (84)	End of intervention; 4-week after intervention
Papadopoulos ES [73]	1996	Lateral epicondylitis	29	Laser (14) vs. placebo (15)	After 4 sessions; after 6 sessions
Vecchio P [74]	1993	Rotator cuff tendinitis	35	Laser (19) vs. placebo (16)	2-week; 4-week; 8-week
Haker E [75]	1991	Lateral epicondylitis	60	Laser (29) vs. placebo (29)	End of intervention; 3-month; 6-month; 12-month
Haker E [76]	1990	Lateral epicondylitis	49	Laser acupuncture (23) vs. placebo (26)	End of intervention; 3-month; 12-month

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*
Ceccherelli F [77]	1989	Myofascial pain	27	Laser (13) vs. placebo (14)	End of intervention; 3-month after intervention
Snyder-Mackler L [78]	1989	Myofascial trigger point pain	24	Laser (13) vs. placebo (11)	Before each session; after each session
Waylonis GW [79]	1988	Fibromyalgia/ chronic myofascial pain	55	Placebo vs. laser acupuncture	6-week after each round of intervention; 60-day; 120-day
Lundeberg T [80]	1987	Lateral epicondylitis	57	Placebo (19) vs. GaAs laser (19) vs. HeNe laser (19)	Every two week; end of intervention; 3-month; 6-month
Snyder-Mackler L [81]	1986	Musculoskeletal trigger point pain	27	Laser (13) vs. placebo (11)	Before each session; after each session

**See appendix B for individual study's outcome measures and summarized results.*

3.3 Quality assessment of included studies

Appendix C shows the methodological assessment of the included studies using the PEDro scale [26]. Thirty studies (61%) were considered as high methodological quality with a moderate cut-off score of 6 [82]. The most common flaws were inadequate allocation concealment (78%), lack of blinded therapists (63%), and lack of intention-to-treat analysis (71%). Despite the possible bias related to these flaws, other criteria were adequately addressed to minimize the risk of bias. Almost all the studies (94%) performed adequate randomization hence reducing possible selection bias. Most of the studies successfully performed blinding of patients (81%) and assessors (63%). Almost three-quarters (73%), provided adequate follow-up data with less than 15% dropout rate, therefore attrition bias was lowered. Inter-rater agreement was an acceptable level and disagreements were resolved by consensus.

Using the risk of bias assessment tool provided by the Cochrane collaboration [27] to evaluate the included studies showed similar results as the PEDro score (see Figure 2). The risk of selection bias and performance bias were mixed as some of the studies have unclear risks due to insufficient description. Other domains remained low risk in all the included studies, except 20% of the studies exhibited high risk in attrition due to the high dropout rates, or non-description of reasons for withdrawals.

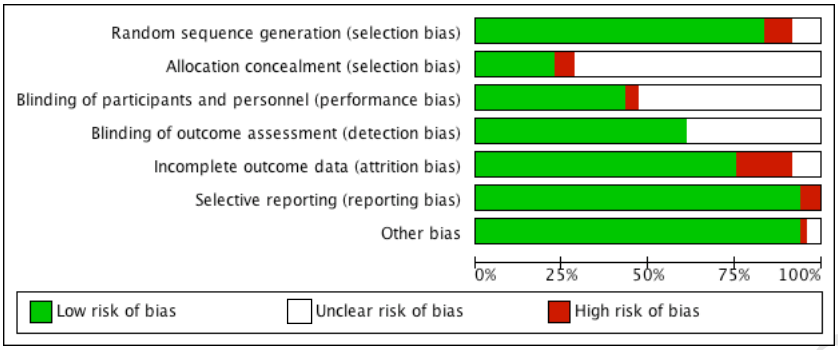


Figure 2. Risk of bias – graphical distribution of the judgments across all included studies

3.4 Effects of laser acupuncture

Thirty-three studies provided sufficient data to calculate effect sizes for key outcome measures using RevMan, and were included in the meta-analysis. These studies show mixed results as reported by the authors, with two-thirds reporting positive effects favoring laser acupuncture, and one-third reporting inconclusive or no effect.

3.4.1 Pain

All 33 studies assessed pain as one of the primary outcome measures. However, due to the heterogeneous characteristics of studies, results for pain scores where sub-categorized into laser acupuncture versus placebo, or laser acupuncture versus other interventions. To account for possible variation among different studies, the random effects model was used and the pooled effects were expressed as standardized mean difference (SMD).

When compared with the placebo intervention, the overall effect for pain favored laser acupuncture, both at the end of intervention (SMD -0.43; -0.74 to -0.12) and at the follow up period (SMD -0.61; -1.12 to -0.10). The pooled effect sizes of laser acupuncture on pain were considered to be small at short-term, but showed a moderate effect at long-term follow up (see Appendix D). Other studies [40, 41, 44, 47, 48, 50, 54, 57, 61, 62, 74, 80] expressed the pain change scores from baseline and showed a similar effect of pain relief at both short-term (SMD -0.53; -0.95 to -0.10) and long-term follow up (SMD -0.77; -1.25 to -0.29). When compared against other interventions, results of pain scores were mixed. Laser acupuncture failed to show significant favorable

effects on pain scores at any time point compared to the control treatment (SMD -0.23; -1.00 to 0.54; SMD -1.43; -3.84 to 0.98).

Nine studies investigated pain by measuring pressure pain threshold [36, 38, 39, 43, 51, 58, 59, 64, 69]. A positive effect indicates the beneficial effects of laser acupuncture as compared to control interventions. Similarly, compared with a placebo group, results showed a strong positive effect in favor of the experimental group at the end of intervention (SMD 1.02; 0.72 to 1.33) and during the follow up period (SMD 0.91; 0.30 to 1.53). Comparing laser acupuncture to other interventions, no short-term (SMD 0.35; -0.01 to 0.71) or long-term effects (SMD 0.20; -0.26 to 0.66) were found on pressure pain threshold (see Appendix D).

Among the studies measuring pain with VAS scale, subgroup analysis of pain scores was performed for the three most common diagnoses, which included myofascial pain or musculoskeletal trigger points syndrome, lateral epicondylitis, and temporomandibular joint pain (Figure 3). The subgroup differences were not significant at the end of intervention and during the follow up period ($p>0.05$). The overall effect of pain in the short-term moderately favored laser acupuncture (SMD -0.49; -0.79 to -0.18). Effects calculated from long-term follow-up almost doubled and suggested a strong effect of pain in favor of laser acupuncture (SMD -0.95; -1.55 to -0.35).

3.4.1.1 Myofascial pain/ musculoskeletal trigger points

Among studies investigating the effectiveness of laser acupuncture for myofascial pain or musculoskeletal trigger points, only six out of thirteen

showed favorable effects at the end of intervention [61, 63, 64, 66, 67, 77]. During the follow up period, four out of six studies demonstrated a positive effect in favor laser acupuncture [39, 59, 63, 77]. Those studies showing no significant effect of laser acupuncture were mostly associated with inadequate reporting of laser parameters [34, 45, 50, 52, 58, 69]. The overall effect of laser acupuncture on pain was positive with a moderate effect at short-term (SMD -0.49; -0.83 to -0.16) and a strong effect at long-term (SMD -0.95; -1.68 to -0.23).

3.4.1.2 Lateral epicondylitis

Two studies examined the effect of laser acupuncture on lateral epicondylitis and showed conflicting results [40, 51]. The overall effects did not suggest any favorable result of laser acupuncture at any time point. The study by Emanet et al [40] reported a positive conclusion during the follow up period yet the effect was not significant (SMD -0.42; -1.00 to 0.16). Again, the laser parameters employed in this study were unclear and incomplete, thus it is not possible to estimate whether or not the dosage was appropriate.

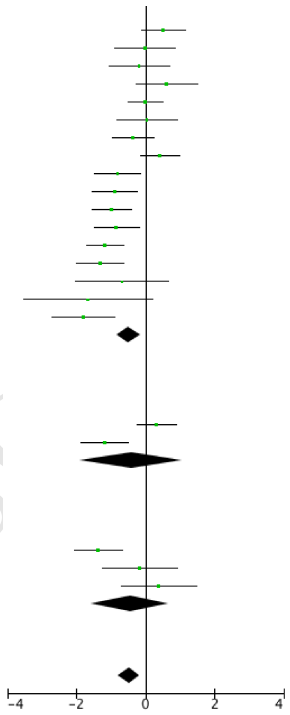
3.4.1.3 Temporomandibular joint pain

Two studies [33, 36] compared laser acupuncture with placebo in treating temporomandibular joint pain at the end of intervention. Results were mixed: one was positive [33], and the other one was inconclusive [36]. The latter study involved two laser acupuncture groups with different dosage applied. The group which received higher dosage showed a better effect of laser acupuncture compared with the lower dosage group; however, neither of them

have a significant effect of pain. During the follow up period, only one study [42] provided data hence outcome effect was not estimated.

A. Pain measured at the end of intervention

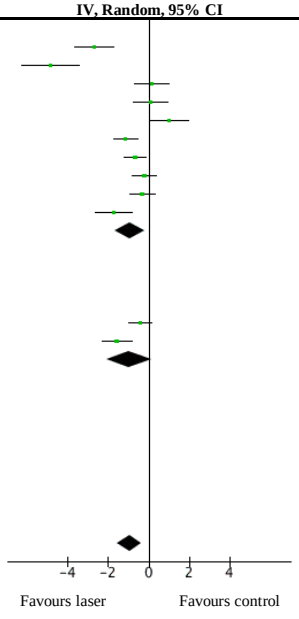
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std.Mean Difference IV, Random, 95% CI
i. Myofascial pain/ musculoskeletal trigger point								
Kannan 2012	2.66	1.23	15	2.18	0.7058	30	5.1%	0.52 [-0.11, 1.15]
Carrasco 2009 (1)	6.73	1.65	10	6.75	1.49	10	4.2%	-0.01 [-0.89, 0.86]
Carrasco 2009 (2)	6.4	2.32	10	6.8	1.74	10	4.2%	-0.19 [-1.07, 0.69]
Carrasco 2009 (3)	7.04	1.72	10	5.97	1.6	10	4.2%	0.62 [-0.29, 1.52]
Dundar 2007	3.2	2.5	32	3.2	2.3	32	5.6%	0.00 [-0.49, 0.49]
Matsutani 2007	4.7	2.9	10	4.6	2.0	10	4.2%	0.04 [-0.84, 0.92]
Kiralp 2006	2.18	1.63	23	2.77	1.57	20	5.2%	-0.36 [-0.97, 0.24]
Altan 2005	4.13	0.58	23	3.92	0.42	25	5.3%	0.41 [-0.16, 0.98]
Ceylan 2004	34.54	23.5	19	54.96	25.89	20	5.0%	-0.81 [-1.46, -0.15]
Ilbuldu 2004 (4)	2.05	1.43	20	3.65	2.03	20	5.0%	-0.89 [-1.55, -0.24]
Gur 2004	3.11	2.29	28	5.79	3.12	26	5.3%	-0.97 [-1.54, -0.40]
Ilbuldu 2004 (5)	2.05	1.43	20	3.71	2.33	20	5.0%	-0.84 [-1.49, -0.19]
Hakguder 2003	3.41	2.0	31	5.77	2.0	31	5.4%	-1.17 [-1.71, -0.62]
Gur 2002	1.27	0.76	20	2.44	0.98	20	4.9%	-1.31 [-2.00, -0.62]
Chen 1997 (6)	1.94	1.87	9	3.25	1.32	3	2.9%	-0.68 [-2.03, 0.67]
Chen 1997 (7)	0.83	1.29	7	3.25	1.32	2	1.9%	-1.66 [-3.54, 0.21]
Ceccherelli 1989	9.46	13.17	13	37.42	16.58	14	4.1%	-1.80 [-2.72, -0.89]
Subtotal (95% CI)			**300**			**303**	**77.7%**	**-0.49 [-0.83, -0.16]**
Heterogeneity: Tau² = 0.34; Chi² = 59.18, df = 16 (P < 0.00001); I² = 73%								
Test for overall effect: Z = 2.87 (P = 0.004)								
ii. Lateral epicondylitis								
Emanet 2010	1.13	0.94	23	0.83	0.88	24	5.3%	0.32 [-0.25, 0.90]
Lam 2007	3.05	1.77	21	5.39	2.12	18	4.9%	-1.18 [-1.87, -0.49]
Subtotal (95% CI)			**44**			**42**	**10.2%**	**-0.42 [-1.89, 1.06]**
Heterogeneity: Tau² = 1.03; Chi² = 10.84, df = 1 (P = 0.0010); I² = 91%								
Test for overall effect: Z = 0.55 (P = 0.58)								
ii. **Temporomandibular joint pain**								
Ferreira 2013	0.05	0.22	20	2.75	2.71	20	4.9%	-1.38 [-2.07, -0.68]
Sattayut 2012 (8)	4.5	2.58	10	5.0	3.38	5	3.6%	-0.17 [-1.24, 0.91]
Sattayut 2012 (9)	6.1	2.29	10	5.0	3.38	5	3.6%	0.39 [-0.70, 1.47]
Subtotal (95% CI)			**40**			**30**	**12.0%**	**-0.45 [-1.57, 0.67]**
Heterogeneity: Tau² = 0.74; Chi² = 8.43, df = 2 (P = 0.01); I² = 76%								
Test for overall effect: Z = 0.79 (P = 0.43)								
Total (95% CI)			**384**			**375**	**100.0%**	**-0.49 [-0.79, -0.18]**
Heterogeneity: Tau² = 0.37; Chi² = 79.89, df = 21 (P < 0.00001); I² = 74%								
Test for overall effect: Z = 3.12 (P = 0.002)								
Test for subgroup differences: Chi² = 0.01, df = 2 (P = 0.99), I² = 0%								



(1) Laser dose: 105J/cm^2; (2) Laser dose: 60J/cm^2; (3) Laser dose: 25J/cm^2; (4) vs placebo; (5) vs dry needling;
(6) Pulsed laser; placebo group data divided ; (7) Continuous laser; placebo group data divided;
(8) High energy laser; placebo group data divided; (9) Low energy laser; placebo group data divided

B. Pain measured during the follow-up period (6 to 26 wks)

Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std.Mean Difference IV, Random, 95% CI
i. Myofascial pain/ musculoskeletal trigger point								
Rayegani 2011 (1)	20.5	4.1231	17	30.7	3.2	16	7.8%	-2.69 [-3.66, -1.71]
Rayegani 2011 (2)	20.5	4.1231	17	40.7	4.0	16	6.4%	-4.85 [-6.27, -3.43]
Carrasco 2009 (3)	7.14	2.68	10	6.75	2.45	10	8.1%	0.15 [-0.73, 1.02]
Carrasco 2009 (4)	5.67	2.99	10	5.4	3.06	10	8.1%	0.09 [-0.79, 0.96]
Carrasco 2009 (5)	6.91	2.24	10	4.63	2.1	10	7.9%	1.01 [0.06, 1.95]
Altan 2005	3.17	0.58	23	3.8	0.51	25	8.9%	-1.14 [-1.75, -0.52]
Gur 2004	4.18	2.65	28	6.29	3.52	26	9.1%	-0.67 [-1.22, -0.12]
Ilbuldu 2004 (6)	2.12	1.9	20	2.59	2.18	20	8.9%	-0.23 [-0.85, 0.40]
Ilbuldu 2004 (7)	2.12	1.9	20	2.89	2.63	20	8.9%	-0.33 [-0.95, 0.30]
Ceccherelli 1989	8.46	10.76	13	35.57	18.28	14	8.1%	-1.74 [-2.64, -0.83]
Subtotal (95% CI)			**168**			**167**	**82.4%**	**-0.95 [-1.68, -0.23]**
Heterogeneity: Tau² = 1.18; Chi² = 78.58, df = 9 (P < 0.00001); I² = 89%								
Test for overall effect: Z = 2.58 (P = 0.01)								
ii. Lateral epicondylitis								
Emanet 2010	0.29	0.47	23	0.57	0.79	24	9.0%	-0.42 [-1.00, 0.16]
Lam 2007	1.48	1.36	21	4.28	2.11	18	8.6%	-1.57 [-2.30, -0.84]
Subtotal (95% CI)			**44**			**42**	**17.6%**	**-0.97 [-2.10, 0.15]**
Heterogeneity: Tau² = 0.55; Chi² = 5.87, df = 1 (P = 0.02); I² = 83%								
Test for overall effect: Z = 1.70 (P = 0.09)								
ii. **Temporomandibular joint pain**								
Katsoulis 2010	3.25	2.248	7	2.65	0.7362	4		Not estimable
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**212**			**209**	**100.0%**	**-0.95 [-1.55, -0.35]**
Heterogeneity: Tau² = 0.95; Chi² = 84.78, df = 11 (P < 0.00001); I² = 87%								
Test for overall effect: Z = 3.09 (P = 0.002)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.97), I² = 0%								



(1) vs ultrasound; (2) vs placebo; (3) Laser dose: 105J/cm^2; (4) Laser dose: 25J/cm^2; (5) Laser dose: 60J/cm^2;
(6) vs dry needling; (7) vs placebo

Figure 3. Forest plot comparison of different diagnoses

3.4.2 Functional outcome

Most of the studies assessed functional improvement using a wide range of scales. Each study could involve multiple results from different functional scales; hence an estimated overall effect size across the studies was not possible. Studies were more likely to report positive effects during the follow up period rather than at the end of the intervention. Only two out of eleven studies [51, 63] showed a positive short-term effect on functional, while six out of eight studies [39, 40, 51, 57, 62, 63] resulted positive at long-term (see appendix D).

Two studies [40, 51] investigated lateral epicondylitis, the pooled effect sizes of handgrip strength were strong in favor of laser acupuncture at both time points, but only significant during the follow up period (MD 5.16; 1.14 to 9.19). In regard to the small number of studies analyzed, it is important not to overlook this significant pooled effect (see Appendix D).

Sensitivity analyses were conducted to explore whether or not the main findings above were affected by any studies with high risk of bias in certain domain. We exclude studies separately with high risk of attrition bias, selection bias and performance bias. No significant difference was found after excluding high-risk studies.

3.5 Appropriateness of laser acupuncture treatment

All included studies were analyzed for the appropriateness of laser parameters used. They were grouped separately into those reporting positive effects and those reporting inconclusive or no effects from trial authors, and displayed along with the parameters used in Tables 2 and 3 respectively. It is notable that four studies [52, 59, 74, 80] reported no significant difference between groups; in contrast their calculated effect sizes from RevMan analysis favored laser acupuncture.

Almost 70% of those reporting positive results reported and fulfilled the clinically appropriate dosage suggested by Baxter et al [17]. Their systematic review stated that laser acupuncture should irradiate at a minimum average output power of 10 mW and apply an energy dose of at least 0.5 J per point.

In contrast, studies reporting inconclusive or no effect of laser acupuncture either failed to describe the parameters comprehensively or applied an inappropriate dosage.

Half of these negative studies are deemed of low methodological quality, with PEDro scores less than 6.

Table 2. Studies reporting positive effect of laser acupuncture

Study	*Average output mW*	*Power density mW/cm²*	*Dose J*	*PEDro*
Studies included in meta-analysis				
Chow RT [62]	300	670	9	10
Chow RT [57]	300	670	9	10
Glazov G [41]	10	50	0.2	9
Yurtkuran M [54]	4	10	0.48	8
Armagan O [56]	50	75	2	8
Gur A [63]	11.2	11.2	2	8
Ceccherelli F [77]	5	?	0.1 or 1	8
Shen X [47]	36 & 200	?	?	7
Oz S [43]*	300	1071	3	7
Lam L [51]	25	208	0.275	7
Shirani AM [48]	17.3 or 1.76	17.3 or 1.76	7.2	6
Hakguder A [66]	5	25.5	0.98	6
Gur A [67]	11.2	11.2	2	6
Ferreira LA [33]	50	1250	4.5	6
Sattayut S [36]	60 or 300	333 or 1666	4 or 20	6
Zhao L [44]	36 & 200	36 & 100	163.2	6
Rayegani SM [39]*	1100	?	?	6
Emanet SK [40]	?	?	?	5
Lin ML [35]	40	50	12	4
Kannan P [34]*	2.4	2.4	0.074	4
Ceylan Y [61]	8	40	1.44	3
Chen SM [69]	15 or 1.5	?	18 or 1.8	2
Studies not included in meta-analysis				
Al-Shenqiti A [65]	100	800	4	8
Conti PCR[70]	100	?	4	7
Tam G [60]*	27	135?	3 to 4	6
Snyder-Mackler L [78]	0.95	0.95	0.02	6
Laaksо EL [71]	10 or 25	278 or 893	1 or 5	5
Snyder-Mackler L [81]	0.95	0.95	0.014	5
Logdberg-Andersson M [72]	8	8	0.5 to 1	5
Wong W [68]	30	107	5.4	5
Mazzetto MO [53]	70	8750	0.72	4

* Laser acupuncture compared to other interventions

? Insufficient details for calculating the missing parameters

Table 3. Studies reporting inconclusive or no effect of laser acupuncture

Study	*Average output mW*	*Power density mW/cm²*	*Dose J*	*PEDro*
Studies included in meta-analysis				
Glazov G [46]	10	50	0.2	9
Vecchio P [74]	30	429	3	9
Dundar U [50]	58	58	7	9
Ilbuldu E [64]*	?	?	2	8
Altan L [59]	?	?	?	7
Carrasco TG [45]	50 or 60 or 70	?	?	6
Lundeberg T [80]	1.56 or 0.07	?	0.09 or 0.004	5
Lee JH [38]	450	6428	27 or 54 or 135	5
Kiralp MZ [58]*	?	?	?	5
Matsutani LA [52]	30	?	?	4
Katsoulis J [42]	40	1000	1.6 to 2.4	2
Studies not included in meta-analysis				
Skorupska E [37]*	0 to 400	?	?	8
Haker E [75]	12	?	0.36	7
Papadopoulos ES [73]	50	400	3	6
Haker E [76]	?	?	0.6	5
Shen X [49]	?	?	?	5
Waylonis GW [79]	1	?	0.02	4
Aigner N [55]	5	5	0.08	4

* Laser acupuncture compared to other interventions

? Insufficient details for calculating the missing parameters

3.5.1 Application site

The most common site of application for laser acupuncture was trigger points (39%). Subgrouping to perform another analysis to examine any difference of the effects on pain with different application sites was performed. There was no significant subgroup difference at the end of intervention and during the follow up period ($p>0.05$). However, only the application at trigger points showed a positive effect in favor of laser acupuncture; this was not seen with application at acupuncture points nor tender points.

(see appendix E).

3.6 Risk of bias across studies

Considering the heterogeneity of the studies, funnel plots were drawn according to different outcome measures. Visual assessment of funnel plots did not show any considerable asymmetry, indicating a comprehensive coverage of publications. Hence the publication and related bias were low in this review.

4 Discussion

This systematic review investigated the clinical effectiveness of laser acupuncture, focusing on the effects on pain and functional outcomes in treating musculoskeletal disorders. The current findings strengthen the evidence from a previous systematic review [17]. The key findings in the current review support the continued use of laser acupuncture for treating musculoskeletal pain. Results from the meta-analysis suggest that the effect of laser acupuncture on pain and functional outcomes tended to be more significant during long-term follow up periods rather than at the end of intervention. These results indicate laser acupuncture may be effective in treating musculoskeletal pain and improving function, where an adequate dosage is used, and that the effects are long lasting, as evidenced by the increase in effect sizes demonstrated in the meta-analysis at 6 to 26 weeks post randomization. It is important to stress that results from the included studies were dependent upon the appropriateness of laser parameters used. Higher methodology quality studies, which also properly reported dosage, showed a more consistent result with a favorable effect of laser acupuncture in terms of both pain and functional outcomes.

To the best of our knowledge, there has been no further evaluation of the latest literature on laser acupuncture since a previous systematic review, Baxter et al [17]. This concluded that laser acupuncture was an effective treatment for myofascial pain with a moderate level of evidence from 18 RCTs that were published before 2005. A massive growth in publications in recent years has resulted in further evidence on the effectiveness of laser acupuncture. Not surprisingly, a large number of clinical trials

were identified from the current literature, most of which were published during the last decade. The total number of eligible studies included in this systematic review was more than twofold that of the last review [17].

4.1 Primary outcomes

The majority of studies reported positive findings for the effects of laser acupuncture for both pain and functional outcomes; in contrast, one-third of reviewed studies reported no benefit. Given the heterogeneity of included studies, meta-analyses were performed using subgroups of studies according to their study populations and follow-up time point. The three most common diagnoses were analyzed separately in order to have a minimum of two studies for each analysis. Sensitivity analyses excluded studies comparing laser acupuncture with other active treatments, as the primary scope of this review was whether or not laser acupuncture is effective, rather than its comparative effectiveness compared to other active treatments.

4.1.1 Myofascial pain/ musculoskeletal trigger points

Ten studies showed positive effects of laser acupuncture for myofascial or trigger points pain: four studies [34, 50, 52, 58] had an individual effect size that did not favor the laser group. Coincidently, all of these studies did not include follow up assessments to investigate possible long-term effects. Given the increased effect sizes at follow up as highlighted here, it is possible that these researchers may have overlooked a potential effect in the longer term: another study [59] found positive effects only during the follow-up period, but not at the end of intervention.

4.1.2 Lateral epicondylitis

Emanet et al [40] showed more favorable effects in the short-term than in the long term. However the individual effect size (for pain) from the forest plot crossed zero at long-term time point, indicating a lack of statistical significance. Although the pooled effects with another study [51] did not suggest any favorable effects for lateral epicondylitis using laser acupuncture to reduce pain, results for hand grip assessment yielded some interesting findings. Both studies investigated the effectiveness of laser acupuncture by evaluating pain and functional outcomes, and appeared to be more homogeneous, so mean difference was used as the pooled effect result. Again, the estimated effect size for functional outcome (handgrip) favored laser acupuncture especially during follow-up period. However, it should be stressed that this analysis is based on two studies examining laser acupuncture, and the result may not be generalized to other conditions.

4.1.3 Temporomandibular joint pain

Results of the three studies reviewed were mixed, and only one of these reported outcomes at long-term. At short-term, the effect was inconclusive. No further analysis was done to compare the effects at different time points.

4.2 Increased long term follow-up effects

Findings among the three different diagnoses showed a consistent trend of better pain-relieving effects during the follow-up period. Pooled effect sizes were doubled during the follow-up period compared to those at the end of intervention. This phenomenon could account for the conflicting results from some of the negative studies. Without taking into consideration the possibility of delayed or long-lasting effects, their

conclusions of lack of effectiveness may be flawed. Results from our analyses included both short-term and long-term follow up data, and separating these data into similar time points to allow more comparable subgroup analyses.

4.3 Weaknesses of negative studies

A number of shortcomings were observed in those five studies [38, 42, 46, 50, 74] that found no significant benefit of laser acupuncture. One study [74] was found to have a mismatch between the calculated individual effect and the authors' conclusion. The effect size (expressed in standard mean difference) for pain favored laser acupuncture, but Vecchio et al reported no benefit. This apparent error was also highlighted by another systematic review [83] which suggested a flaw in their analysis. In another study on back pain, Glazov and colleagues performed a *post hoc* analysis [41] on their data which challenged the results of their original study [46]. They suggested that the randomization failed to create comparable groups and resulted in an imbalanced baseline characteristic that responded differently to the intervention. The PEDro quality rating of the study by Katsoulis et al [42] was exceptionally low (2 out of 10 PEDro score) representing a major performance bias. The remaining two studies [38, 50] applied laser acupuncture around the neck and upper trapezius muscles area. The parameters selected in both studies were similar to the other two positive studies [57, 66] targeting neck region, but the authors' conclusions were only based upon results measured at short term. The consequences of these apparent methodological flaws may be an underestimation of the true effect of laser acupuncture from these studies.

4.4 Clinical relevance of laser parameter

Variation in application of the laser acupuncture intervention could very likely account for a certain degree of difference in outcomes. Such clinical heterogeneity is an issue to be considered when evaluating the effectiveness of a therapy. Laser acupuncture has been suggested to be a dosage-dependent modality [16, 21]; these sources suggest that the energy delivered to the target point by laser acupuncture has to reach a threshold in order to produce a desired effect. Thus the dosages taken from the included studies may explain the observed difference in outcomes. Characteristics of the laser beam and the application site of laser would directly affect the actual energy received by the target point [10, 14]. While detailed discussion of the potential mechanisms of laser acupuncture is beyond the scope of this review, the importance of accurate selecting and reporting of parameters is paramount to understand and interpret the results of individual studies.

Unfortunately, the quality of reporting of parameters and dosages varied among the studies included in this review: five studies neither stated the power density nor the irradiated area [40, 58, 59, 64, 75]. This brings into question whether or not an appropriate dosage was applied. Reporting of these parameters is essential as recommended by the WALT guideline [28] so as to determine the appropriateness of the dosage. In addition, unclear reporting of parameters was more commonly seen among studies with negative or inconclusive results (Table 2 and 3).

It is challenging to draw meaningful conclusions concerning an effective dosage window from these studies due to the variation in the application of laser acupuncture, and the wide dosage range employed. This systematic review covered different

musculoskeletal conditions and each condition may have required a distinct parameter and dosage regime for clinical effectiveness. Site of application is a key factor in selection of parameters, given that there may be a specific acupuncture point for different diagnosis. In this review, the point of application was not limited to acupuncture points, but also included trigger and tender point applications, since there exists a wide range of evidence suggesting overlapping with acupuncture points [84-86]. It seems unwise to exclude those studies using trigger points or tender points even though the existence of these specific points is still controversial [85, 87, 88]. A subgroup analysis based on different application site was performed however no obvious difference could be seen between groups. Application on acupuncture points, trigger points, and tender points appeared equally effective.

4.5 Quality of included studies in our review

The number and proportion of trials rated as high methodological quality doubled in this review, compared to a previous review [17]. Over two-thirds of the 49 included RCTs in this review were high quality studies, while the previous review had less than one-third of the studies categorized as high quality. Considering this growing number of higher quality studies in this body of literature, the findings of this systematic review were expected to be more robust.

There was an apparent relationship between levels of methodological quality and reported results. Two thirds of high quality (PEDro ≥6) studies reported beneficial effects of laser acupuncture, which is similar to the proportion for all included studies. Lower quality studies appeared to show more conflicting results, with equal numbers of studies reporting benefits (n=9) or no benefit (n=9). This methodological

heterogeneity should be considered when assessing the overall pooled effect in the meta-analysis. However, it should be stressed that the sensitivity analyses, excluding those studies with high risk of bias in various domains, failed to show any differences in overall findings that conflicted with the effects estimated.

4.6 Limitation

The limitations of this review include potential bias from the heterogeneity and methodological quality of the included studies. These problems were anticipated in designing the methodology of this review, and as a result different subgroup analyses were initiated to address this limitation. Another limitation of this review is that some of the studies have high risk of bias in some of the domains; however the sensitivity analyses suggested no major effects upon the results. Lastly, even though non-English publications were excluded, the funnel plot assessment did not detect any potential publication bias. Although this kind of visual assessment is considered prone to error [89], it is one of the most common methods adopted for detecting publication bias owing to its simplicity [31]. Given the large number of included studies in this meta-analysis, using funnel plot could be capable to detect possible bias.

4.7 Recommendations

Using the GRADE system [90], the strength of recommendation is not only based on the quality of the evidence, but also other factors which should not outweigh the benefit of the treatment. Using pain and functional outcomes to assess the clinical effectiveness of laser acupuncture, most of the included studies are high quality RCTs

and accounted for high quality of evidence. Yet the quality of evidence was downgraded (-2) due to inconsistency and imprecision of the results for both pain and functional outcome measures [32]. Owing to the possible dose response for pain-relieving effects, and a large effect from functional outcome, the quality of evidence was upgraded (+1). As a result, there is a moderate quality of evidence supporting the effectiveness of laser acupuncture for the treatment of pain and functional outcome in musculoskeletal disorders. It suggests a moderate confidence that the estimated effect from meta-analysis is likely to be close to the true effect. Serious adverse events have been seldom reported for laser acupuncture given its non-invasive nature; this is in keeping with reports in all the included studies. Based upon this systematic review, strong recommendation for laser acupuncture can be made for its effectiveness for improving musculoskeletal pain and functional outcomes at 6 to 26 weeks.

5 Conclusion

Overall, the evidence is sufficiently robust to determine the effectiveness of laser acupuncture at long-term for musculoskeletal conditions. Trials reporting negative or inconclusive results, neither provided enough evaluation nor follow-up to the participant to a sufficient time point. These trials did not allow complete evaluation for pain and functional outcomes and their conclusions only based upon results measured at short-term. For these, it highlights the importance of providing a sufficient course of treatment to allow laser acupuncture to work effectively in the clinical situation.

Although the evidence does not allow us to determine an effective dosage window for laser acupuncture, the possible range of applications was largely adjusted and designed to fit specific musculoskeletal conditions. To foster the development of clinical guidelines, future research should carefully define the study population and provide rationale for the parameters chosen. This would not only facilitate pooling of data for meta-analysis, but also more precise analysis for a specific condition or application site. With the improving quality of evidence over time, more robust recommendations for clinical application of laser acupuncture can be anticipated in the future.

6 Reference

1. Burden of musculoskeletal diseases at the start of the millennium: report of a WHO scientific group. Geneva: World Health Organization; 2003.

2. Vos T, Aboyans V, Dherani M, Diaz-Torne C, Dolk H, Dorsey ER, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the global burden of disease study 2010. Lancet. 2012;380(9859):2163.

3. Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. Bull World Health Organ. 2003;81(9):646-56.

4. Brooks PM. The burden of musculoskeletal disease - a global perspective. Clin Rheumatol. 2006;25(6):778-81.

5. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain. 2006;10(4):287-333.

6. Rickards LD. Therapeutic needling in osteopathic practice: an evidence-informed perspective. Int J Osteopath Med. 2009;12(1):2-13.

7. Su D, Li L. Trends in the use of complementary and alternative medicine in the United States: 2002-2007. J Health Care Poor Underserved. 2011;22(1):296-310.

8. Xue CC, Zhang AL, Lin V, Da Costa C, Story DF. Complementary and alternative medicine use in Australia: a national population-based survey. J Altern Complement Med. 2007 Jul-Aug;13(6):643-50.

9. Han J-S, Ho Y-S. Global trends and performances of acupuncture research. Neurosci Biobehav Rev. 2011;35(3):680-7.

10. Whittaker P. Laser acupuncture: past, present, and future. Lasers Med Sci. 2004;19(2):69-80.

11. Litscher G. High-tech laser acupuncture is Chinese medicine. Med Acupunct. 2008;20(4):245-54.

12. Plog FMW. Biophysical application of the laser beam. Lasers Surg Med. 1980;1:21.

13. Zhou YC. An advanced clinical trial with laser acupuncture anesthesia for minor operations in the oro-maxillofacial region. Lasers Surg Med. 1984;4(3):297.

14. Chang WD, Wu JH, Yang WJ, Jiang JA. Therapeutic effects of low-level laser on lateral epicondylitis from differential interventions of Chinese-Western medicine: systematic review. Photomed Laser Surg. 2010;28(3):327-36.

15. Peplow PV, Chung TY, Baxter GD. Laser photobiomodulation of proliferation of cells in culture: a review of human and animal studies. Photomed Laser Surg. 2010;28 Suppl 1(S1):S3-S-40.

16. Litscher G, Opitz G. Technical parameters for laser acupuncture to elicit peripheral and central effects: state-of-the-art and short guidelines based on results from the Medical University of Graz, the German academy of acupuncture, and the scientific literature. Evid Based Complement Alternat Med. 2012;2012:697096.

17. Baxter GD, Bleakley C, McDonough S. Clinical effectiveness of laser acupuncture: a systematic review. J Acupunct Meridian Stud. 2008;1(2):65.

18. WALT. Recommended treatment doses for low level laser therapy - laser class 3B, 904 nm GaAs lasers. [Internet]: World Association for Laser Therapy; 2010 [updated 2010 Apr; cited Feb 13, 2013]; Available from: http://waltza.co.za/wp-content/uploads/2012/08/Dose_table_904nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf.

19. WALT. Recommended treatment doses for low level laser therapy - laser class 3 B, 780 - 860nm GaAlAs lasers. [Internet]: World Association for Laser Therapy; 2010 [updated 2010 Apr; cited 2013 Feb 13]; Available from: http://waltza.co.za/wp-content/uploads/2012/08/Dose_table_780-860nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf.

20. Chow RT, Johnson MI, Lopes-Martins RAB, Bjordal JM. Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. Lancet. 2009;374(9705):1897-908.

21. David Baxter G. Laser acupuncture: effectiveness depends upon dosage. Acupunct Med. 2009;27(3):92.

22. Jang H, Lee H. Meta-analysis of pain relief effects by laser irradiation on joint areas. Photomed Laser Surg. 2012;30(8):405-17.

23. Lorenzini L, Giuliani A, Giardino L, CalzÃ L. Laser acupuncture for acute inflammatory, visceral and neuropathic pain relief: an experimental study in the laboratory rat. Res Vet Sci. 2010;88(1):159-65.

24. Erthal V, da Silva MD, Cidral-Filho FJ, Santos AR, Nohama P. ST36 laser acupuncture reduces pain-related behavior in rats: involvement of the opioidergic and serotonergic systems. Lasers Med Sci. 2013.

25. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Ann Intern Med. 2009;151(4):W65-W94.

26. PEDro scale. [Internet]: Physiotherapy Evidence Database; 1999 [updated 1999 June 21; cited 2012 Feb 13]; Available from: http://www.pedro.org.au/wp-content/uploads/PEDro_scale.pdf.

27. Shuster JJ, Green S. Review: Cochrane handbook for systematic reviews for interventions, version 5.1.0. The Cochrane Collaboration; 2011 [updated March 2011]; Available from: http://www.cochrane-handbook.org/.

28. WALT. Consensus agreement on the design and conduct of clinical studies with low level laser therapy and light therapy for musculoskeletal pain and disorders. [Internet]: World Association for Laser Therapy; 2010 [updated 2004 Nov; cited Apr 1, 2013]; Available from: http://waltza.co.za/wp-content/uploads/2012/08/walt_standard_for_conduct_of_randomized_controlled_trials.pdf.

29. Review manager (RevMan) [Computer program]. Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.

30. Cohen J. Statistical power analysis for the behavioral sciencies: Routledge; 1988.

31. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-34.

32. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, et al. Grade guidelines: 3. rating the quality of evidence. J Clin Epidemiol. 2011;64(4):401-6.

33. Ferreira LA. Laser acupuncture in patients with temporomandibular dysfunction: a randomized controlled trial. Lasers Med Sci. 2013:1-10.

34. Kannan P. Management of myofascial pain of upper trapezius: a three group comparison study. Glob J Health Sci. [Clinical Trial

Comparative Study]. 2012 Sep;4(5):46-52.

35. Lin ML, Wu HC, Hsieh YH, Su CT, Shih YS, Lin CW, et al. Evaluation of the effect of laser acupuncture and cupping with ryodoraku and visual analog scale on low back pain. Evid Based Complement Alternat Med. 2012;2012.

36. Sattayut S, Bradley P. A study of influence of low intensity laser therapy on painful temporomandibular disorder patients. Laser Ther. 2012;21(3):183-92.

37. Skorupska E, Lisinski P, Samborski W. The effectiveness of the conservative versus myofascial pain physiotherapy in tennis elbow patients: double-blind randomized trial of 80 patients. J Musculoskelet Pain. 2012;20(1):41-50.

38. Lee JH, Han JT. The dose-dependent effect of an 830-nm, 450-mW low-level laser therapy on the myofacial trigger point of the upper trapezius muscle: a randomized, double-blinded, clinical trial. J Phys Ther Sci. 2011;23(6):933-5.

39. Rayegani SM, Bahrami MH, Samadi B, Sedighipour L, Mokhtarirad MR, Eliaspoor D. Comparison of the effects of low energy laser and ultrasound in treatment of shoulder myofascial pain syndrome: a randomized single-blinded clinical trial. Eur J Phys Rehabil Med. [Article]. 2011 Sep;47(3):381-90.

40. Emanet SK, Altan LI, Yurtkuran M. Investigation of the effect of gaas laser therapy on lateral epicondylitis. Photomed Laser Surg. 2010;28(3):397-403.

41. Glazov G. The influence of baseline characteristics on response to a laser acupuncture intervention: an exploratory analysis. Acupunct Med. 2010 Mar;28(1):6-11.

42. Katsoulis J, Ausfeld-Hafter B, Windecker-Gétaz I, Katsoulis K, Blagojevic N, Mericske-Stern R. Laser acupuncture for myofascial pain of the masticatory muscles. A controlled pilot study. Schweiz Monatsschr Zahnmed. 2010;120(3):213-25.

43. Öz S, Gökçen-Röhlig B, Saruhanoglu A, Tuncer EB. Management of myofascial pain: low-level laser therapy versus occlusal splints. J Craniofac Surg. 2010;21(6):1722-8.

44. Zhao L, Shen X, Cheng K, Deng H, Ding G, Tan M, et al. Validating a nonacupoint sham control for laser treatment of knee osteoarthritis. Photomed Laser Surg. 2010 Jun;28(3):351-6.

45. Carrasco TG, Guerisoli LD, Guerisoli DM, Mazzetto MO. Evaluation of low intensity laser therapy in myofascial pain syndrome. Cranio. 2009;27(4):243-7.

46. Glazov G, Schattner P, Lopez D, Shandley K. Laser acupuncture for chronic non-specific low back pain: a controlled clinical trial. Acupunct Med. 2009 Sep;27(3):94-100.

47. Shen X, Zhao L, Ding G, Tan M, Gao J, Wang L, et al. Effect of combined laser acupuncture on knee osteoarthritis: a pilot study. Lasers Med Sci. 2009;24(2):129-36.

48. Shirani AM, Gutknecht N, Taghizadeh M, Mir M. Low-level laser therapy and myofacial pain dysfunction syndrome: a randomized controlled clinical trial. Lasers Med Sci. 2009;24(5):715-20.

49. Shen XY, Ding GH, Wu F, Wang LZ, Zhao L, Wang M, et al. Effects of 650 nm - 10.6 μm combined laser acupuncture-moxibustion on knee osteoarthritis: a randomized, double-blinded and placebo-controlled clinical trial. J Acupunct Tuina Sci. 2008;6(5):315-7.

50. Dundar U, Evcik D, Samli F, Pusak H, Kavuncu V. The effect of gallium arsenide aluminum laser therapy in the management of cervical myofascial pain syndrome: a double blind, placebo-controlled study. Clin Rheumatol. 2007;26(6):930-4.

51. Lam LKY, Cheing GLY. Effects of 904-nm low-level laser therapy in the management of lateral epicondylitis: a randomized controlled trial. Photomed Laser Surg. 2007;25(2):65-71.

52. Matsutani LA, Marques AP, Ferreira EAG, Assumpção A, Lage LV, Casarotto RA, et al. Effectiveness of muscle stretching exercises with and without laser therapy at tender points for patients with fibromyalgia. Clin Exp Rheumatol. 2007;25(3):410-5.

53. Mazzetto MO, Carrasco TG, Bidinelo EF, Andrade Pizzo RC, Mazzetto RG. Low intensity laser application in temporomandibular disorders: a phase I double-blind study. Cranio [serial on the Internet]. 2007; (3): Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/304/CN-00611304/frame.html.

54. Yurtkuran M, Konur S, Ozcakir S, Bingol U. Laser acupuncture in knee osteoarthritis: a double-blind, randomized controlled study. Photomed Laser Surg. 2007;25(1):14-20.

55. Aigner N, Fialka C, Radda C, Vecsei V. Adjuvant laser acupuncture in the treatment of whiplash injuries: a prospective, randomized placebo-controlled trial. Wien Klin Wochenschr. 2006 Mar;118(3-4):95-9.

56. Armagan O, Tascioglu F, Ekim A, Oner C. Long-term efficacy of low level laser therapy in women with fibromyalgia: a placebo-controlled study. J Back Musculoskelet Rehabil. 2006;19(4):135-40.

57. Chow RT, Heller GZ, Barnsley L. The effect of 300 mW, 830 nm laser on chronic neck pain: a double-blind, randomized, placebo-controlled study. Pain. 2006;124(1-2):201-10.

58. Kiralp MZ, Ari H, Karabekir I, Dursun H. Comparison of low intensity laser therapy and trigger point injection in the management of myofascial pain syndrome. Pain Clinic. 2006;18(1):63-6.

59. Altan L, Bingöl U, Aykaç M, Yurtkuran M. Investigation of the effect of GaAs laser therapy on cervical myofascial pain syndrome. Rheumatol Int [serial on the Internet]. 2005; (1): Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/915/CN-00510915/frame.html.

60. Tam G. Effects of LLLT on the periarthritis of the shoulder: a clinical stydy on differents with, corticosteriod injections or a wait-and-see policy. Progress in Biomedical Optics and Imaging - Proceedings of SPIE; 2005; Florence.

61. Ceylan Y, Hizmetli S, Siliğ Y. The effects of infrared laser and medical treatments on pain and serotonin degradation products in patients with myofascial pain syndrome. A controlled trial. Rheumatol Int [serial on the Internet]. 2004; (5): Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/365/CN-00502365/frame.html http://link.springer.com/article/10.1007%2Fs00296-003-0348-6.

62. Chow RT, Barnsley L, Heller GZ, Siddall PJ. A pilot study of low-power laser therapy in the management of chronic neck pain. J Musculoskelet Pain. 2004;12(2):71-81.

63. Gur A, Sarac AJ, Cevik R, Altindag O, Sarac S. Efficacy of 904 nm gallium arsenide low level laser therapy in the management of chronic myofascial pain in the neck: a double-blind and randomize-controlled trial. Lasers Surg Med. 2004;35(3):229-35.

64. Ilbuldu E, Cakmak A, Disci R, Aydin R. Comparison of laser, dry needling, and placebo laser treatments in myofascial pain syndrome. Photomed Laser Surg. 2004;22(4):306-11.

65. Al-Shenqiti A, Oldham J. The use of low level laser therapy (LLLT) in the treatment of trigger points that are associated with rotator cuff tendonitis. Window on the Laser Medicine World; 2003; Bellingham: SPIE-Int Soc Optical Engineering.

66. Hakgüder A, Birtane M, Gürcan S, Kokino S, Turan FN. Efficacy of low level laser therapy in myofascial pain syndrome: an algometric and thermographic evaluation. Lasers Surg Med [serial on the Internet]. 2003; (5): Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/820/CN-00469820/frame.html.

67. Gür A, Karakoç M, Nas K, Çevik R, Saraç J, Demir E. Efficacy of low power laser therapy in fibromyalgia: a single-blind, placebo-controlled trial. Lasers Med Sci. 2002;17(1):57-61.

68. Wong W, Xiao S, Ip WY, Guo X, editors. Effects of a laser acupuncture therapy on treating pain. Proceedings of SPIE - The International Society for Optical Engineering; 2001; Florence.

69. Chen SM, Lin CP, Kuan TS, Chen JT, Hong CZ. Cold laser therapy on myofascial trigger points. 8th world congress of the international rehabilitation medicine association. 40128 Bologna: Monduzzi Editore; 1997. p. 605-10.

70. Conti PCR. Low level laser therapy in the treatment of temporomandibular disorders (TMD): a double-blind pilot study. Cranio. 1997;15(2):144-9.

71. Laakso EL, Richardson C, Cramond T. Pain scores and side effects in response to low level laser therapy (LLLT) for myofascial trigger points. Laser Ther. 1997;9(2):67-72.

72. Lögdberg-Andersson M, Mützell S, Hazel Å. Low level laser therapy (LLLT) of tendinitis and myofascial pains - a randomized, double-blind, controlled study. Laser Ther. 1997;9(2):79-85.

73. Papadopoulos ES, Smith RW, Cawley MID, Mani R. Low-level laser therapy does not aid the management of tennis elbow. Clin Rehabil. 1996;10(1):9-11.

74. Vecchio P, Cave M, King V, Adebajo AO, Smith M, Hazleman BL. A double-blind-study of the effectiveness of low-level laser treatment of rotator cuff tendinitis. Br J Rheumatol. [Article]. 1993 Aug;32(8):740-2.

75. Haker EHK, Lundeberg TCM. Lateral epicondylalgia - report of noneffective midlaser treatment. Arch Phys Med Rehabil. [Article]. 1991 Nov;72(12):984-8.

76. Haker E, Lundeberg T. Laser treatment applied to acupuncture points in lateral humeral epicondylalgia. A double-blind study. Pain. 1990;43(2):243-7.

77. Ceccherelli F, Altafini L, Lo Castro G, Avila A, Ambrosio F, Giron GP. Diode laser in cervical myofascial pain: a double-blind study versus placebo. Clin J Pain. 1989;5(4):301-4.

78. Snyder-Mackler L, Barry AJ, Perkins AI, Soucek MD. Effects of helium-neon laser irradiation on skin resistance and pain in patients with trigger points in the neck or back. Phys Ther. 1989;69(5):336-41.

79. Waylonis GW, Wilke S, O'Toole D, Waylonis DA, Waylonis DB. Chronic myofascial pain: management by low-output helium-neon laser therapy. Arch Phys Med Rehabil. 1988;69(12):1017-20.

80. Lundeberg T, Haker E, Thomas M. Effect of laser versus placebo in tennis elbow. Scand J Rehabil Med. 1987;19(3):135-8.

81. Snyder-Mackler L, Bork C, Bourbon B, Trumbore D. Effect of helium-neon laser on musculoskeletal trigger points. Phys Ther. 1986;66(7):1087-90.

82. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther. 2003;83(8):713.

83. Tumilty S, Munn J, McDonough S, Hurley DA, Basford JR, Baxter GD. Low level laser treatment of tendinopathy: a systematic review with meta-analysis. Photomed Laser Surg. 2010;28(1):3-16.

84. Birch S. Trigger point – acupuncture point correlations revisited. J Altern Complement Med. 2003;9(1):91-103.

85. Ahn AC, Colbert AP, Anderson BJ, Martinsen OG, Hammerschlag R, Cina S, et al. Electrical properties of acupuncture points and meridians: a systematic review. Bioelectromagnetics. 2008 May;29(4):245-56.

86. Melzack R, Stillwell DM, Fox EJ. Trigger points and acupuncture points for pain: correlations and implications. Pain. 1977;3(1):3-23.

87. Wick F, Wick N, Wick MC. Morphological analysis of human acupuncture points through immunohistochemistry. Am J Phys Med Rehabil. 2007;86(1):7-11.

88. Han J-S. Acupuncture analgesia: areas of consensus and controversy. Pain. 2011;152(3):S41-S8.

89. Terrin N, Schmid CH, Lau J. In an empirical evaluation of the funnel plot, researchers could not visually identify publication bias. J Clin Epidemiol. 2005;58(9):894-901.

90. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-6.

Appendices

Appendix A – Search strategy

Phase 1	Phase 2	Phase 3
1. acupunc*.mp.	18. exp pain/	29. exp clinical trial/
2. exp acupuncture/	19. exp “wounds and injuries”/	30. clinical trial.mp.
3. acupoint*.mp.	20. disorder.mp.	31. exp research design/
4. exp acupuncture points/	21. musculoskeletal.mp.	32. research design.mp.
5. exp acupuncture therapy/	22. injur*.mp.	33. random allocation/
6. trigger.mp.	23. pain.mp.	34. random*.mp.
7. exp trigger points/	24. exp musculoskeletal diseases/	35. double-blind method/
8. or/1-7	25. tend*.mp.	36. single-blind method/
9. therap*.mp.	26. backache.mp.	37. blind*.mp.
10. treatment.mp.	27. or/18-26	38. placebo*.mp.
11. or/9,10	28. and/17,27	39. placebos/
12. and/8,11		40. or/29-39
13. exp laser therapy, low-level/		41. human/
14. laser*.mp.		
15. LLLT.mp.		42. and/40,41
16. or/13-15		
17. and/12,16		43. and/28,42

Appendix B – Characteristics of the included studies – extended table

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Ferreira LA [33]	2013	Temporomandibular joint disorder	40	Laser acupuncture (20) vs. placebo (20)	Monthly until intervention completed	Pain – VAS Pain upon palpation – VAS Symptoms evolution	Both groups showed significant fewer symptoms after Rx. Laser group showed significant faster reduction in pain intensity comparing with placebo group.
Kannan P [34]	2012	Myofascial pain	45	Ultrasound (15) vs. laser (15) vs. ischemic compression (15)	End of intervention	Pain – VAS Tenderness upon palpation Movement of cervical spine	All groups showed significant improvement after Rx. Laser group had a significant reduction in pain compared to other two groups.
Lin ML [35]	2012	Low back pain	60	Laser acupuncture (21) vs. placebo (21)	After each session	Pain – VAS Ryodoraku value	Both groups showed significant less pain after Rx but no between group differences. There was a rebound of Ryodoraku value in laser group but not in placebo group.
Sattayut S [36]	2012	Temporomandibular joint disorder	30	Low energy density laser (10) vs. high energy density laser (10) vs. placebo (10)	After each session	PPT Maximum mouth opening MPQ Symptom severity index – VAS Jaw kinesiology – EMG	There were a greater number of patient reported recoveries in laser groups compared to placebo group. Laser groups showed a higher PPT and larger EMG amplitude.

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Skorupska E [37]	2012	Lateral epicondylitis	80	LLLT (40) vs. ultrasound (40) (trigger point application vs. anatomical site application; 20 in each subgroup)	End of intervention; 12-month	Pain – VAS Grip strength DASH questionnaire	All groups showed a significant less pain after Rx. Ultrasound group using trigger point application showed a more significant improvement in grip strength comparing to other three groups.
Lee JH [38]	2011	Myofascial trigger point pain	24	Laser (12) vs. placebo (12)	End of intervention	PPT	There was a significant higher PPT after 5 minutes Rx in laser group but not after 1 minute or 2 minutes Rx.
Rayegani SM [39]	2011	Myofascial pain	49	Laser (17) vs. ultrasound (16) vs. placebo laser (16)	6-week	Pain – VAS PPT Degree of disability – NDI	Laser group showed significant less pain and improved NDI score after Rx comparing to other two groups.
Emanet SK [40]	2010	Lateral epicondylitis	47	Laser acupuncture (24) vs. placebo (23)	End of intervention; 12-week after intervention	Pain – VAS PPT DASH questionnaire Grip strength NHP questionnaire PRTEE test	Both groups showed significant improvement in all outcome measures after Rx. Improvement retained in laser group at 12-week later.
Glazov G [41]	2010	Low back pain	100	Laser acupuncture (45) vs. placebo (45)	After each session; 6-week after intervention; 6-month after intervention	Change in pain – VAS Disability – ODI Patient global assessment Depression anxiety stress scale Subjective well-being – PWI-A Level of exercise Medication use	After adjustment for covariates, laser group showed significant less pain at 6-week follow up compared with placebo group.
Katsoulis J [42]	2010	Tendomyopathy	11	Laser (7) vs. placebo (4)	3-month after intervention	Pain – VAS Pain – verbal scale	All groups showed a significant less pain after Rx.

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Oz S [43]	2010	Myofascial pain	40	Laser (20) vs. occlusal splint (20)	End of intervention	Pain – VAS PPT Pain upon palpation/ mandibular movement – verbal scale	Both groups showed significant improvement in all parameter after Rx but no significant between two groups.
Zhao L [44]	2010	Knee osteoarthritis	40	Laser on acupuncture point (19) vs. Laser on sham point (17)	2-week; 4-week	Global improvement WOMAC Adverse effect Medication use	Laser group using acupuncture point showed significant better improvement in WOMAC score after 2-week Rx comparing with placebo group. No significant difference observed after 4-week.
Carrasco TG [45]	2009	Myofascial pain	60	Laser (30) vs. placebo (30) – 3 parameter groups;10 in each group	After 4 sessions; after 8 Rx; 15-day after intervention; 1-month after intervention	Pain – VAS	Both groups showed significant less pain after Rx but no significant between two groups.
Glazov G [46]	2009	Low back pain	100	Laser acupuncture (45) vs. placebo (45)	After each session; 6-week after intervention; 6-month after intervention	Pain – VAS Disability – ODI Patient global assessment Depression anxiety stress scale Subjective well-being – PWI-A Level of exercise Medication use	Both groups showed significant less pain and improvement in ODI score after Rx but no between group differences seen.
Shen X [47]	2009	Knee osteoarthritis	40	Laser acupuncture (20) vs. placebo (20)	2-week; 4-week	Global improvement WOMAC Adverse effect Medication use	Laser group using acupuncture point showed significant better improvement in WOMAC score after 2-week Rx compared with placebo group.

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Shirani AM [48]	2009	Myofascial pain	16	Laser acupuncture (8) vs. placebo (8)	After first session; 1-week; the day with complete pain relief	Change in Pain – VAS	Laser group showed significant less pain compared with placebo group.
Shen X [49]	2008	Knee osteoarthritis	48	Laser acupuncture (24) vs. placebo (24)	2-week; 4-week	Global improvement WOMAC Adverse effect Medication use	Both groups showed significant improvement in all outcome measures after Rx but no significant between two groups.
Dundar U [50]	2007	Myofascial pain	64	Laser acupuncture (32) vs. placebo (32)	4-week	Pain at rest/ movement/ night – VAS Active ROM Degree of disability – NDI	Both groups showed significant improvement in all outcome measures after Rx but no significant between two groups.
Lam L [51]	2007	Lateral epicondylitis	39	Laser acupuncture (21) vs. placebo (18)	After 5 sessions; end of intervention; 3-month after intervention	Pain – VAS Maximum grip strength PPT DASH questionnaire	Laser group showed a greater improvement from all outcome measures after Rx compared to placebo group.
Matsutani LA [52]	2007	Fibromyalgia	20	Laser (10) vs. no laser (10)	End of intervention	Pain – VAS PPT Life quality – FIQ SF-36	Both groups showed significant improvement in all outcome measures after Rx but no significant between two groups.
Mazzetto MO [53]	2007	Temporomandibular joint disorder	48	Laser (24) vs. placebo (24)	After 4 sessions; after 8 sessions; 30-day after intervention	Pain upon palpation – VAS	Laser group showed significant less pain after Rx comparing with placebo group.

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Yurtkuran M [54]	2007	Knee osteoarthritis	55	Laser (27) vs. placebo (25)	2-week; 12-week	Pain during movement – VAS WOMAC 50-foot walking time Knee circumference NHP questionnaire Medial tenderness score	Both groups showed significant improvement in all outcome measures after Rx. Laser group showed a significant decrease in knee circumference after 2-week.
Aigner N [55]	2006	Whiplash injury	50	Laser acupuncture (23) vs. placebo (22)	After each session; end of intervention; 8-12 months after injury	Cervical ROM Subjective symptoms	No significant difference observed at any time point between two groups.
Armagan O [56]	2006	Fibromyalgia	32	LLLT (16) vs. placebo (16)	End of intervention; 6-month after intervention	Global improvement No. of tender point Life quality – FIQ Morning stiffness Total myalgia score	LLLT group showed significant better in FIQ, global improvement, total myalgia after Rx and 6-month later. But placebo group only showed improvement in number of tender point and morning stiffness.
Chow RT [57]	2006	Chronic neck pain	90	Laser (45) vs. placebo (45)	7-week; 12-week	Change in pain – VAS NPNQ MPQ SF-36 NPAD Self-assessed improvement	Laser group showed a greater improvement from most of the outcome measures after Rx compared to placebo group.
Kiralp MZ [58]	2006	Myofascial pain	43	Laser (23) vs. trigger point injection (20)	End of intervention; 6-month after intervention	Pain – VAS/ verbal pain scale PPT	Both groups showed significant improvement in all outcome measures after Rx but no significant between two groups.

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Altan L [59]	2005	Myofascial pain	53	Laser (23) vs. placebo (25)	2-week; 12-week after intervention	Pain – VAS Trigger point tenderness Movement of cervical spine	Both groups showed significant improvement in all outcome measures after Rx but no significant between two groups.
Tam G [60]	2005	Periarthritis of shoulder	60	Corticosteroid injection (20) vs. LLLT (21) vs. wait-and-see policy (18)	3-week; 6-week; 12-week; 26-week; 52-week	Pain during the day – VAS General improvement PPT Shoulder disability Shoulder ROM Severity of main complaint	Corticosteroid injection group showed better improvement for all outcome measures at week 6 compared with the other two groups. Beyond week 26, LLLT group showed better result than the other two groups.
Ceylan Y [61]	2004	Myofascial pain	46	Laser (19) vs. placebo (20)	End of intervention	Pain upon palpation – VAS Seretonin level	Laser group showed significant less pain after Rx comparing with placebo group. Higher seretonin level was significant higher in laser group.
Chow RT [62]	2004	Chronic neck pain	20	Laser (10) vs. placebo (10)	7-week; 12-week	Pain – VAS NPNQ MPQ Self-assessed improvement	Laser group showed a greater improvement from pain related outcome measures after Rx comparing to placebo group. No significant difference observed from the result of SF-36.
Gur A [63]	2004	Myofascial pain	60	Laser (30) vs. placebo (30)	2-week; 3-week; 12-week	Pain at rest/ movement – VAS Number of trigger point NPAD Back depression inventory NHP questionnaire Self-assessed improvement	Laser group showed a greater improvement from all outcome measures after Rx. Only SAI and VAS score were significant comparing to placebo group.

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Ilbuldu E [64]	2004	Trigger point pain	60	Placebo laser (20) vs. dry needling (20) vs. laser (20)	End of intervention; 6-month	Pain – VAS PPT Cervical ROM Analgesic use NHP questionnaire	Laser group showed significant improvement in VAS and NHP score at end of intervention but not at 6-month.
Al-Shenqiti A [65]	2003	Rotator cuff tendinitis	55	Laser (26) vs. placebo (29)	End of intervention; 3-month	Pain – VAS PPT ROM Shoulder pain and disability index	Laser group showed a greater improvement from all outcome measures after Rx comparing to placebo group.
Hakguder A [66]	2003	Myofascial pain	62	Laser (31) vs. no laser (31)	End of intervention; 3-week after intervention	Pain – VAS PPT Thermography	Laser group showed significant less pain after Rx comparing with placebo group. Other outcome measures were not significant but favorable to laser group.
Gur A [67]	2002	Fibromyalgia	40	Laser (20) vs. placebo (20)	End of intervention	Pain – VAS Number of tender point Skin fold tenderness Sleep disturbance Muscle spasm Fatigue	Laser group showed significant less pain after Rx comparing with placebo group. Other outcome measures were not significant but favorable to laser group.
Wong W [68]	2001	Carpal tunnel syndrome	12	Laser (12) vs. placebo (12)	End of intervention	Pain – VAS Nerve conduction test MPQ Grip strength Pinch test Physical examination	Laser group showed a greater improvement from all outcome measures except pinch test after one stage of Rx comparing to placebo group.

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Chen SM [69]	1997	Myofascial pain	21	Placebo (5) vs. continuous laser (7) vs. pulsed laser (9)	End of intervention	Pain – VAS PPT Cervical ROM	All groups showed a significant less pain after Rx. Both laser groups showed a more significant improvement in PPT and ROM compared to placebo group.
Conti PCR [70]	1997	Temporomandibular joint disorder	20	Laser (10) vs. placebo (10)	After each session	Pain – VAS Mandibular function – active ROM	Laser group showed significant improvement in pain (myogeneous subgroup) and ROM (arthrogeneous subgroup) after Rx.
Laaksо EL [71]	1997	Myofascial trigger point pain	41	Red laser (15) vs. Infrared (IR) laser (16) vs. placebo (10)	Before each session; after each session	Pain – VAS	All groups showed a significant less pain after Rx. Between group differences were not significant
Logdberg-Andersson M [72]	1997	Tendinitis & myofascial pain	176	Laser (92) vs. placebo (84)	End of intervention; 4-week after intervention	Pain – VAS PPT	Laser group showed a greater improvement from all outcome measures after Rx.
Papadopoulos ES [73]	1996	Lateral epicondylitis	29	Laser (14) vs. placebo (15)	After 4 sessions; after 6 sessions	Pain – VAS Marcy wedge pro exerciser	No significant difference observed at any time point between two groups.
Vecchio P [74]	1993	Rotator cuff tendinitis	35	Laser (19) vs. placebo (16)	2-week; 4-week; 8-week	Change in pain at rest/ movement/ night – VAS Scoring of painful arc Pain on resisted abduction Shoulder ROM Functional limitation	Both groups showed improvement in all outcome measures after Rx but not significant between groups.

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Haker E [75]	1991	Lateral epicondylitis	60	Laser (29) vs. placebo (29)	End of intervention; 3-month; 6-month; 12-month	Pain – NRS Physical examination - Palpation/ resisted testing/ passive stretching Grip strength Lifting test	No significant difference observed at any time point between groups.
Haker E [76]	1990	Lateral epicondylitis	49	Laser acupuncture (23) vs. placebo (26)	End of intervention; 3-month; 12-month	Pain – NRS Grip strength	No significant difference observed at any time point between groups.
Ceccherelli F [77]	1989	Myofascial pain	27	Laser (13) vs. placebo (14)	End of intervention; 3-month after intervention	Pain – VAS MPQ	Laser group showed significant less pain after Rx and at 3-month comparing with placebo group.
Snyder-Mackler L [78]	1989	Myofascial trigger point pain	24	Laser (13) vs. placebo (11)	Before each session; after each session	Pain – VAS Skin resistance	Laser group showed significant less pain and increase in skin resistance after Rx.
Waylonis GW [79]	1988	Fibromyalgia/ chronic myofascial pain	55	Placebo vs. laser acupuncture	6-week after each round of intervention; 60-day; 120-day	MPQ Detailed questionnaire – medication use/ effect on work/ recreational performance	No significant difference observed at any time point between groups.

First author	*Year*	*Diagnosis*	*n*	*Interventions*	*Follow-up*	*Outcome measures*	*Results*
Lundeberg T [80]	1987	Lateral epicondylitis	57	Placebo (19) vs. GaAs laser (19) vs. HeNe laser (19)	Every two week; end of intervention; 3-month; 6-month	Pain – VAS Grip strength Pain on wrist dorsiflexion/ weight/ load Patient and medical assessment of outcome Nerve conduction	No significant difference observed at any time point between groups.
Snyder-Mackler L [81]	1986	Musculoskeletal trigger point pain	27	Laser (13) vs. placebo (11)	Before each session; after each session	Skin resistance	Laser group showed significant increase in skin resistance after Rx.

Abbreviations: DASH – Disability of the arm, shoulder and hand; EMG – Electromyography; FIQ – Fibromyalgia impact questionnaire; MPQ – McGill pain questionnaire; NDI – Neck disability index; NHP – Nottingham health profile; NRS – Numeric rating scale; NPAD – Neck Pain Disability Scale; NPNQ – Northwick Park Neck Pain Questionnaire; ROM – Range of motion; SF-36 – 36-item Short-form health survey; ODI – Oswestry disability index; PPT – Pressure pain threshold; PRTEE – Patient related tennis elbow evaluation; PWI-A – Personal well-being index (adult); VAS – Visual Analogue Scale; WOMAC – Western Ontario and McMaster Universities Arthritis Index

Appendix C - Quality assessment using PEDro scale with itemized criteria

	PEDro criteria*											
First author	(1)	2	3	4	5	6	7	8	9	10	11	**Score**
Ferreira LA [33]	Y	Y		Y	Y		Y			Y	Y	**6**
Kannan P [34]	Y	Y						Y		Y	Y	**4**
Lin ML [35]	Y	Y		Y						Y	Y	**4**
Sattayut S [36]	Y	Y			Y	Y		Y		Y	Y	**6**
Skorupska E [37]	Y	Y		Y	Y		Y	Y	Y	Y	Y	**8**
Lee JH [38]	Y	Y			Y		Y	Y		Y		**5**
Rayegani SM [39]	Y	Y	Y	Y	Y		Y				Y	**6**
Emanet SK [40]	Y			Y	Y		Y	Y		Y		**5**
Glazov G [41]	Y	Y	Y	Y	Y	Y	Y	Y		Y	Y	**9**
Katsoulis J [42]							Y	Y				**2**
Oz S [43]	Y	Y	Y		Y		Y	Y		Y	Y	**7**
Zhao L [44]	Y	Y	Y	Y	Y					Y	Y	**6**
Carrasco TG [45]	Y	Y			Y	Y	Y			Y	Y	**6**
Glazov G [46]	Y	Y	Y	Y	Y	Y	Y	Y		Y	Y	**9**
Shen X [47]	Y	Y	Y	Y	Y		Y			Y	Y	**7**
Shirani AM [48]	Y	Y		Y	Y		Y			Y	Y	**6**
Shen X [49]	Y	Y		Y	Y			Y		Y		**5**
Dundar U [50]	Y	Y	Y	Y	Y		Y	Y	Y	Y	Y	**9**
Lam L [51]	Y	Y		Y	Y			Y	Y	Y	Y	**7**
Matsutani LA [52]	Y	Y		Y						Y	Y	**4**
Mazzetto MO [53]	Y	Y			Y	Y				Y		**4**
Yurtkuran M [54]	Y	Y	Y	Y	Y		Y	Y		Y	Y	**8**
Aigner N [55]		Y			Y			Y		Y		**4**
Armagan O [56]	Y	Y		Y	Y		Y	Y	Y	Y	Y	**8**
Chow RT [57]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**10**
Kiralp MZ [58]	Y	Y		Y				Y		Y	Y	**5**
Altan L [59]	Y	Y		Y	Y		Y	Y		Y	Y	**7**
Tam G [60]	Y	Y	Y				Y	Y		Y	Y	**6**
Ceylan Y [61]	Y	Y								Y	Y	**3**
Chow RT [62]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**10**

Gur A [63]	Y	Y	Y	Y		Y	Y	Y	Y	Y	**8**
Ilbuldu E [64]	Y	Y	Y	Y		Y	Y	Y	Y	Y	**8**
Al-Shenqiti A [65]	Y	Y	Y	Y	Y	Y	Y		Y	Y	**8**
Hakguder A[66]	Y	Y	Y			Y	Y		Y	Y	**6**
Gur A [67]	Y	Y	Y	Y			Y	Y		Y	**6**
Wong W [68]	Y	Y		Y			Y		Y	Y	**5**
Chen SM [69]	Y	Y					Y				**2**
Conti PCR [70]	Y	Y	Y	Y		Y	Y	Y	Y		**7**
Laaskso EL [71]		Y		Y	Y	Y			Y		**5**
Logdberg-Andersson M [72]	Y			Y	Y	Y	Y		Y		**5**
Papadopoulos ES [73]	Y	Y		Y	Y		Y	Y	Y		**6**
Vecchio P [74]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**9**
Haker E [75]	Y	Y	Y	Y	Y	Y					**5**
Haker E [76]	Y	Y		Y	Y	Y	Y		Y	Y	**7**
Ceccherelli F [77]	Y	Y	Y	Y	Y		Y	Y	Y	Y	**8**
Snyder-Mackler L [78]		Y		Y	Y		Y	Y	Y		**6**
Waylonis GW [79]	Y	Y		Y			Y		Y		**4**
Lundeberg T [80]	Y	Y		Y	Y	Y				Y	**5**
Snyder-Mackler L [81]		Y	Y		Y	Y		Y		Y		**5**

*PEDro criteria:		4	Baseline comparability	8	Adequate follow-up
(1)	Eligibility criteria	5	Blind subjects	9	Intention-to-treat analysis
2	Random allocation	6	Blind therapists	10	Between-group comparisons
3	Concealed allocation	7	Blind assessors	11	Point estimates and variability

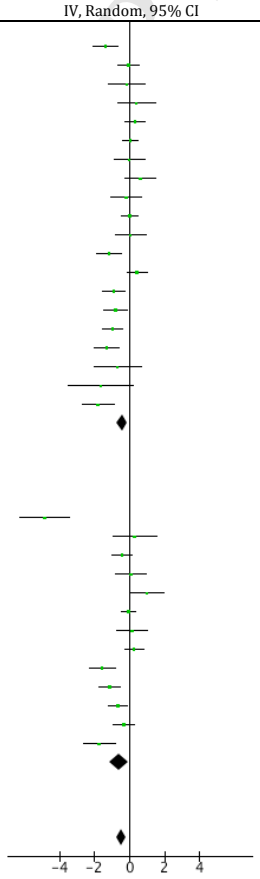
Y – Criteria met; (1) – Eligibility criteria item does not contribute to total score

Appendix D – Forest plots of outcome measures

1. Effects on pain scores

1.1 Laser acupuncture vs placebo

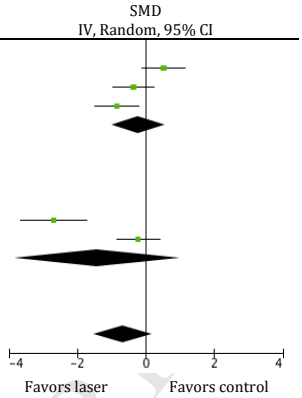
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD IV, Random, 95%CI
1.1.1 Measured at the end of intervention								
Ferreira 2013	0.05	0.22	20	2.75	2.71	20	3.2%	-1.38 [-2.07, -0.68]
Lin 2012	3.11	1.54	21	3.2	1.84	21	3.4%	-0.05 [-0.66, 0.55]
Sattayut 2012 (1)	4.5	2.58	10	5.0	3.38	5	2.5%	-0.17 [-1.24, 0.91]
Sattayut 2012 (2)	6.1	2.29	10	5.0	3.38	5	2.5%	0.39 [-0.70, 1.47]
Emanet 2010	1.13	0.94	23	0.83	0.88	24	3.5%	0.32 [-0.25, 0.90]
Glazov 2009	3.55	2.437	43	3.45	2.4669	44	3.7%	0.04 [-0.38, 0.46]
Carrasco 2009 (3)	6.73	1.65	10	6.75	1.49	10	2.9%	-0.01 [-0.89, 0.86]
Carrasco 2009 (4)	7.04	1.72	10	5.97	1.6	10	2.8%	0.62 [-0.29, 1.52]
Carrasco 2009 (5)	6.4	2.32	10	6.8	1.74	10	2.9%	-0.19 [-1.07, 0.69]
Dundar 2007	3.2	2.5	32	3.2	2.3	32	3.6%	0.00 [-0.49, 0.49]
Matsutani 2007	4.7	2.9	10	4.6	2.0	10	2.9%	0.04 [-0.84, 0.92]
Lam 2007	3.05	1.77	21	5.39	2.12	18	3.3%	-1.18 [-1.87, -0.49]
Altan 2005	4.13	0.58	23	3.92	0.42	25	3.5%	0.41 [-0.16, 0.98]
Ilbuldu 2004	2.05	1.43	20	3.65	2.03	20	3.3%	-0.89 [-1.55, -0.24]
Ceylan 2004	34.54	23.5	19	54.96	25.89	20	3.3%	-0.81 [-1.46, -0.15]
Gur 2004	3.11	2.29	28	5.79	3.12	26	3.5%	-0.97 [-1.54, -0.40]
Gur 2002	1.27	0.76	20	2.44	0.98	20	3.3%	-1.31 [-2.00, -0.62]
Chen 1997 (6)	1.94	1.87	9	3.25	1.32	3	2.0%	-0.68 [-2.03, 0.67]
Chen 1997 (7)	0.83	1.29	7	3.25	1.32	2	1.4%	-1.66 [-3.54, 0.21]
Ceccherelli 1989	9.46	13.17	13	37.42	16.58	14	2.8%	-1.80 [-2.72, -0.89]
Subtotal (95% CI)			359			339	60.3%	-0.43 [-0.74, -0.12]
Heterogeneity: $Tau^2 = 0.33$; $Chi^2 = 68.26$, df = 19 (P < 0.00001); $I^2 = 72\%$								
Test for overall effect: Z = 2.71 (P = 0.007)								
1.1.2 Measured during the follow-up period (6 to 26 weeks)								
Rayegani 2011	20.5	4.1231	17	40.7	4.0	16	1.9%	-4.85 [-6.27, -3.43]
Katsoulis 2010	3.25	2.248	7	2.65	0.7362	4	2.2%	0.29 [-0.95, 1.53]
Emanet 2010	0.29	0.47	23	0.57	0.79	24	3.5%	-0.42 [-1.00, 0.16]
Carrasco 2009 (8)	5.67	2.99	10	5.4	3.06	10	2.9%	0.09 [-0.79, 0.96]
Carrasco 2009 (9)	6.91	2.24	10	4.63	2.1	10	2.7%	1.01 [0.06, 1.95]
Glazov 2009	3.95	2.437	43	4.1	2.6313	44	3.7%	-0.06 [-0.48, 0.36]
Carrasco 2009 (10)	7.14	2.68	10	6.75	2.45	10	2.9%	0.15 [-0.73, 1.02]
Yurtkuran 2007	5.58	2.36	27	4.81	3.49	25	3.5%	0.26 [-0.29, 0.80]
Lam 2007	1.48	1.36	21	4.28	2.11	18	3.2%	-1.57 [-2.30, -0.84]
Altan 2005	3.17	0.58	23	3.8	0.51	25	3.4%	-1.14 [-1.75, -0.52]
Gur 2004	4.18	2.65	28	6.29	3.52	26	3.5%	-0.67 [-1.22, -0.12]
Ilbuldu 2004	2.12	1.9	20	2.89	2.63	20	3.4%	-0.33 [-0.95, 0.30]
Ceccherelli 1989	8.46	10.76	13	35.57	18.28	14	2.8%	-1.74 [-2.64, -0.83]
Subtotal (95% CI)			252			246	39.7%	-0.61 [-1.12, -0.10]
Heterogeneity: $Tau^2 = 0.72$; $Chi^2 = 82.70$, df = 12 (P < 0.00001); $I^2 = 85\%$								
Test for overall effect: Z = 2.33 (P = 0.02)								
Total (95% CI)			611			585	100.0%	-0.49 [-0.76, -0.22]
Heterogeneity: $Tau^2 = 0.46$; $Chi^2 = 151.41$, df = 32 (P < 0.00001); $I^2 = 79\%$								
Test for overall effect: Z = 3.57 (P = 0.0004)								
Test for subgroup differences: $Chi^2 = 0.36$, df = 1 (P = 0.55), $I^2 = 0\%$								



(1) High energy laser; placebo group data divided; (2) Low energy laser; placebo group data divided; (3) Laser dose: 105J/cm²; (4) Laser dose: 25J/cm²; (5) Laser dose: 60J/cm²; (6) Pulsed laser; placebo group data divided; (7) Continuous laser; placebo group data divided; (8) Laser dose: 60J/cm²; (9) Laser dose: 25J/cm²; (10) Laser dose: 105J/cm²

1.2 Laser acupuncture vs other control interventions

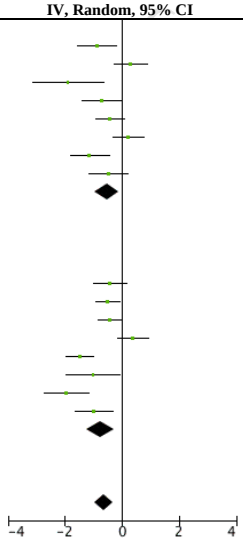
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD IV, Random, 95%CI
1.2.1 Measured at the end of intervention								
Kannan 2012	2.66	1.23	15	2.18	0.7058	30	20.5%	0.52 [-0.11, 1.15]
Kiralp 2006	2.18	1.63	23	2.77	1.57	20	20.7%	-0.36 [-0.97, 0.24]
Ilbuldu 2004	2.05	1.43	20	3.71	2.33	20	20.4%	-0.84 [-1.49, -0.19]
Subtotal (95% CI)			58			70	61.6%	-0.23 [-1.00, 0.54]
Heterogeneity: $Tau^2 = 0.36$; $Chi^2 = 9.00$, df = 2 (P = 0.01); $I^2 = 78\%$								
Test for overall effect: Z = 0.58 (P = 0.56)								
1.2.1 Measured during the follow-up period (6 to 26 weeks)								
Rayegani 2011	20.5	4.1231	17	30.7	3.2	16	17.8%	-2.69 [-3.66, -1.71]
Ilbuldu 2004	2.12	1.9	20	2.59	2.18	20	20.6%	-0.23 [-0.85, 0.40]
Subtotal (95% CI)			37			36	38.4%	-1.43 [-3.84, 0.98]
Heterogeneity: $Tau^2 = 2.85$; $Chi^2 = 17.49$, df = 1 (P < 0.0001); $I^2 = 94\%$								
Test for overall effect: Z = 1.16 (P = 0.25)								
Total (95% CI)			95			106	100.0%	-0.66 [-1.51, 0.18]
Heterogeneity: $Tau^2 = 0.81$; $Chi^2 = 31.42$, df = 4 (P < 0.00001); $I^2 = 87\%$								
Test for overall effect: Z = 1.54 (P = 0.12)								
Test for subgroup differences: $Chi^2 = 0.86$, df = 1 (P = 0.35), $I^2 = 0\%$								



2. Effects on change in pain scores

2.1 Laser acupuncture vs placebo

Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD IV, Random, 95%CI
2.1.1 Measured at the end of intervention								
Zhao 2010	-49.21	34.19	19	-11.99	47.78	17	6.0%	-0.88 [-1.57, -0.20]
Emanet 2010	-54.0	36.0	23	-65.0	35.0	24	6.6%	0.30 [-0.27, 0.88]
Shirani 2009	-5.375	2.6152	8	-1.25	1.2817	8	3.7%	-1.89 [-3.13, -0.66]
Shen 2009	-49.0	34.0	19	-13.0	62.0	16	6.0%	-0.72 [-1.41, -0.03]
Dundar 2007	-24.0	20.0	32	-16.0	18.0	32	7.0%	-0.42 [-0.91, 0.08]
Yurtkuran 2007	-18.0	31.0	27	-25.0	35.0	25	6.8%	0.21 [-0.34, 0.75]
Ceylan 2004	-27.41	14.41	19	-11.44	13.03	20	6.1%	-1.14 [-1.82, -0.46]
Vecchio 1993	-3.9	3.0512	19	-2.2	4.0	16	6.1%	-0.47 [-1.15, 0.20]
Subtotal (95% CI)			**166**			**158**	**48.4%**	**-0.53 [-0.95, -0.10]**
Heterogeneity: Tau² = 0.25; Chi² = 23.43, df = 7 (P = 0.001); I² = 70%								
Test for overall effect: Z = 2.44 (P = 0.01)								
2.1.2 Measured during the follow-up period (6 to 26 weeks)								
Emanet 2010	-87.0	22.0	23	-76.0	28.0	24	6.6%	-0.43 [-1.01, 0.15]
Glazov 2010 (1)	-35.2	45.2463	43	-12.4	45.7694	44	7.3%	-0.50 [-0.92, -0.07]
Glazov 2010 (2)	-35.0	46.5578	43	-14.8	47.0961	44	7.3%	-0.43 [-0.85, -0.00]
Yurtkuran 2007	-14.0	37.0	27	-30.0	47.0	25	6.7%	0.37 [-0.17, 0.92]
Chow 2006	-2.7	1.9971	45	0.3	1.9971	45	7.1%	-1.49 [-1.96, -1.02]
Chow 2004	-65.9	34.8483	10	-29.82	33.1723	10	4.8%	-1.02 [-1.96, -0.07]
Lundeberg 1987 (3)	-2.6	0.2	19	-2.2	0.2	19	5.6%	-1.96 [-2.75, -1.17]
Lundeberg 1987 (4)	-2.4	0.2	19	-2.2	0.2	19	6.1%	-0.98 [-1.66, -0.30]
Subtotal (95% CI)			**229**			**230**	**51.6%**	**-0.77 [-1.25, -0.29]**
Heterogeneity: Tau² = 0.38; Chi² = 39.72, df = 7 (P < 0.00001); I² = 82%								
Test for overall effect: Z = 3.16 (P = 0.002)								
Total (95% CI)			**395**			**388**	**100.0%**	**-0.65 [-0.97, -0.34]**
Heterogeneity: Tau² = 0.31; Chi² = 66.29, df = 15 (P < 0.00001); I² = 77%								
Test for overall effect: Z = 4.04 (P < 0.0001)								
Test for subgroup differences: Chi² = 0.55, df = 1 (P = 0.46), I² = 0%								



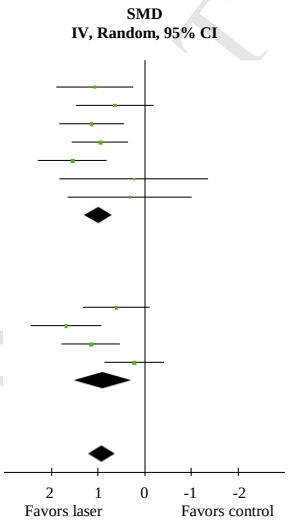
(1) Pain at baseline imputed for missing value; posthoc analysis; (2) Pain at last assessment imputed for missing value; posthoc analysis
(3) Ga-As laser; (4) He-Ne laser

3. Effects on pressure pain threshold

3.1 Laser acupuncture vs placebo

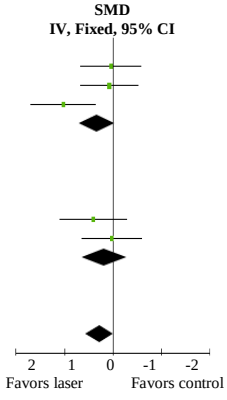
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD IV, Random, 95%CI
3.1.1 Measured at the end of intervention								
Sattayut 2012	93.9	30.387	20	61.1	27.57	10	8.5%	1.08 [0.27, 1.90]
Lee 2011	2.14	0.64	12	1.7	0.66	12	8.3%	0.65 [-0.17, 1.48]
Lam 2007	2.59	0.99	21	1.49	0.87	18	10.6%	1.15 [0.47, 1.83]
Altan 2005	80.26	2.54	23	77.69	2.69	25	12.2%	0.97 [0.36, 1.57]
Ilbuldu 2004	3.99	1.22	20	2.45	0.62	20	10.0%	1.56 [0.84, 2.28]
Chen 1997 (1)	2.53	0.4	7	2.4	0.82	2	3.0%	0.24 [-1.34, 1.82]
Chen 1997 (2)	2.74	0.99	9	2.4	0.82	3	4.1%	0.33 [-0.99, 1.64]
Subtotal (95% CI)			**112**			**90**	**56.6%**	**1.02 [0.72, 1.33]**
Heterogeneity: Tau² = 0.00; Chi² = 5.13, df = 6 (P = 0.53); I² = 0%								
Test for overall effect: Z = 6.58 (P < 0.00001)								
3.1.2 Measured during the follow-up period (6 to 26 weeks)								
Rayegani 2011	41.0	32.9848	17	24.4	16.0	16	10.3%	0.62 [-0.08, 1.32]
Lam 2007	3.8	1.26	21	1.87	0.91	18	9.5%	1.70 [0.95, 2.44]
Altan 2005	81.97	3.03	23	78.47	2.88	25	11.9%	1.17 [0.55, 1.78]
Ilbuldu 2004	2.26	0.52	20	2.13	0.58	20	11.8%	0.23 [-0.39, 0.85]
Subtotal (95% CI)			**81**			**79**	**43.4%**	**0.91 [0.30, 1.53]**
Heterogeneity: Tau² = 0.28; Chi² = 10.18, df = 3 (P = 0.02); I² = 71%								
Test for overall effect: Z = 2.91 (P = 0.004)								
Total (95% CI)			**193**			**169**	**100.0%**	**0.95 [0.66, 1.24]**
Heterogeneity: Tau² = 0.08; Chi² = 15.68, df = 10 (P = 0.11); I² = 36%								
Test for overall effect: Z = 6.47 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.10, df = 1 (P = 0.76), I² = 0%								

(1) Continuous laser; placebo group data divided; (2) Pulsed laser; placebo group data divided



3.2 Laser acupuncture vs other control interventions

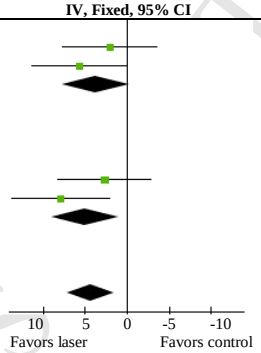
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD IV, Fixed, 95%CI
3.2.1 Measured at the end of intervention								
Oz 2010	28.8917	7.0851	20	28.5467	6.5037	20	21.1%	0.05 [-0.57, 0.67]
Kiralp 2006	2.766	4.34	23	2.414	4.18	20	22.5%	0.08 [-0.52, 0.68]
Ilbuldu 2004	3.99	1.22	20	2.51	1.57	20	18.4%	1.03 [0.37, 1.70]
Subtotal (95% CI)			**63**			**60**	**62.0%**	**0.35 [-0.01, 0.71]**
Heterogeneity: Chi² = 5.72, df = 2 (P = 0.06); I² = 65%								
Test for overall effect: Z = 1.91 (P = 0.06)								
3.2.2 Measured during the follow-up period (6 to 26 weeks)								
Rayegani 2011	41.0	32.9848	17	29.0	22.8	16	17.0%	0.41 [-0.28, 1.10]
Ilbuldu 2004	2.26	0.52	20	2.24	0.73	20	21.1%	0.03 [-0.59, 0.65]
Subtotal (95% CI)			**37**			**36**	**38.0%**	**0.20 [-0.26, 0.66]**
Heterogeneity: Chi² = 0.64, df = 1 (P = 0.42); I² = 0%								
Test for overall effect: Z = 0.85 (P = 0.39)								
Total (95% CI)			**100**			**96**	**100.0%**	**0.29 [0.01, 0.58]**
Heterogeneity: Chi² = 6.63, df = 4 (P = 0.16); I² = 40%								
Test for overall effect: Z = 2.03 (P = 0.04)								
Test for subgroup differences: Chi² = 0.26, df = 1 (P = 0.61), I² = 0%								



4. Effects on functional scores

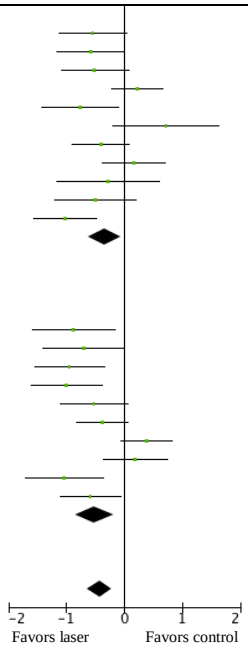
4.1 Hand grip

Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95%CI
4.1.1 Measured at the end of intervention								
Emanet 2010	22.58	11.6	23	20.45	7.68	24	25.4%	2.13 [-3.52, 7.78]
Lam 2007	25.29	8.26	21	19.56	9.75	18	24.7%	5.73 [0.01, 11.45]
Subtotal (95% CI)			**44**			**42**	**50.1%**	**3.91 [-0.11, 7.93]**
Heterogeneity: Chi² = 0.77, df = 1 (P = 0.38); I² = 0%								
Test for overall effect: Z = 1.90 (P = 0.06)								
4.1.2 Measured during the follow-up period (6 to 26 weeks)								
Emanet 2010	25.63	10.91	23	22.91	8.1	24	26.6%	2.72 [-2.79, 8.23]
Lam 2007	29.57	8.96	21	21.61	9.7	18	23.3%	7.96 [2.06, 13.86]
Subtotal (95% CI)			**44**			**42**	**49.9%**	**5.16 [1.14, 9.19]**
Heterogeneity: Chi² = 1.62, df = 1 (P = 0.20); I² = 38%								
Test for overall effect: Z = 2.51 (P = 0.01)								
Total (95% CI)			**88**			**84**	**100.0%**	**4.53 [1.69, 7.38]**
Heterogeneity: Chi² = 2.58, df = 3 (P = 0.46); I² = 0%								
Test for overall effect: Z = 3.12 (P = 0.002)								
Test for subgroup differences: Chi² = 0.19, df = 1 (P = 0.66), I² = 0%								



4.2 Scale expressed in raw score

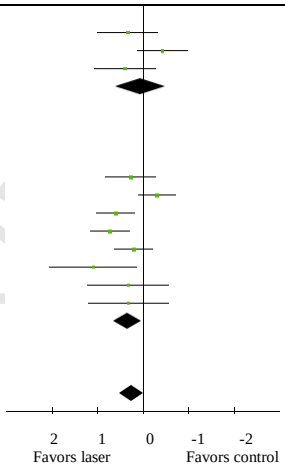
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD IV, Random, 95%CI
4.2.1 Measured at the end of intervention								
Emanet 2010 DASH	30.16	16.4	23	37.96	11.27	24	4.9%	-0.55 [-1.13, 0.04]
Emanet 2010 NHP	113.03	92.63	23	167.4	92.63	24	4.9%	-0.58 [-1.16, 0.01]
Emanet 2010 PRTEE	42.53	16.66	23	49.89	11.27	24	4.9%	-0.51 [-1.09, 0.07]
Glazov 2009 ODI	25.0	11.8652	38	22.3	12.1945	40	5.8%	0.22 [-0.22, 0.67]
Lam 2007 DASH	23.41	15.05	21	37.26	20.45	18	4.4%	-0.76 [-1.42, -0.11]
Matsutani 2007 FIQ	5.6	1.5	10	4.1	2.4	10	3.2%	0.72 [-0.19, 1.63]
Dundar 2007 NDI	18.8	10.9	32	23.7	12.9	32	5.4%	-0.41 [-0.90, 0.09]
Yurtkuran 2007 NHP	7.26	5.58	27	6.31	5.76	25	5.1%	0.17 [-0.38, 0.71]
Matsutani 2007 SF-36	59.3	17.9	10	64.7	18.9	10	3.3%	-0.28 [-1.16, 0.60]
Armagan 2006 FIQ	58.5	10.3	16	63.63	9.59	16	4.2%	-0.50 [-1.21, 0.20]
Gur 2004 NHP	41.48	26.19	30	69.61	27.92	30	5.1%	-1.03 [-1.57, -0.49]
Subtotal (95% CI)			**253**			**253**	**51.1%**	**-0.34 [-0.63, -0.06]**
Heterogeneity: Tau² = 0.13; Chi² = 24.13, df = 10 (P = 0.007); I² = 59%								
Test for overall effect: Z = 2.37 (P = 0.02)								
4.2.2 Measured during the follow-up period (6 to 26 weeks)								
Rayegani 2011 NDI (1)	13.0	16.4924	17	37.8	36.0	16	4.1%	-0.87 [-1.59, -0.15]
Rayegani 2011 NDI (2)	13.0	16.4924	17	27.6	24.0	16	4.2%	-0.70 [-1.40, 0.01]
Emanet 2010 DASH	18.09	12.74	23	30.5	12.94	24	4.7%	-0.95 [-1.56, -0.34]
Emanet 2010 PRTEE	26.84	14.06	23	40.77	13.42	24	4.7%	-1.00 [-1.61, -0.39]
Emanet 2010 NHP	76.55	81.17	23	127.0	105.13	24	4.9%	-0.53 [-1.11, 0.06]
Glazov 2009 PWI-A	64.2	18.1355	40	71.1	17.9705	42	5.8%	-0.38 [-0.82, 0.06]
Glazov 2009 ODI	27.1	12.1695	38	22.4	12.1945	40	5.8%	0.38 [-0.07, 0.83]
Yurtkuran 2007 NHP	7.58	5.41	27	6.44	6.27	25	5.1%	0.19 [-0.35, 0.74]
Lam 2007 DASH	15.79	11.59	21	31.58	17.98	18	4.3%	-1.04 [-1.72, -0.37]
Gur 2004 NHP	56.41	29.18	30	72.48	24.66	30	5.3%	-0.59 [-1.10, -0.07]
Subtotal (95% CI)			**259**			**259**	**48.9%**	**-0.51 [-0.84, -0.19]**
Heterogeneity: Tau² = 0.19; Chi² = 29.42, df = 9 (P = 0.0006); I² = 69%								
Test for overall effect: Z = 3.09 (P = 0.002)								
Total (95% CI)			**512**			**512**	**100.0%**	**-0.42 [-0.63, -0.21]**
Heterogeneity: Tau² = 0.15; Chi² = 54.15, df = 20 (P < 0.0001); I² = 63%								
Test for overall effect: Z = 3.94 (P < 0.0001)								
Test for subgroup differences: Chi² = 0.61, df = 1 (P = 0.43), I² = 0%								



(1) vs placebo; (2) vs ultrasound

4.3 Scale expressed in change in score

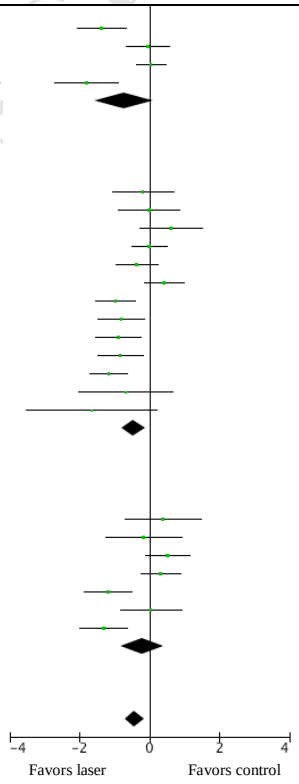
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD IV, Random, 95%CI
4.3.1 Measured at the end of intervention								
Zhao 2010 WOMAC	26.16	11.73	19	13.93	49.27	17	8.2%	0.34 [-0.32, 1.00]
Shen 2009 WOMAC	25.0	32.0	19	4.0	65.0	16	8.0%	0.41 [-0.26, 1.09]
Yurtkuran 2007 WOMAC	5.0	24.0	27	13.0	11.0	25	9.7%	-0.42 [-0.97, 0.13]
Subtotal (95% CI)			**65**			**58**	**26.0%**	**0.08 [-0.47, 0.63]**
Heterogeneity: Tau² = 0.13; Chi² = 4.63, df = 2 (P = 0.10); I² = 57%								
Test for overall effect: Z = 0.30 (P = 0.76)								
4.3.2 Measured during the follow-up period (6 to 26 weeks)								
Yurtkuran 2007 WOMAC	8.0	19.0	27	2.0	23.0	25	9.8%	0.28 [-0.27, 0.83]
Chow 2006 SF-36 MCS	2.4	8.987	45	5.4	10.9841	45	11.9%	-0.30 [-0.71, 0.12]
Chow 2006 NPQ	3.5	5.3256	45	0.6	3.9942	45	11.8%	0.61 [0.19, 1.03]
Chow 2006 NPAD	15.2	17.3083	45	3.1	14.9784	45	11.7%	0.74 [0.31, 1.17]
Chow 2006 SF-36 PCS	3.2	8.6542	45	1.3	8.6542	45	11.9%	0.22 [-0.20, 0.63]
Chow 2004 NPQ	0.12	0.1138	10	0.0070	0.0791	10	5.2%	1.10 [0.15, 2.06]
Chow 2004 SF-36 PCS	4.0	8.2219	10	1.71	3.7947	10	5.8%	0.34 [-0.54, 1.23]
Chow 2004 SF-36 MCS	1.71	3.7947	10	0.0	6.0083	10	5.8%	0.33 [-0.56, 1.21]
Subtotal (95% CI)			**237**			**235**	**74.0%**	**0.37 [0.07, 0.67]**
Heterogeneity: Tau² = 0.10; Chi² = 16.80, df = 7 (P = 0.02); I² = 58%								
Test for overall effect: Z = 2.39 (P = 0.02)								
Total (95% CI)			**302**			**293**	**100.0%**	**0.29 [0.03, 0.56]**
Heterogeneity: Tau² = 0.11; Chi² = 23.51, df = 10 (P = 0.009); I² = 57%								
Test for overall effect: Z = 2.19 (P = 0.03)								
Test for subgroup differences: Chi² = 0.79, df = 1 (P = 0.37), I² = 0%								



Appendix E – Forest plots of subgroup analysis of different application site of laser acupuncture

1. Pain measured at the end of intervention

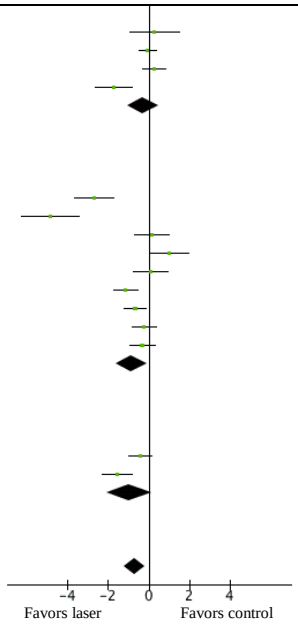
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD IV, Random, 95%CI
1.1 Acupuncture point								
Ferreira 2013	0.05	0.22	20	2.75	2.71	20	4.4%	-1.38 [-2.07, -0.68]
Lin 2012	3.11	1.54	21	3.2	1.84	21	4.7%	-0.05 [-0.66, 0.55]
Glazov 2009	3.55	2.437	43	3.45	2.4669	44	5.3%	0.04 [-0.38, 0.46]
Ceccherelli 1989	9.46	13.17	13	37.42	16.58	14	3.7%	-1.80 [-2.72, -0.89]
Subtotal (95% CI)			**97**			**99**	**18.1%**	**-0.74 [-1.59, 0.11]**
Heterogeneity: Tau² = 0.64; Chi² = 22.01, df = 3 (P < 0.0001); I² = 86%								
Test for overall effect: Z = 1.70 (P = 0.09)								
1.2 Trigger point								
Carrasco 2009 (1)	6.4	2.32	10	6.8	1.74	10	3.8%	-0.19 [-1.07, 0.69]
Carrasco 2009 (2)	6.73	1.65	10	6.75	1.49	10	3.8%	-0.01 [-0.89, 0.86]
Carrasco 2009 (3)	7.04	1.72	10	5.97	1.6	10	3.7%	0.62 [-0.29, 1.52]
Dundar 2007	3.2	2.5	32	3.2	2.3	32	5.1%	0.00 [-0.49, 0.49]
Kiralp 2006	2.18	1.63	23	2.77	1.57	20	4.7%	-0.36 [-0.97, 0.24]
Altan 2005	4.13	0.58	23	3.92	0.42	25	4.8%	0.41 [-0.16, 0.98]
Gur 2004	3.11	2.29	28	5.79	3.12	26	4.9%	-0.97 [-1.54, -0.40]
Ceylan 2004	34.54	23.5	19	54.96	25.89	20	4.5%	-0.81 [-1.46, -0.15]
Ilbuldu 2004 (4)	2.05	1.43	20	3.65	2.03	20	4.5%	-0.89 [-1.55, -0.24]
Ilbuldu 2004 (5)	2.05	1.43	20	3.71	2.33	20	4.6%	-0.84 [-1.49, -0.19]
Hakguder 2003	3.41	2.0	31	5.77	2.0	31	4.9%	-1.17 [-1.71, -0.62]
Chen 1997 (6)	1.94	1.87	9	3.25	1.32	3	2.5%	-0.68 [-2.03, 0.67]
Chen 1997 (7)	0.83	1.29	7	3.25	1.32	2	1.6%	-1.66 [-3.54, 0.21]
Subtotal (95% CI)			**242**			**229**	**53.5%**	**-0.46 [-0.80, -0.12]**
Heterogeneity: Tau² = 0.23; Chi² = 34.64, df = 12 (P = 0.0005); I² = 65%								
Test for overall effect: Z = 2.67 (P = 0.008)								
1.3 Tender point								
Sattayut 2012 (8)	6.1	2.29	10	5.0	3.38	5	3.2%	0.39 [-0.70, 1.47]
Sattayut 2012 (9)	4.5	2.58	10	5.0	3.38	5	3.2%	-0.17 [-1.24, 0.91]
Kannan 2012	2.66	1.23	15	2.18	0.7058	30	4.6%	0.52 [-0.11, 1.15]
Emanet 2010	1.13	0.94	23	0.83	0.88	24	4.8%	0.32 [-0.25, 0.90]
Lam 2007	3.05	1.77	21	5.39	2.12	18	4.4%	-1.18 [-1.87, -0.49]
Matsutani 2007	4.7	2.9	10	4.6	2.0	10	3.8%	0.04 [-0.84, 0.92]
Gur 2002	1.27	0.76	20	2.44	0.98	20	4.4%	-1.31 [-2.00, -0.62]
Subtotal (95% CI)			**109**			**112**	**28.4%**	**-0.21 [-0.83, 0.40]**
Heterogeneity: Tau² = 0.52; Chi² = 27.33, df = 6 (P = 0.0001); I² = 78%								
Test for overall effect: Z = 0.68 (P = 0.49)								
Total (95% CI)			**448**			**440**	**100.0%**	**-0.43 [-0.71, -0.16]**
Heterogeneity: Tau² = 0.33; Chi² = 86.13, df = 23 (P < 0.00001); I² = 73%								
Test for overall effect: Z = 3.07 (P = 0.002)								
Test for subgroup differences: Chi² = 1.00, df = 2 (P = 0.61), I² = 0%								



(1) Laser dose: 60J/cm^2 ; (2) Laser dose: 105J/cm^2; (3) Laser dose: 25J/cm^2; (4) vs placebo; (5) vs dry needling;
(6) Pulsed laser; placebo group data divided; (7) Continuous laser; placebo group data divided;
(8) Low energy laser; placebo group data divided; (9) High energy laser; placebo group data divided

2. Pain measured during the follow-up period (6 to 26 weeks)

Study or Subgroup	Laser Mean	Laser SD	Laser Total	Placebo Mean	Placebo SD	Placebo Total	Weight	SMD IV, Random, 95%CI
2.1 Acupuncture point								
Katsoulis 2010	3.25	2.248	7	2.65	0.7362	4	5.4%	0.29 [-0.95, 1.53]
Glazov 2009	3.95	2.437	43	4.1	2.6313	44	7.6%	-0.06 [-0.48, 0.36]
Yurtkuran 2007	5.58	2.36	27	4.81	3.49	25	7.4%	0.26 [-0.29, 0.80]
Ceccherelli 1989	8.46	10.76	13	35.57	18.28	14	6.4%	-1.74 [-2.64, -0.83]
Subtotal (95% CI)			**90**			**87**	**26.7%**	**-0.29 [-1.05, 0.47]**
Heterogeneity: Tau² = 0.45; Chi² = 14.55, df = 3 (P = 0.002); I² = 79%								
Test for overall effect: Z = 0.74 (P = 0.46)								
2.2 Trigger point								
Rayegani 2011 (1)	20.5	4.1231	17	30.7	3.2	16	6.2%	-2.69 [-3.66, -1.71]
Rayegani 2011 (2)	20.5	4.1231	17	40.7	4.0	16	4.9%	-4.85 [-6.27, -3.43]
Carrasco 2009 (3)	7.14	2.68	10	6.75	2.45	10	6.5%	0.15 [-0.73, 1.02]
Carrasco 2009 (4)	6.91	2.24	10	4.63	2.1	10	6.3%	1.01 [0.06, 1.95]
Carrasco 2009 (5)	5.67	2.99	10	5.4	3.06	10	6.5%	0.09 [-0.79, 0.96]
Altan 2005	3.17	0.58	23	3.8	0.51	25	7.2%	-1.14 [-1.75, -0.52]
Gur 2004	4.18	2.65	28	6.29	3.52	26	7.4%	-0.67 [-1.22, -0.12]
Ilbuldu 2004 (6)	2.12	1.9	20	2.59	2.18	20	7.2%	-0.23 [-0.85, 0.40]
Ilbuldu 2004 (7)	2.12	1.9	20	2.89	2.63	20	7.2%	-0.33 [-0.95, 0.30]
Subtotal (95% CI)			**155**			**153**	**59.1%**	**-0.87 [-1.64, -0.10]**
Heterogeneity: Tau² = 1.21; Chi² = 73.34, df = 8 (P < 0.00001); I² = 89%								
Test for overall effect: Z = 2.21 (P = 0.03)								
2.3 Tender point								
Emanet 2010	0.29	0.47	23	0.57	0.79	24	7.3%	-0.42 [-1.00, 0.16]
Lam 2007	1.48	1.36	21	4.28	2.11	18	6.9%	-1.57 [-2.30, -0.84]
Subtotal (95% CI)			**44**			**42**	**14.2%**	**-0.97 [-2.10, 0.15]**
Heterogeneity: Tau² = 0.55; Chi² = 5.87, df = 1 (P = 0.02); I² = 83%								
Test for overall effect: Z = 1.70 (P = 0.09)								
Total (95% CI)			**289**			**282**	**100.0%**	**-0.71 [-1.21, -0.22]**
Heterogeneity: Tau² = 0.80; Chi² = 103.25, df = 14 (P < 0.00001); I² = 86%								
Test for overall effect: Z = 2.82 (P = 0.005)								
Test for subgroup differences: Chi² = 1.49, df = 2 (P = 0.47), I² = 0%								



(1) vs ultrasound; (2) vs placebo; (3) Laser dose: 105J/cm^2; (4) Laser dose: 25J/cm^2; (5) Laser dose: 60J/cm^2; (6) vs dry needling; (7) vs placebo