Pain Research and Management

Management of Chronic Pain: Integrating Manual Therapy, Dry Needling, and Exercise

Lead Guest Editor: César Fernández-de-las-Peñas
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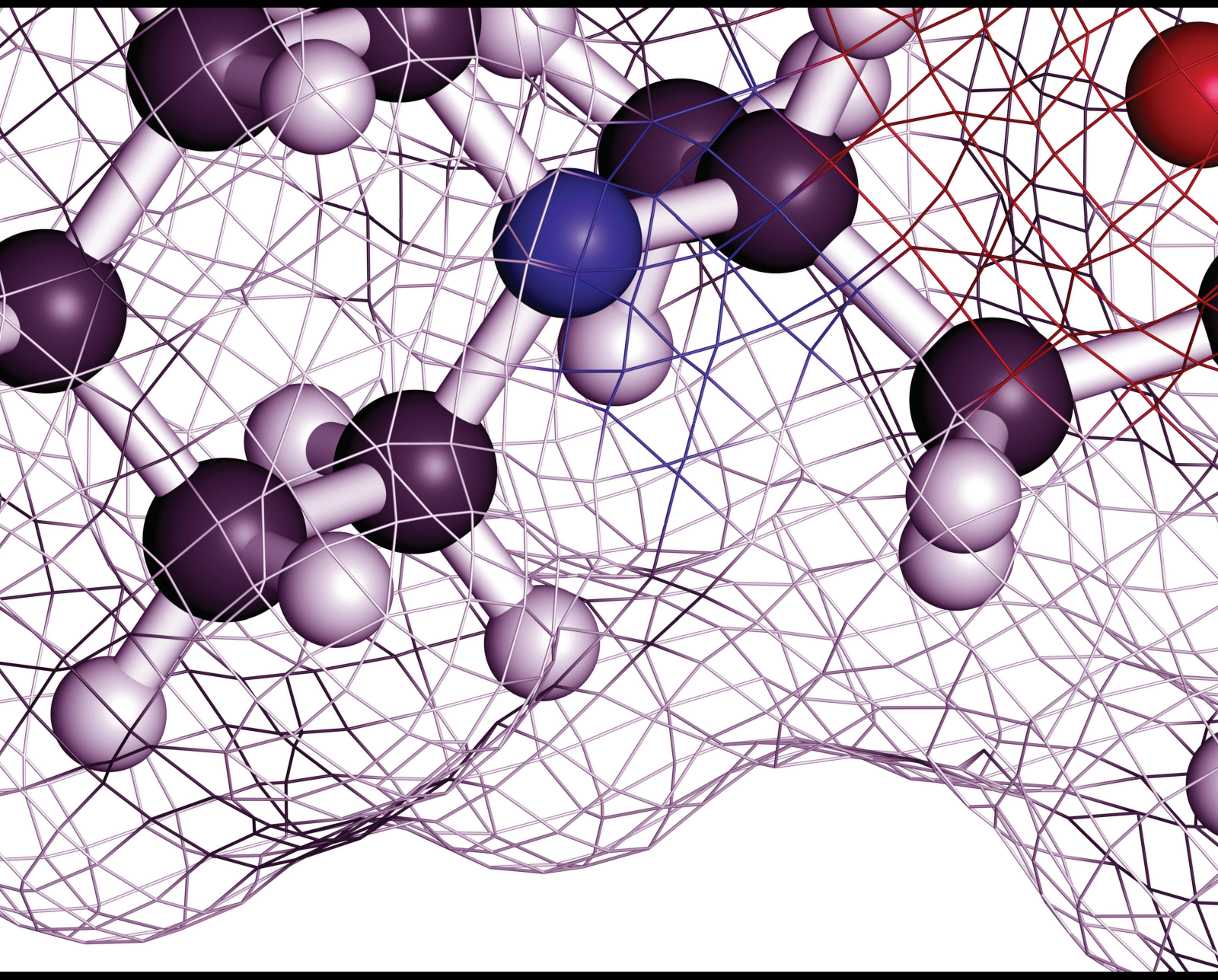

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Contents

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Review Article

Acupuncture for Chronic Pain-Related Depression: A Systematic Review and Meta-Analysis

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Objective. The aim of this systematic review was to summarize and evaluate the existing evidence on the effectiveness and safety of acupuncture in relieving chronic pain-related depression (CPRD). *Methods*. We searched seven online databases to identify eligible randomized controlled trials (RCTs) of acupuncture for CPRD published before September 2020. We included studies that used acupuncture as the intervention group, with or without a control group, and the control group was treated with conventional drugs. Meta-analysis was performed using RevMan 5.3 software. For outcomes, assessments were performed using the Hamilton Depression Scale (HAMD), Visual Analogue Scale (VAS), and adverse events. *Results*. Eight studies involving 636 participants were identified and included in the meta-analysis. The results showed that single acupuncture treatment and drug treatment have the same effect in improving the HAMD score (MD = −0.14, 95% CI = [−0.88, 0.59], $P = 0.71$) and alleviating the VAS score (MD = −0.42, 95% CI = [−1.10, −0.27], $P = 0.23$), but acupuncture treatment is safer (OR = 0.03, 95% CI = [0.01, 0.21], $P = 0.0003$). In addition, acupuncture combined with drugs (control group) is more beneficial than single-drug treatment in improving the HAMD score (MD = −2.95, 95% CI = [−3.55, −2.36], $P < 0.00001$) and alleviating the VAS score (MD = −1.06, 95% CI = [−1.65, −0.47], $P = 0.0004$). *Conclusion*. Acupuncture is an effective and safe treatment for CPRD, and acupuncture combined with drug therapy is more effective than single-drug therapy. Nevertheless, the conclusions were limited due to the low quality and a small number of included studies.

1. Introduction

Chronic pain (CP) is defined as pain that continues beyond 3 months. Internationally, no less than 20% of adults (18–65 years) and more than 33% of older adults (>65 years) suffer from CP [1]. In addition, the latest estimates claim that CP affects approximately 1.5 billion people worldwide, and these numbers are rising steadily [2]. In the United States, CP is thought to affect more than 116 million adults, which is higher than the combined prevalence of heart disease, diabetes, and cancer [2]. Due to the high prevalence of CP, it has brought a heavy economic burden to the healthcare system and society. In European countries, pain caused by chronic low back pain and musculoskeletal diseases has been proven to cost up to 2% of the gross domestic product (GDP) [3], while in the United States, the annual cost of CP treatment can be as high as $635 billion [4]. In addition, CP can not only lead to a reduction in the quality of life of patients but also has a huge negative impact on the mental health of patients. Studies have shown that CP is often accompanied by a wide range of mental disorders, of which depression is one of the more common comorbidities [5].

Depression, the fourth leading cause of disability worldwide, is defined as a psychological problem characterized by negative mood, hopelessness, and despair [6, 7]. In most developed countries, the lifetime prevalence of major depression is 16.2% [8]. Additionally, it is estimated that depression and its related diseases will become the main contributor to the global burden of disease by 2030 [9]. According to reports, the average prevalence of major depression in CP patients is about 50% [9], and the anxiety or major depression of patients with pain increases 2.5–10

times compared with the general population [10, 11]. This striking level of comorbidity suggests that there may be a bidirectional relationship between CP and depression. That is, CP can cause negative emotions such as anxiety and depression, and negative emotions can also lead to and accelerate pain. The existence of pain has a significant negative impact on the clinical management of depression, making the treatment of depression more complicated, and depression has a similar impact on the clinical management of pain [12, 13].

In this study, CPRD was defined as a type of comorbid depression associated with CP, with clinical manifestations of CP and depression. Depression can be caused by pain, or depression itself exists and is accompanied by pain symptoms, both of which are considered in this study. Although the pathogenesis of CPRD is still unclear, in primary care, the guidelines suggest CPRD is primarily managed with antidepressants and painkillers [14–16]. These therapies are associated with low remission rates and high dropout rates [17], and the use of these drugs is also limited by serious side effects, such as dependence, gastrointestinal reactions, and allergies [18]. In addition, psychotherapy is considered to be a safe and effective treatment method, but the clinical application of psychotherapy is limited by the lack of qualified therapists. Therefore, it is an urgent research question to find an alternative treatment that can alleviate relieve both depressive symptoms and coexisting pain [5].

Acupuncture, an alternative nondrug treatment, is an important part of traditional Chinese medicine and involves the use of thin needles to stimulate specific acupoints on the human body. In China, acupuncture has been widely used to treat diseases for at least 3000 years. In addition, acupuncture is also one of the most popular alternative therapies in the world. Modern research has shown that acupuncture can stimulate the neuroendocrine of the body by stimulating specific points on the body. Therefore, acupuncture has a satisfactory therapeutic effect on diseases involving neuroendocrine pathological changes (such as chronic pain, menopause, depression, and insomnia) [19, 20], with a very rare occurrence of adverse events.

Although the benefits of acupuncture treatment of CP and depression have been widely reported [21–24], a recent meta-analysis on acupuncture for chronic pain with depression found that acupuncture is efficient and safe therapy [25]. However, the experimental group of the study consisted of single acupuncture and acupuncture combined with other therapies, and the study did not perform a subgroup analysis of the interventions of the experimental group. These factors affected the accuracy of the conclusions of the study. Therefore, we conducted this study to evaluate the existing evidence from RCTs to separately evaluate the effectiveness and safety of acupuncture and acupuncture-related comprehensive therapies for CPRD.

2. Methods

This systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement and was registered at PROSPERO (number CRD42019146188) [26].

2.1. Search Strategy. We searched digital databases for RCTs which evaluated the effectiveness of acupuncture for CPRD, including Embase, PubMed, Cochrane Library, WanFang, CNKI, VIP, and the Chinese SinoMed Database (up to September 2020). The keywords used for the search consist of three parts: chronic pain (e.g., musculoskeletal pain, back pain), depression (e.g., depression, affective disorder, affective symptoms, mood), and acupuncture (e.g., acupuncture, electroacupuncture needling, acupoint). The complete search terms are shown in Supplementary Materials. References of related articles were manually checked for potential eligible RCTs for inclusion.

2.2. Inclusion and Exclusion Criteria. Studies were included if the following situations were met: (1) types of studies: Only RCTs of acupuncture therapy for CPRD were included. RCTs were published in English or Chinese; (2) types of participants: Participants met the diagnosis of depression and chronic pain at the same time; (3) type of intervention: The only experimental treatments allowed are manual acupuncture or electroacupuncture alone, or either of these combined with the control group (drugs); (4) types of control groups: The control group should be conventional drug therapy, and the method, dosage, and course of treatment were reported in detail. There are no restrictions on the drugs used here, including western medicine and Chinese herbal medicine, and they may also include drugs that are no longer used in some countries (for example, Deanxit); (5) types of outcome measures: primary outcomes were Hamilton Depression Scale (HAMD) and Visual Analogue Scale (VAS), the secondary outcome was adverse events; (6) Full text should be available.

The exclusion situations included the following: (1) Non-RCTs; (2) RCTs that compared different kinds of acupuncture; (3) duplicate studies; (4) case reports; (5) animal experiments.

2.3. Data Extraction. Two authors (Jianyu You, Haiyan Li) independently extracted relevant data from studies that met the inclusion criteria. Key information included the first author, publication year, sample size, baseline characteristics of participants, intervention, major outcomes (measured at the end of treatment), and adverse events. If there is any uncertainty, we will resolve it through discussion or consultation with the corresponding author (Rixin Chen).

2.4. Quality Assessment. The quality and risk of bias (ROB) of the included RCTs were independently evaluated by two authors (Jianyu You, Haiyan Li) using the Cochrane risk of bias assessment tool [27]. The contents include (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; (7) other sources of bias. For each item,

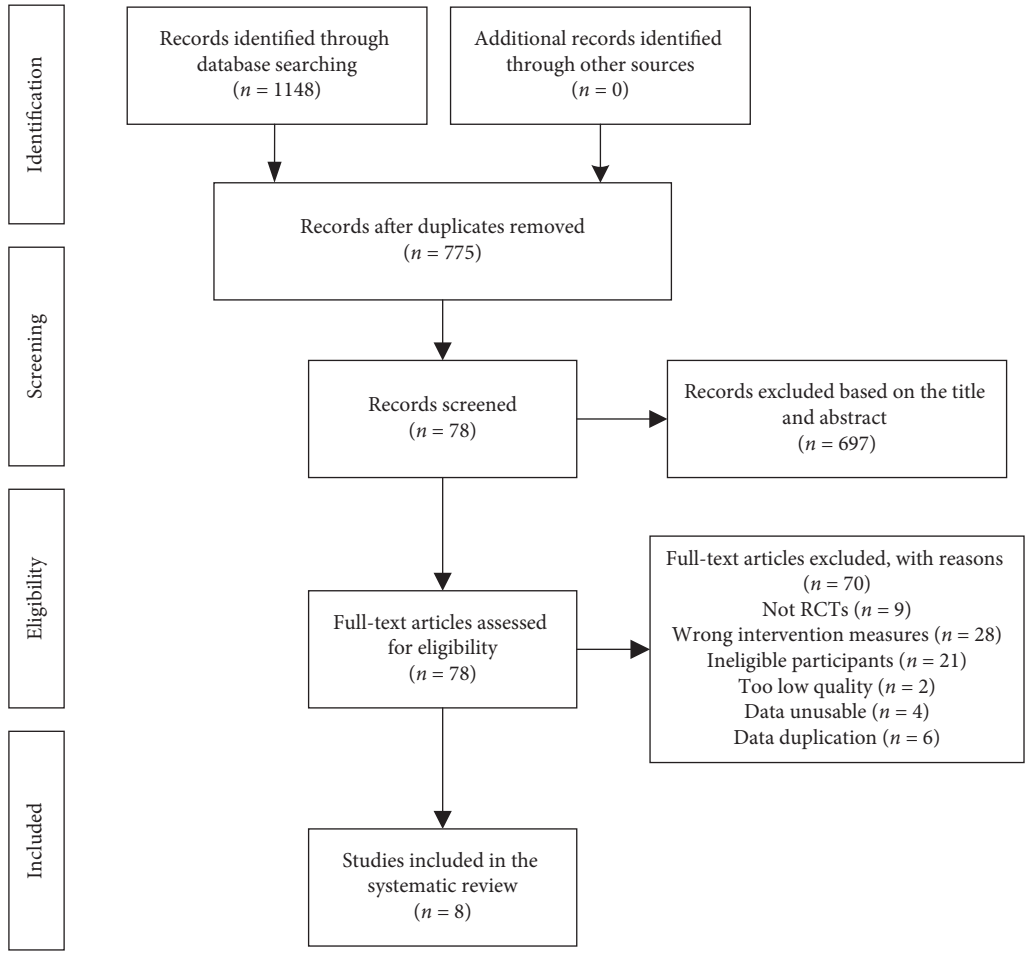

Figure 1: Flow diagram of the study.

ROB was graded as high, unclear, or low. Discrepancies were resolved through discussion with the corresponding author (Rixin Chen).

2.5. Statistical Analysis. Data analysis was performed using Reviewer Manager software. For continuous data (HAMD and VAS), we estimated the combined mean difference (MD) with 95% confidence intervals (CI); for the dichotomous data (adverse events), we calculated the combined odds ratio (OR) with 95% CI. Heterogeneity was evaluated by Higgins I^2 test and chi-square test. When $I^2 \leq 50\%$, $P \geq 0.10$, and the fixed effect model was applied; otherwise, the random effect model was used, and subgroup analysis was performed to explore heterogeneity. Subgroup analyses were carried out according to the different intervention measures. If the number of included studies was insufficient, we did not assess publication bias.

3. Results

3.1. Literature Search Results. A total of 1148 studies were retrieved from all initial searches. 775 studies remained after we excluded 373 duplicates, and 697 studies were eliminated based on the title and abstract. Then, the eligibility of the remaining 78 studies was evaluated by scanning the full text. Finally, 8 RCTs [28–35] met the inclusion criteria and were included in the systematic review. The screening process is shown in Figure 1.

3.2. Basic Information of Included Studies. We included a total of 8 RCTs, involving 636 participants, including 316 in the experimental group and 320 in the control group. All studies were conducted in China, including one article [29] published in English and seven published in Chinese. The sample size of included studies ranges from 40 to 128. There were three studies [28, 29, 33] that compared single acupuncture with drugs, and the remaining five studies compared acupuncture-combined drugs with drugs. One study [28] used electroacupuncture, and the other seven studies used manual acupuncture. Characteristics of included studies are shown in Table 1.

3.3. Quality Assessment. Among all the included 8 RCTs, five studies [29–31, 33, 34] used a random number table to generate random sequences for grouping and were assessed as low ROB. One study [35] was randomized according to the order of admission of participants and was assessed as having a high ROB. The remaining studies did not mention the method or details of random

Table 1: Characteristics of included studies.

Study	Sample size	Mean age (SD)	Sex (male/female)	Diagnosis	Interventions' group	Control group	Treatment period	Outcomes
Huang and Luo [28]	65	30.39 ± 7.01	25/40	Depression: CCMD-2-R CP : CD	EA	Medicine (amitriptyline)	T: once a day, six times per week for 6 weeks, 20 min C: once a day for 6 weeks	HAMD, AE
Cao et al. [29]	60	NR	23/37	CD	MA	Medicine (Deanxit)	T: once a day, five times per week for 4 weeks, 30 min C: twice a day for the first 10 days and once a day for the next 18 days for 4 weeks	HAMD, VAS, AE
Liu et al. [30]	90	T: 47 ± 8 C: 48 ± 8	T: 15/30 C: 16/29	Depression: CCMD-3 CP : CD	MA + C	Medicine (SSRI antidepressants)	T: once every two days for 4 weeks, 30 min; drug treatment was the same as the control group C: once a day for 4 weeks	HAMD, VAS
Zhao et al. [31]	60	NR	T: 12/18 C: 11/19	Depression: CD CP : ICHD	MA + C	Medicine (diclofenac sodium)	T: twice a day, 6 times a week for 30 days, 30 minutes; drug treatment was the same as the control group C: once a day for 30 days	HAMD
Ma et al. [32]	128	T: 39.93 ± 12.93 C: 38.69 ± 14.19	T: 27/37 C: 29/35	Depression: ICD-10 CP : CD	MA + C	Medicine (duloxetine + benzodiazepines)	T: five times per week for 8 weeks, 20 min; drug treatment was the same as the control group C: duloxetine once a day for 8 weeks, benzodiazepines were used according to the needs of the disease	HAMD, VAS, AE
Yu et al. [33]	40	T: 41 ± 8 C: 40 ± 7	T: 6/14 C: 8/12	Depression: CD CP : CCMD-3	MA	Medicine (Deanxit)	T: once a day, six times a week for 8 weeks, 50 min : twice a day for 8 weeks	HAMD, VAS, AE

Table 1: Continued.

Study	Sample size	Mean age (SD)	Sex (male/female)	Diagnosis	Interventions' group	Control group	Treatment period	Outcomes
Luo et al. [34]	84	T: 57.15 ± 11.26 C: 57.39 ± 11.58	T: 22/20 C: 23/19	CD	MA + C	Medicine (Chinese herbal medicine)	T: once a day for 4 weeks, 30 min; drug treatment was the same as the control group C: one dose a day for 4 weeks	HAMD, VAS, AE
Huang et al. [35]	109	T: 45.36 ± 2.78 C: 45.72 ± 2.79	T: 24/31 C: 22/32	Chinese diagnostic criteria	MA + C	Medicine (Deanxit or fluoxetine + olanzapine)	T: five times a week for 2 months, 30 min; drug treatment was the same as the control group C: moderate depression: Deanxit twice a day for two months; severe depression: fluoxetine once a day for two months, olanzapine was used according to the needs of the disease	HAMD, AE

AE: adverse events; C: control group; CCMD: Chinese Classification of Mental Disorders; CD: clinical diagnosis; EA: electroacupuncture; HAMD: Hamilton Depression Scale; ICD: International Classification of Diseases; ICHD: International Classification of Headache Disorders; MA: manual acupuncture; NR: not reported; T: therapy group; VAS: Visual Analogue Scale.

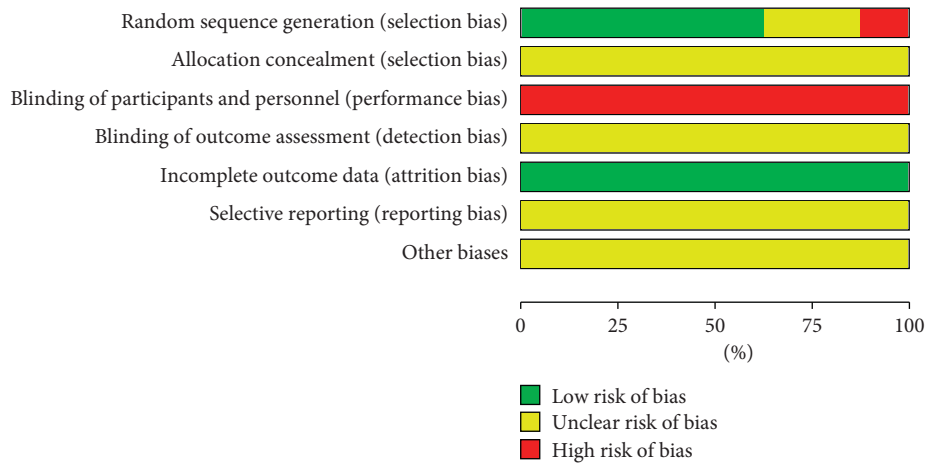

Figure 2: Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

sequence generation and were judged as unclear ROB. No studies mentioned the details of the use of allocation concealment, and all studies were assessed as unclear ROB. Due to the characteristics of acupuncture therapy, it is difficult to perform blinding operations. Therefore, all studies were judged to have a high ROB in blinding. No study reported the blinding details about outcome assessment, and all studies were considered to have an unclear ROB. All studies had no loss of outcome data and were considered to have a low ROB. Since all included studies have no published protocol or trial registration records, the reporting bias of all included studies was considered to have an unclear ROB. All studies were judged as unclear ROB due to a lack of clear evidence to show the existence of other biases. The ROB summary is presented in Figures 2 and 3.

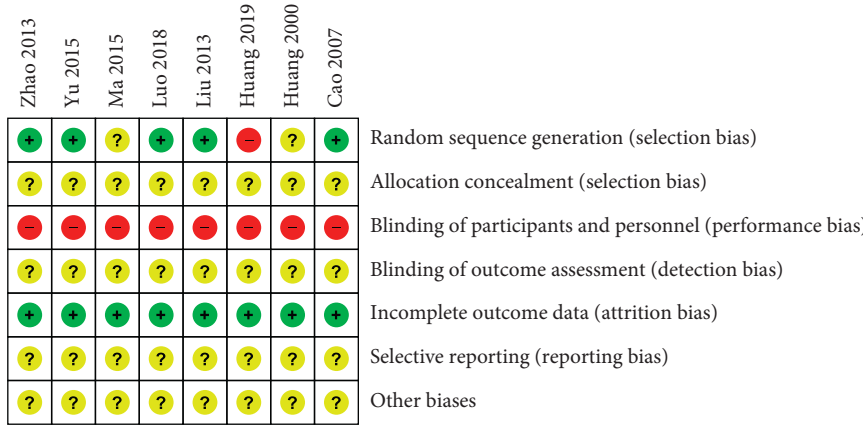

Figure 3: Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

3.4. HAMD Score. All studies evaluated the severity of depression by using the HAMD score. Three studies [28, 29, 33] compared acupuncture with drugs, and five studies [30–32, 34, 35] compared acupuncture combination drugs with drugs alone. Due to the high heterogeneity ($P < 0.00001$, $I^2 = 82\%$), we used a random-effects model. The results show that experimental groups could further relieve depression compared with control groups (MD = −1.97, 95% CI = [−3.14, −0.80], $P < 0.00001$). Subgroup analysis also showed that acupuncture combination drugs are statistically significantly better than single drugs (MD = −2.95, 95% CI = [−3.55, −2.36], $P < 0.00001$). However, acupuncture only was not statistically superior to drugs alone (MD = −0.14, 95% CI [−0.88, 0.59], $P = 0.71$) (Figure 4).

3.5. VAS Score. Five studies [29, 30, 32–34] evaluated pain intensity by using the VAS score. Two studies [29, 33] compared acupuncture with drugs, aND three studies [30, 32, 34] compared acupuncture combination drugs with drugs alone. The random-effects model was used due to the heterogeneity in the data ($P = 0.001$, $I^2 = 77\%$). The results show that experimental groups could further relieve pain compared with the control group (MD = −0.83, 95% CI = [−1.35, −0.32], $P = 0.001$). Subgroup analysis also showed that acupuncture combination drugs are statistically significantly better than drugs (MD = −1.06, 95% CI = [−1.65, −0.47], $P = 0.0004$). However, there was no statistically significant difference between acupuncture and oral drugs (MD = −0.42, 95% CI = [−1.10, −0.27], $P = 0.23$, heterogeneity: $P = 0.17$, $I^2 = 46\%$) (Figure 5).

3.6. Adverse Events. Six studies [28, 29, 32–35] reported the occurrence of adverse events, of which only four studies [29, 32–34] reported the exact number of adverse events. Two studies [29, 33] compared acupuncture with drugs, and two studies [32, 34] compared acupuncture combination drugs with drugs alone. Obvious heterogeneity was found among these RCTs ($P = 0.005$, $I^2 = 77\%$), and the random-effects model showed no statistical difference in adverse events between the experimental group and the control group (OR = 0.26, 95% CI = [0.06, 1.13], $P = 0.07$). In addition, subgroup analysis also showed the same results between acupuncture combination drugs and drugs (OR = 0.72, 95% CI = [0.40, 1.32], $P = 0.29$). However, single acupuncture treatment has a lower incidence of adverse events compared to oral drugs (OR = 0.03, 95% CI = [0.01, 0.21], $P = 0.0003$) (Figure 6).

3.7. Publication Bias. Since the number of included studies did not exceed 10, funnel plots were not used to measure publication bias.

4. Discussion

Depression and pain are the most common psychological and physical symptoms in primary care, respectively. In addition, depression and pain often coexist (30%–50% cooccurrence) [36]. Pain has a negative impact on the prognosis and treatment of depression and vice versa. There is a significant correlation between the severity of pain and the degree of depression [37]. Although the specific pathogenesis of depression and pain is still unclear, current experimental evidence suggests that the pathophysiological processes of depression and pain overlap in many aspects. For example, the brain structures involved in pain and depression shared neural circuits, and neurochemicals play an important role in the formation of pain and depression [6, 37, 38].

Acupuncture is a part of Traditional Chinese Medicine (TCM), which has the advantages of easy operation, safety, economy, and reliable efficacy [39]. At present, acupuncture has been widely used in the clinical treatment of various diseases in many countries around the world, among which chronic pain and depression are common diseases treated by acupuncture [23]. The mechanism of acupuncture analgesia is quite complex, involving the entire nervous system from the periphery to the center. Modern research has shown that acupuncture analgesia is related to the interaction of a variety of biologically active molecules in the pain process,

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI	Year
2.1.1 Acupuncture vs. drugs									
Huang 2000	11.64	1.42	30	12.01	2.11	35	15.1	−0.37 [−1.23, 0.49]	2000
Cao 2007	12.07	6.92	30	12.9	6.01	30	7.1	−0.83 [−4.11, 2.45]	2007
Yu 2015	11.95	2.44	20	11.2	2.57	20	12.7	0.75 [−0.80, 2.30]	2015
Subtotal (95% CI)			*80*			*85*	*34.9*	*−0.14 [−0.88, 0.59]*	
Heterogeneity: $tau^2 = 0.00$, $chi^2 = 1.70$, df = 2 ($P = 0.43$); $I^2 = 0\%$									
Test for overall effect: $Z = 0.38$ ($P = 0.71$)									
2.1.2 Acupuncture + drugs vs. drugs									
Zhao 2013	7.82	2.09	30	10.53	4.4	30	12.0	−2.71 [−4.45, −0.97]	2013
Liu 2013	10.84	3.86	45	14.33	4.12	45	12.4	−3.49 [−5.14, −1.84]	2013
Ma 2015	9.02	4.36	64	11.3	4.98	64	12.5	−2.28 [−3.90, −0.66]	2015
Luo2018	4.32	1.41	42	7.06	2.59	42	15.0	−2.74 [−3.63, −1.85]	2018
Huang 2019	15.39	2.64	55	19.16	4.62	54	13.2	−3.77 [−5.19, −2.35]	2019
Subtotal (95% CI)			*236*			*235*	*65.1*	*−2.95 [−3.55, −2.36]*	
Heterogeneity: $tau^2 = 0.00$, $chi^2 = 2.64$, df = 4 ($P = 0.62$); $I^2 = 0\%$									
Test for overall effect: $Z = 9.74$ ($P < 0.00001$)									
Total (95% CI)			*316*			*320*	*100.0*	*−1.97 [−3.14, −0.80]*	
Heterogeneity: $tau^2 = 2.15$; $chi^2 = 38.29$, df = 7 ($P < 0.00001$); $I^2 = 82\%$									
Test for overall effect: $Z = 3.31$ ($P = 0.0009$)									
Test for subgroup differences: $chi^2 = 33.95$, df = 1 ($P < 0.00001$); $I^2 = 97.1\%$									

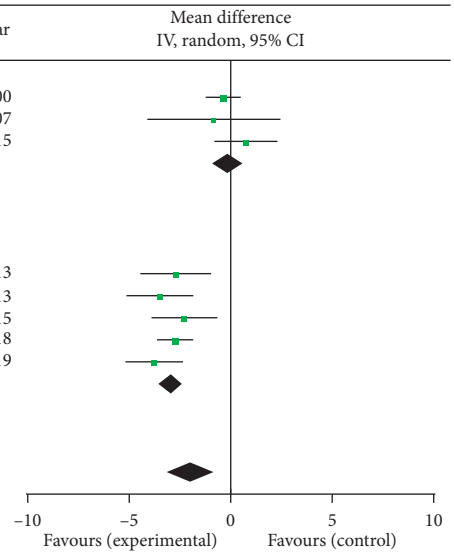

Figure 4: Meta-analysis for the HAMD score of acupuncture versus the control group.

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI	Year
2.2.1 Acupuncture vs. drugs									
Cao 2007	2.34	1.43	30	2.4	1.43	30	17.4	−0.06 [−0.78, 0.66]	2007
Yu 2015	2.15	1.18	20	2.91	1.07	20	17.8	−0.76 [−1.46, −0.06]	2015
Subtotal (95% CI)			*50*			*50*	*35.1*	*−0.42 [−1.10, 0.27]*	
Heterogeneity: $tau^2 = 0.11$, $chi^2 = 1.86$, df = 1 ($P = 0.17$); $I^2 = 46\%$									
Test for overall effect: $Z = 1.19$ ($P = 0.23$)									
2.2.2 Acupuncture + drugs vs. drugs									
Liu 2013	0.93	0.78	45	2.53	1.09	45	22.9	−1.60 [−1.99, −1.21]	2013
Ma 2015	2.75	1.46	64	3.44	1.64	64	20.5	−0.69 [−1.23, −0.15]	2015
Luo2018	2.29	1.01	42	3.12	1.25	42	21.4	−0.83 [−1.32, −0.34]	2018
Subtotal (95% CI)			*151*			*151*	*64.9*	*−1.06 [−1.65, −0.47]*	
Heterogeneity: $tau^2 = 0.22$, $chi^2 = 9.55$, df = 2 ($P = 0.008$); $I^2 = 79\%$									
Test for overall effect: $Z = 3.51$ ($P = 0.0004$)									
Total (95% CI)			*201*			*201*	*100*	*−0.83 [−1.35, −0.32]*	
Heterogeneity: $tau^2 = 0.26$; $chi^2 = 17.69$, df = 4 ($P = 0.001$); $I^2 = 77\%$									
Test for overall effect: $Z = 3.18$ ($P = 0.001$)									
Test for subgroup differences: $chi^2 = 1.94$, df = 1 ($P = 0.16$); $I^2 = 48.5\%$									

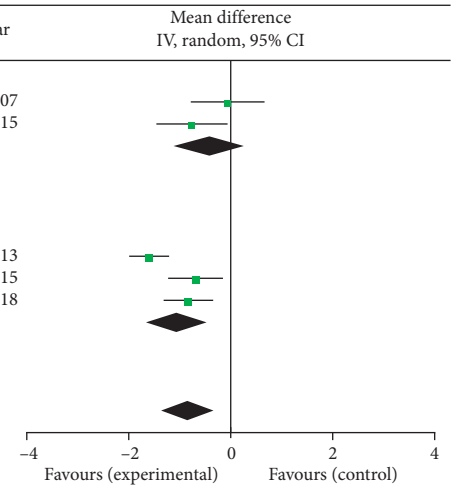

Figure 5: Meta-analysis for the VAS score of acupuncture versus the control group.

Study or subgroup	Experimental Events	Total	Control Events	Total	Weight (%)	Odds ratio M-H, random, 95% CI	Year
1.3.1 Acupuncture vs. drugs							
Cao 2007	1	30	20	30	20.9	0.02 [0.00, 0.15]	2007
Yu 2015	0	20	3	20	14.5	0.12 [0.01, 2.53]	2015
Subtotal (95% CI)		*50*		*50*	*35.3*	*0.03 [0.01, 0.21]*	
Total events	1		23				
Heterogeneity: $tau^2 = 0.13$, $chi^2 = 1.07$, df = 1 ($P = 0.30$); $I^2 = 7\%$							
Test for overall effect: $Z = 3.65$ ($P = 0.0003$)							
1.3.2 Acupuncture + drugs vs. drugs							
Ma 2015	23	64	28	64	34.0	0.72 [0.35, 1.47]	2015
Luo2018	7	42	9	42	30.7	0.73 [0.25, 2.19]	2018
Subtotal (95% CI)		*106*		*106*	*64.7*	*0.72 [0.40, 1.32]*	
Total events	30		37				
Heterogeneity: $tau^2 = 0.00$, $chi^2 = 0.00$, df = 1 ($P = 0.98$); $I^2 = 0\%$							
Test for overall effect: $Z = 1.06$ ($P = 0.29$)							
Total (95% CI)		*156*		*156*	*100*	*0.26 [0.06, 1.13]*	
Total events	31		60				
Heterogeneity: $tau^2 = 1.54$; $chi^2 = 12.79$, df = 3 ($P = 0.005$); $I^2 = 77\%$							
Test for overall effect: $Z = 1.80$ ($P = 0.07$)							
Test for subgroup differences: $chi^2 = 9.87$, df = 1 ($P = 0.002$); $I^2 = 89.9\%$							

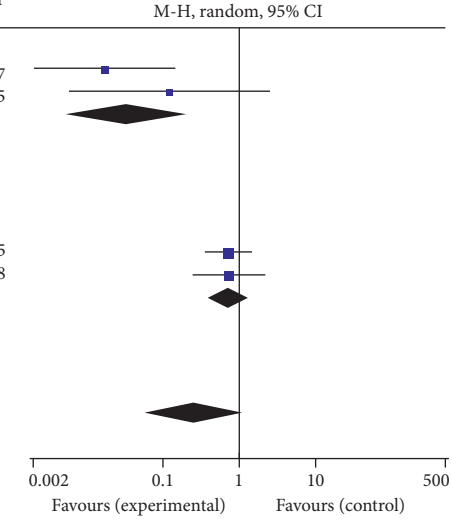

Figure 6: Meta-analysis for adverse events of acupuncture versus the control group.

including neurotransmitters, inflammatory mediators, cell signaling molecules and neuropeptides, etc. [39–41]. At the same time, relevant depression research also affirmed the antidepressant effects of acupuncture [42]. Recent studies have provided laboratory-based evidence that acupuncture treatment can increase the expression of 5-HT1A receptors in the cortex, hippocampus, thalamus, and hypothalamus, as well as the expression of 5-HT1B in the cortex and thalamus. Therefore, acupuncture can effectively relieve depression symptoms [19, 43].

In the present study, we included 8 RCTs to compare the effects of acupuncture and oral drugs, as well as acupuncture-combined oral drugs and oral drugs. With respect to improving the depression symptoms, the HAMD score was used to indicate the intensity of depression. All RCTs evaluated HAMD scores using the same scale, so we reported the results using the mean difference (MD) of HAMD. Our pooled analysis indicated that acupuncture-combined oral drugs were more effective than single oral drugs. However, there was no statistically significant difference between acupuncture and oral drugs. With respect to reducing pain, the VAS score was used to indicate the intensity of pain. Five RCTs evaluated VAS scores using the same scale, so we reported the results using the mean difference (MD) of VAS. Our pooled analysis indicated that acupuncture combined with oral drugs was more effective than single oral drugs. However, the combined data showed no significant difference between acupuncture and oral drugs. In this study, four RCTs reported relevant adverse events with the exact number. The results showed that there was no significant difference in adverse reactions between the experimental group and the control group. Additionally, the subgroup analysis also showed the same results between acupuncture combination drugs and single drugs. However, single acupuncture treatment has a lower incidence of adverse events compared to oral drugs. Therefore, we can cautiously recommend that acupuncture is a safe treatment for CPRD. Based on the results of our included studies, we suggest that acupuncture is an effective and safe alternative therapy for CPRD.

This systematic review has several limitations. Firstly, the insufficient number of RCTs were included in our systematic review, and most of the RCTs had a relatively small sample size. This limitation may lead to inaccurate research evidence. Secondly, the quality of the included RCTs was not satisfactory. Some studies lack the details of random sequence generation, and no RCTs mentioned the use of allocation concealment and blind details, which may lead to imprecise evidence in our study. Thirdly, there was considerable heterogeneity in our study. Subgroup analyses were used to explore the source of heterogeneity. Lastly, all RCTs were conducted in China, which may lead to publication bias and affect the validity and reliability of this systematic review.

5. Conclusions

The results of our current systematic review and meta-analysis show that compared with drug treatment, single acupuncture treatment has the same effect in reducing pain and relieving symptoms of depression in patients with CPRD, but the incidence of adverse reactions of acupuncture treatment is smaller. In addition, acupuncture combined with drug therapy has a better effect than a single drug. However, due to the insufficient number of included studies, low methodological quality, and heterogeneity of results, further studies using large- and high-quality samples are needed to confirm the role of acupuncture for CPRD.

Data Availability

All data generated or analyzed during this study are included within this published article and its supplementary information files.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Jianyu You conceived the article, analyzed the data, and wrote the final manuscript. Jianyu You and Haiyan Li screened the studies, extracted the data, and assessed the risk of bias. Dingyi Xie and Mingren Chen gave suggestions on the structure of the article. Rixin Chen provided methodological guidance. All authors read and approved this manuscript.

Acknowledgments

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Supplementary Materials

Supplemental materials explain the complete search process. Our search process consists of three parts: chronic pain (e.g., musculoskeletal pain and back pain), depression (e.g., depression and affective disorder), and acupuncture (e.g., acupuncture and electroacupuncture). (*Supplementary Materials*)

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Research Article

Is Dry Needling Effective When Combined with Other Therapies for Myofascial Trigger Points Associated with Neck Pain Symptoms? A Systematic Review and Meta-Analysis

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Objective. To evaluate the effects of combining dry needling with other physical therapy interventions versus the application of the other interventions or dry needling alone applied over trigger points (TrPs) associated to neck pain. *Databases and Data Treatment*. Electronic databases were searched for randomized controlled trials where at least one group received dry needling combined with other interventions for TrPs associated with neck pain. Outcomes included pain intensity, pain-related disability, pressure pain thresholds, and cervical range of motion. The risk of bias (RoB) was assessed using the Cochrane risk of bias tool, methodological quality was assessed with PEDro score, and the quality of evidence was assessed by using the GRADE approach. Between-groups mean differences (MD) and standardized mean difference (SMD) were calculated. *Results*. Eight trials were included. Dry needling combined with other interventions reduced pain intensity at short-term (SMD −1.46, 95% CI −2.25 to −0.67) and midterm (SMD −0.38, 95% CI −0.74 to −0.03) but not immediately after or at long-term compared with the other interventions alone. A small effect on pain-related disability was observed at short-term (SMD −0.45, 95% CI −0.87 to −0.03) but not at midterm or long-term. The inclusion of dry needling was also effective for improving pressure pain thresholds only at short-term (MD 112.02 kPa, 95% CI 27.99 to 196.06). No significant effects on cervical range of motion or pain catastrophism were observed. *Conclusion*. Low-to-moderate evidence suggests a positive effect to the combination of dry needling with other interventions for improving pain intensity, pain-related disability, pressure pain thresholds, and cervical range of motion in people with neck pain associated with TrPs at short-term. No midterm or long-term effects were observed.

1. Introduction

Neck pain is the fourth ranked condition in number of years lived with disability [1] and has a lifetime prevalence of 70% and a point prevalence of 20% in the general population [2]. Physical therapy is often considered the first treatment option for people with neck pain. Different therapeutic strategies, e.g., cervical spine mobilizations and manipulations [3], thoracic manipulations [4], therapeutic exercise [5], or education [6], have shown to be effective for the treatment of neck pain. However, evidence supporting the use of other therapies proposed for the management of neck pain, such as dry needling, is still limited [7].

It is important to note that clinicians do not usually treat patients with neck pain with just one isolated intervention, and multimodal approaches are generally advocated. In fact, clinical practice guidelines for physical therapy management of people with neck pain recommend a combination of manual therapy combined with exercise as a potential therapeutic strategy for this population [8, 9]. Some systematic reviews have shown that the combination of two interventions seems to be more effective than the application of each intervention alone [10, 11]; however, others did not [12]. There are few systematic reviews and meta-analyses supporting an effect of dry needling for the management of neck pain [7, 13]. These reviews included trials investigating the isolated application of dry needling for patients with neck pain. No meta-analysis investigating the effects of adding dry needling to other physical therapy interventions for the management of trigger points (TrPs) associated to neck pain exists.

Therefore, the current systematic review and meta-analysis compares the effects of combining dry needling with other physical therapy interventions vs. application of other physical therapy interventions or dry needling alone applied over TrPs associated with neck pain symptoms.

2. Methods

This systematic review and meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [14]. The international OPS Registry registration link is https://doi.org/10.17605/OSF.IO/4J8H5.

2.1. Systematic Literature Search. Electronic literature searches were conducted on MEDLINE, CINAHL, PubMed, PEDro, Cochrane Library, SCOPUS, and Web of Science databases from their inception to 20 July 2020. When databases allowed limits, searches were restricted to randomized clinical trials. We also screened the reference lists of the identified trials. Bibliographical database search strategies were conducted with the assistance of an experienced health science librarian.

2.1.1. Population. Adults with myofascial TrPs in the cervical muscles associated with neck pain symptoms of musculoskeletal origin older than 18 years of age.

2.1.2. Intervention. Any form of muscular dry needling combined with other physical therapy interventions. Acupuncture was excluded.

2.1.3. Comparators. Acceptable comparator was the other physical therapy intervention applied alone, the intervention combined with sham dry needling, or the application of just dry needling alone.

2.1.4. Outcomes. The primary outcome measure was pain intensity or pain-related disability. Secondary outcomes included pressure pain thresholds or cervical range of motion. The search strategy for each database is available in Supplementary Table 1.

2.2. Selection Criteria. The systematic review included randomized clinical trials where at least one group received any form of dry needling combined with another intervention in people with TrPs associated with neck pain. Due to the heterogeneity in the terminology, we included the following diagnostic terms in the current meta-analysis: neck pain, myofascial neck pain, myofascial pain syndrome, and whiplash-associated pain.

The eligible criteria included adult population (>18 years old) with at least at one active TrP associated with neck pain symptoms, one group receiving dry needling targeting TrPs combined with other physiotherapy interventions, an acceptable comparator with other interventions alone or combined with sham/placebo or dry needling alone, and the primary outcome of the trial should include pain intensity (e.g., as measured with a visual analogue scale or numerical pain rate scale) or pain-related disability (e.g., as assessed with a specific-disease questionnaire). Secondary outcomes included pain sensitivity (e.g., pressure pain thresholds) or cervical range of motion (e.g., assessed with a goniometer). We excluded clinical trials including pain associated with neurological disorders (e.g., poststroke pain), postoperative neck pain and studies not published as a journal article, retrospective designs, pilot studies, needling using a traditional Chinese medicine approach, or use of injection therapy (e.g., lidocaine injection).

2.3. Screening, Selection Process, and Data Extraction. Articles identified from the different databases were independently reviewed by two authors. First, the duplicates were removed. Second, title and abstract of the articles were screened for potential eligibility. Third, a full-text read of potentially eligible studies was conducted. Authors were required to achieve a consensus on the included trials. In case of discrepancy between both reviewers, a third author participated in the process to reach the consensus for including or not including the study.

Data from each trial including study design, sample size, population, interventions, outcomes, and follow-ups were extracted independently by 2 authors in a standardized form. Both authors had to achieve a consensus on each item on the

data-extraction form. If disagreement occurred, a third author participated in the determination.

2.4. Assessment of Methodological Quality and Risk of Bias. Risk of bias and methodological quality of the included trials were independently assessed by two authors using the Cochrane risk of bias (RoB) assessment tool [15] and the Physiotherapy Evidence Database (PEDro) scale [16], respectively.

The RoB tool includes the following items: selection bias (randomization sequence generation and allocation concealment), performance bias (blinding participants and blinding therapists), detection bias (blinding outcome assessor), attrition bias (incomplete outcome data), reporting bias (source of funding bias/selecting outcome reporting), and other bias (sample size) [15]. Each item was classified as low risk, high risk, or unclear according to the Cochrane collaboration's tool [15].

The PEDro score evaluates the quality of the trial by assessing the following items: random allocation, concealed allocation, baseline between-groups similarity, participants blinding, therapists blinding, assessors blinding, dropouts, intention-to-treat statistical analysis, between-groups statistical comparison, point measures, and variability data [16]. A trial was considered of high-quality when the PEDro score was ≥6 over 10 points.

2.5. Level of Evidence. To evaluate the quality of the evidence, we used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach [17]. The evidence level was classified as high, moderate, low, or very low based on the following items: presence of the study limitations (RoB), indirectness of evidence, inconsistency of results/unexplained heterogeneity, imprecision of results, and high probability of publication bias [18]. The level of evidence was classified as high quality when all items were negative, moderate quality when one item included serious risk, low quality when two items showed serious risk or one item showed very serious risk, or very low quality when three or more items have serious risk or two or more showed very serious risk. This process was also independently performed by two authors, with the participation of a third one if discrepancy occurred.

2.6. Data Synthesis and Analysis. The meta-analysis was conducted using the Review Manager statistical software (RevMan version 5.3). Data synthesis was presented by groups according to the inclusion of TrP dry needling with other interventions vs. the same intervention alone or vs. TrP dry needling alone and by the follow-up period as immediately after, at short-term, midterm, and long-term, if data were available.

We extracted the sample size, means, and standard deviations for each variable. When the trial reported only standard errors, they were converted to standard deviations. When necessary, the mean scores and standard deviations were estimated from graphs. Also, if the trial presented nonparametric values (median and interquartile range), they were converted to means and standard deviations [19, 20].

The between-groups mean differences (MD) of the trials were converted to SMD, with their 95% confidence intervals (CI). A random-effects model was used to determine the overall effect size (SMD). An effect size (SMD) of 0.8 or greater was considered large, between 0.5 and 0.8 as moderate, and between 0.2 and 0.5 as small. In general, P values < 0.05 were considered statistically significant [21]. The calculation of the effect size on pain and related-disability were obtained immediate after (less than one week) just one session and at short-term (1–12 weeks), midterm (12–24 weeks), and long-term (>24 weeks).

Cervical range of motion was pooled for each movement, i.e., flexion, extension, lateral-flexion, and rotation. When the trial calculated the total range of motion or either side separately for lateral-flexion and rotation, the mean was used in the main analysis.

The heterogeneity of the studies was assessed using the I^2 statistic. The Cochrane group has established the following interpretation of the I^2 statistic: 0%–40% may not be relevant/important heterogeneity; 30%–60% suggests moderate heterogeneity, 50%–90% represents substantial heterogeneity, and 75–100% considerable heterogeneity [22].

3. Results

3.1. Study Selection. The electronic searches identified 557 potential studies for review. After removing duplicates, 324 studies remained. Three hundred fifteen ($n = 315$) were excluded based on examination of their titles or abstracts, leaving 9 articles for full-text analysis [23–31]. One trial was excluded due to the objective of the study was to observe the effectiveness on postneedling soreness [23]. A total of 8 trials [24–31] were included in the systematic review and in the quantitative analysis (Figure 1).

3.2. Study Characteristics. The characteristics of the participants of the included studies are shown in Table 1. All studies targeted active TrPs (i.e., those which referred pain reproduced the patient's symptoms) with the needle, five (62.5%) targeted TrPs in the posterior neck muscles from a pragmatic viewpoint [25–27, 29, 31], two just the upper trapezius muscle [24, 30], and the last one the upper trapezius and levator scapulae [28]. Although all trials included one group receiving dry needling, two did not report the presence of local twitch responses during the needling intervention [26, 27]. All clinical trials specified that dry needling was applied by a physical therapist. The combination of the interventions was grouped since six trials compared the combination of dry needling with other interventions against the application of that intervention alone [26–31], and the remaining two compared the combination of dry needling with other interventions against dry needling alone [24, 25]. There was heterogeneity in the complementary interventions since three trials used best evidence-based physical therapy approaches [26, 28, 31], two trials included just stretching [29, 30], one just exercise [27], one

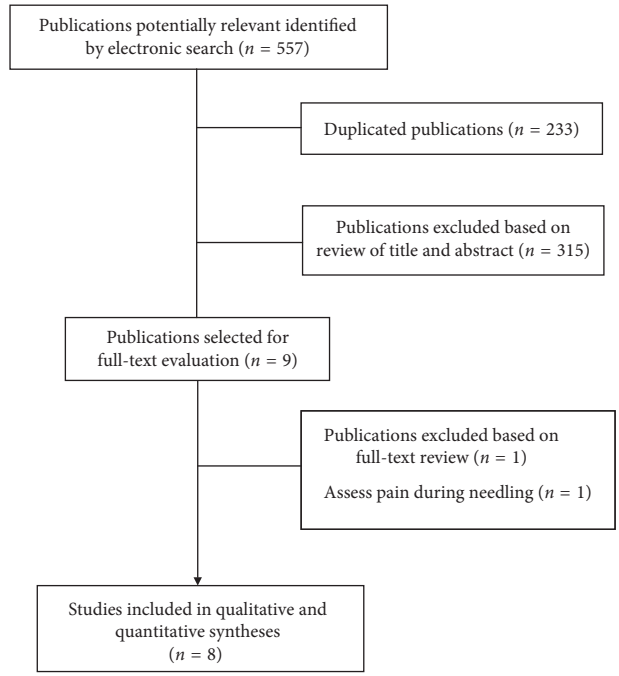


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow diagram.

pain neuroscience education [25], and the last one the application of percutaneous electrical nerve stimulation [24] (Table 1). All trials included pain intensity as the primary outcome, whereas six (62.5%) also assessed pain-related disability. Secondary outcomes (pressure pain thresholds and cervical range of motion) were assessed in five trials. In addition, pain catastrophizing was also assessed in three trials [25, 27, 31]; therefore, pooling data were also conducted. Supplementary Table 2 summarizes the characteristics of dry needling interventions applied in each trial.

4. Methodological Quality

The methodological quality scores ranged from 6 to 9 (mean: 7.2; SD: 1.1) out of a maximum of 10 points; therefore, all studies were considered of high methodological quality (≥6 points). No trial was able to blind the therapists. The most frequent bias was blinding participants since only three trials were able to do [26–28]. Table 2 represents the details of the PEDro scale of each trial.

4.1. Risk of Bias. The details of the risk of bias assessment of the included trials are displayed in Figure 2. No trial was able to blind therapists, and all trials had an unclear bias in the item of blinding participants. In general, the risk of bias of the included trials in the current meta-analysis was low.

4.2. Dry Needling Combined with Other Therapies on Pain Intensity. Dry needling combined with other physical therapy interventions did not exhibit a significant effect (MD −0.55 points, 95% CI −1.64 to 0.55, $P = 0.33$, $Z = 0.98$, $n = 159$) for reducing pain intensity immediately after one single treatment session when compared with other interventions or dry needling alone, although this analysis was based on just one trial each (Figure 3(a)).

At short-term follow-up, the meta-analysis found that dry needling combined with other interventions showed a significant large effect (MD −1.76 points, 95% CI −2.66 to −0.86; SMD −1.46, 95% CI −2.25 to −0.67, $P = 0.001$, $Z = 3.83$, $N = 550$, 6 trials) for reducing pain intensity as compared to the other interventions alone or dry needling alone but with considerable heterogeneity ($I^2 = 94\%$) between the studies (Figure 3(b)). The effect was positive in both comparisons, dry needling combined with other interventions vs. the other interventions alone (MD −1.84 points, 95% CI −2.83 to −0.85), and dry needling with other interventions vs. dry needling alone (MD −1.21 points, 95% CI −2.15 to −0.27).

The results revealed that dry needling combined with other interventions exhibited a significant small effect (MD −0.52 points, 95% CI −0.79 to −0.25; SMD −0.38, 95% CI −0.74 to −0.03, $P = 0.002$, $Z = 3.72$, $n = 237$) for decreasing pain intensity at midterm than the other interventions or dry needling alone and without heterogeneity ($I^2 = 0\%$) between the trials (Figure 3(c)). The effect was significant for dry needling combined with other interventions vs. the other interventions alone (MD −0.52 points, 95% CI −0.80 to −0.24) but not for dry needling combined with other therapy vs. dry needling alone (MD −0.53 points, 95% CI −1.78 to 0.25).

No significant effect on pain (MD −1.30 points, 95% CI −3.27 to 0.66; SMD −0.64, 95% CI −1.20 to −0.08, $P = 0.19$, $Z = 1.30$, $n = 324$) was observed at the long-term follow-up for the inclusion of dry needling with other interventions

Table 1: Characteristics of the sample of included studies.

Study	Diagnosis	Group	Total (male/female)	Age (SD), y	Pain duration
DN plus other therapies vs. other therapies alone					
Tough et al., 2010 [26]	Whiplash-associated disorders	G1: TrP-DN + standardized physical therapy	20 (9/11)	34.2 (10.8)	6.8 (4.3) wk.
		G2: sham DN + standardized physical therapy	21 (8/13)	36.9 (10.9)	7.3 (4.7) wk.
Sterling et al., 2015 [27]	Chronic whiplash-associated disorders	G1: TrP-DN + exercise therapy	40 (16/24)	41.5 (11.1)	20.6 (18.0) mo.
		G2: sham TrP-DN + exercise therapy	40 (10/30)	41.7 (12.3)	15.9 (12.8) mo.
Cerezo Tellez et al., 2016 [29]	Chronic mechanical neck pain	G1: TrP-DN + passive stretching	64	48 (15.7)	>6 mo.
		G2: passive stretching	64	52 (16.6)	>6 mo.
Cerezo-Tellez et al., 2016 [30]	Neck pain in office workers	G1: TrP-DN + passive stretching	22 (5/17)	40.1 (13.1)	NR
		G2: passive stretching	22 (3/19)	47 (16.2)	NR
Gallego-Sendarrubias et al., 2020 [28]	Chronic mechanical neck pain	G1: TrP-DN + manual therapy	47 (13/34)	34.1 (7.6)	>3 mo.
		G2: sham TrP-DN + manual therapy	53 (24/29)	34.6 (8.9)	>3 mo.
Stieven et al., 2020 [31]	Chronic neck pain	G1: TrP-DN + guideline based physical therapy	58 (14/44)	39.3 (9.9)	36.1 (12.4) mo.
		G2: guideline based physical therapy	58 (18/40)	36.9 (11.5)	41.6 (14.1) mo.
DN plus other therapies vs. DN alone					
León-Hernández et al., 2016 [24]	Chronic myofascial neck pain	G1: DN alone	31 (7/24)	23.32 (4.77)	16.03 (17.23) mo.
		G2: DN + PENS	31 (9/22)	26.81 (9.63)	19.36 (19.23) mo.
Valiente-Castrillo et al., 2020 [25]	Chronic myofascial neck pain	G1: TrP-DN	20 (4/16)	40.33 (11.94)	43.39 (56.54) mo.
		G2: TrP-DN + pain neuroscience education	21 (2/19)	40.35 (7.97)	64.94 (62.93) mo.
		G3: usual care (N/A)	19 (3/16)	42.35 (9.43)	56.29 (67.74) mo.

TrP, trigger point; DN, dry needling; SDN, superficial dry needling; PENS, percutaneous electrical nerve stimulation; G, group; Y, years; NR, not reported; mo., months; wk., weeks.

Table 2: Score of randomized clinical trials with the PEDro scale.

	1	2	3	4	5	6	7	8	9	10	Total
Tough et al., 2010 [26]	Y	Y	Y	Y	N	Y	N	Y	Y	Y	8/10
Sterling et al., 2015 [27]	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9/10
Cerezo-Tellez et al., 2016 [29]	Y	N	Y	N	N	Y	Y	N	Y	Y	6/10
Cerezo-Tellez et al., 2016 [30]	Y	N	Y	N	N	Y	Y	N	Y	Y	6/10
León-Hernández et al., 2016 [24]	Y	N	Y	N	N	Y	Y	Y	Y	Y	7/10
Gallego-Sendarrubias et al., 2020 [28]	Y	N	Y	Y	N	N	Y	N	Y	Y	6/10
Stieven et al., 2020 [31]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/10
Valiente-Castrillo et al., 2020 [25]	Y	N	Y	N	N	Y	Y	Y	Y	Y	7/10

1, random allocation of participants; 2, concealed allocation; 3, similarity between groups at baseline; 4, participant blinding; 5, therapist blinding; 6, assessor blinding; 7, fewer than 15% dropouts; 8, intention-to-treat analysis; 9, between-group statistical comparisons; 10, point measures and variability data.

(Figure 3(d)). Furthermore, considerable heterogeneity between the trials was observed ($I^2 = 98\%$). Table 3 summarizes the main results and raw data of the included studies.

4.3. Dry Needling Combined with Other Therapies on Related-Disability. A significant effect on related-disability for the combination of dry needling with other interventions was observed at short-term (SMD −0.45, 95% CI −0.87 to −0.03, $P = 0.5$, $Z = 2.09$, $n = 506$, Figure 4(a)) but not at midterm (SMD −0.16, 95% CI −0.44 to 0.11, $P = 0.25$, $Z = 1.14$, $n = 237$, Figure 4(b)) and long-term (SMD −0.32, 95% CI −0.97 to 0.29, $P = 0.35$, $Z = 0.94$, $n = 324$, Figure 4(c)). The heterogeneity between trials was considerable ($I^2 = 81\%$) at short-term, not relevant ($I^2 = 11\%$) at midterm, and considerable ($I^2 = 88\%$) at long-term.

At short-term, a significant effect on pain-related disability was found when compared the combined application of dry needling against dry needling alone (SMD −0.77, 95% CI −1.40 to −0.13), but this analysis was based on just one trial (Figure 4(a)). Table 3 details the main results and raw data of the included studies.

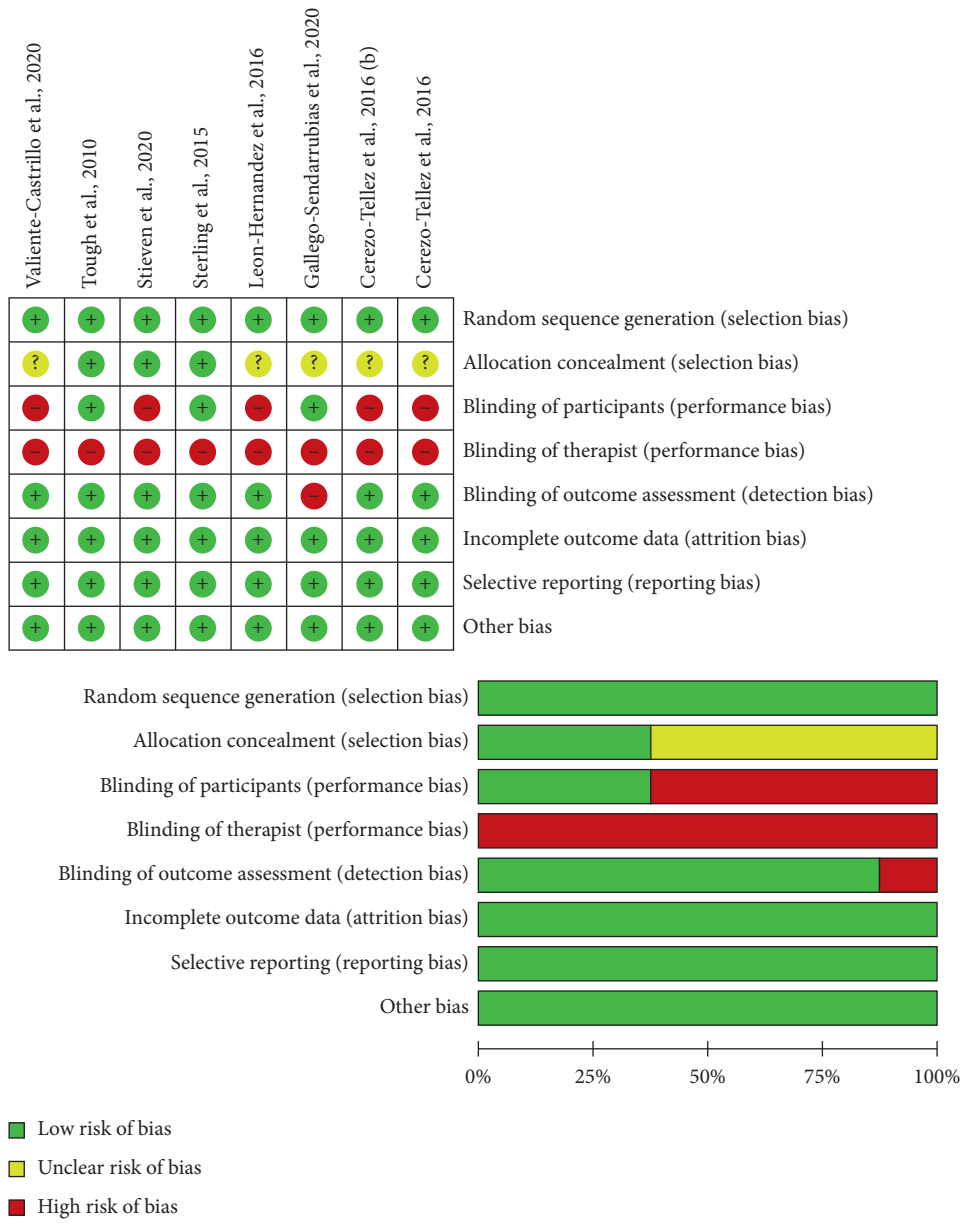
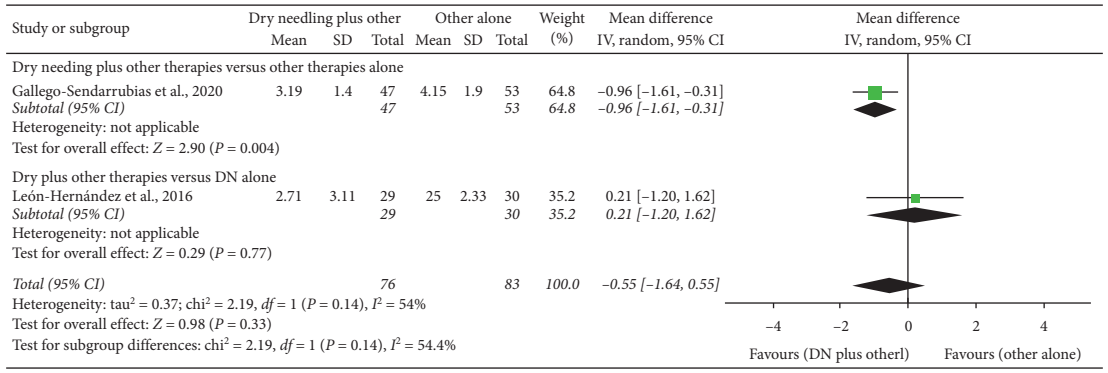


Figure 2: Plot of risk of bias of the included studies.

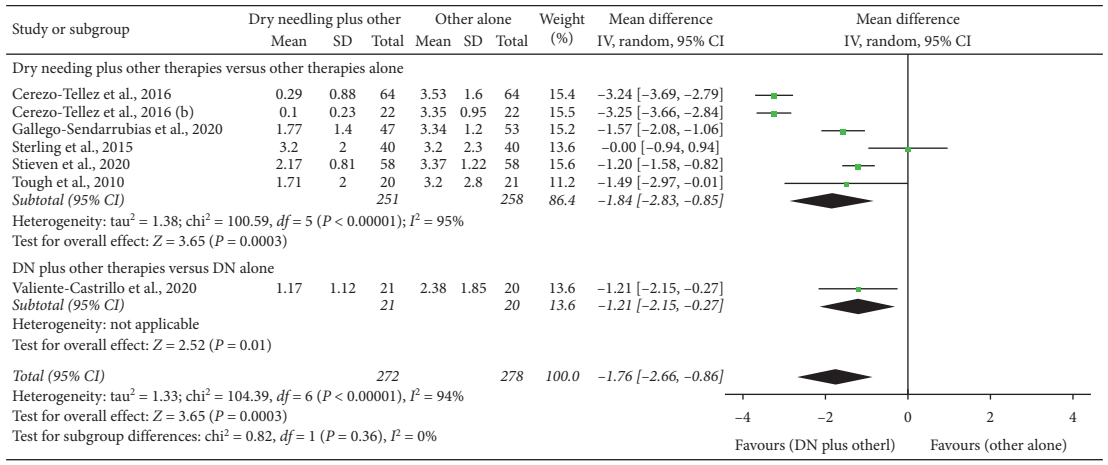
4.4. Dry Needling Combined with Other Therapies on Pressure Pain Thresholds. The meta-analysis found that dry needling in combination with other therapies did not exhibit a significant effect for increasing pressure pain thresholds immediately after (MD 89.93 kPa, 95% CI −25.97 to 205.64, $P = 0.13$, $Z = 1.52$, $n = 159$, Figure 5(a)), at mid-term (MD 32.10 kPa, 95% CI −21.68 to 85.88, $P = 0.24$, $Z = 1.17$, $n = 80$, Figure 5(c)), and at long-term (MD 53.26 kPa, 95% CI −66.28 to 172.80, $P = 0.38$, $Z = 0.87$, $n = 208$, Figure 5(d)).

At short-term, dry needling combined with other therapies exhibited a significant effect (MD 112.02 kPa, 95% CI 27.99 to 196.06, $P = 0.009$, $Z = 2.61$, $n = 352$) for increasing pressure pain threshold when compared with the other interventions alone, although with considerable heterogeneity ($I^2 = 92\%$) between the studies (Figure 5(b)).

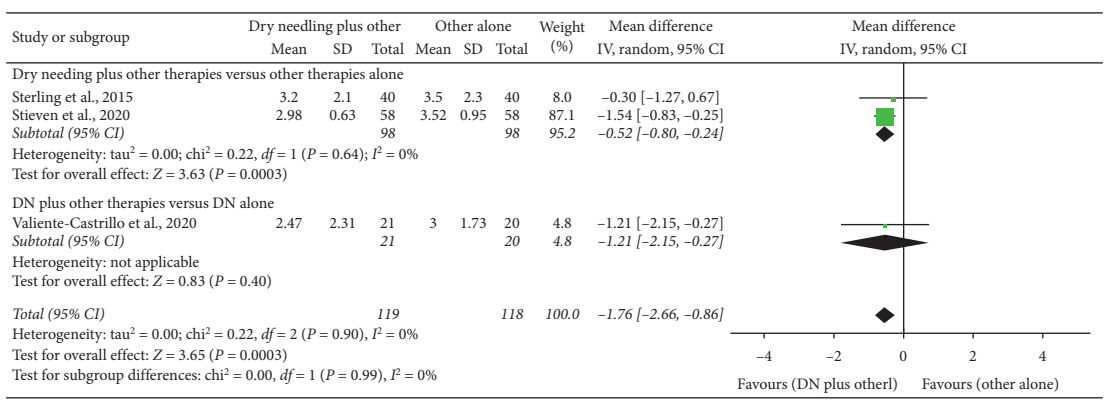
4.5. Dry Needling Combined with Other Therapies on Cervical Range of Motion. Dry needling combined with other interventions did not show a significant effect immediately after the intervention on the cervical range of motion when compared with the other interventions alone: flexion (MD 3.33, 95% CI −0.28 to 6.97, $n = 159$, $Z = 1.81$, $P = 0.08$, Figure 6(a). 1); extension (MD 2.43, 95% CI −1.30 to 6.16, $n = 159$, $Z = 1.28$, $P = 0.20$, Figure 6(b). 1); rotation (MD −0.03, 95% CI −5.71 to 5.64, $n = 159$, $Z = 0.01$, $P = 0.99$, Figure 6(c). 1); and lateral-flexion (MD 2.13, 95% CI −1.14 to 5.41, $n = 159$, $Z = 1.28$, $P = 0.20$, Figure 6(d)). Similarly, no significant effects at long-term were either observed for flexion (MD 2.89, 95% CI −4.67 to 10.45, $n = 208$, $Z = 0.75$, $P = 0.45$, Figure 6(a). 3); extension (MD 1.67, 95% CI −7.94 to 11.27, $n = 208$, $Z = 0.34$, $P = 0.73$, Figure 6(b). 3); and rotation (MD 4.25, 95% CI −3.78 to 12.26, $n = 208$, $Z = 1.04$,



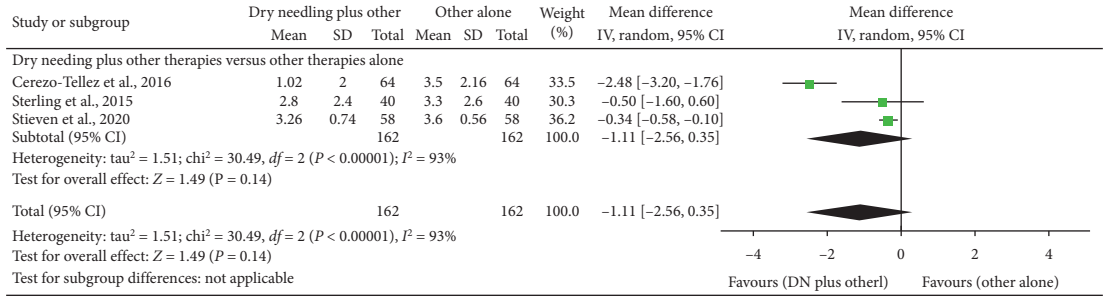
(a)



(b)



(c)



(d)

Figure 3: Comparison (mean differences) between the effects of dry needling combined with other interventions against other interventions on pain intensity (a) immediately after, (b) at short-term, (c) at midterm, and (d) at long-term.

Table 3: Main results and raw data of the included studies.

Study	Outcome/Group	Baseline mean (SD)	Immediate, less than one week after a single session	Short-term, 1–12 weeks, mean (SD)	Midterm, 12–24 weeks, mean (SD)	Long-term, >24 weeks, mean (SD)
Dry needling combined with other interventions vs. other intervention alone						
Tough et al., 2010 [26]	Pain (VAS, 0–10)	4.9 (1.6)	—	1.71 (2.0) (6 wk)	—	—
	G1	5.0 (1.6)	—	3.2 (2.8) (6 wk)	—	—
	G2	18.6 (8.7)	—	8.4 (7.8) (6 wk)	—	—
	Disability (NDI)					
	G1		—		—	—
	G2	20.5 (7.6)	—	11.9 (8.8) (6 wk)	—	—
Sterling et al., 2015 [27]	Pain (NPRS, (0–10)					
	G1	5.6 (2.2)	—	3.2 (2.0) (6 wk)	3.2 (2.1) (12 wk)	2.8 (2.4) (54 wk)
	G2	5.4 (2.0)	—	3.2 (2.3) (6 wk)	3.5 (2.3) (12 wk)	3.3 (2.6) (54 wk)
	Disability (NDI, %)					
	G1	42.9 (15.2)	—	32.2 (16.8) (6 wk)	30.8 (17.1) (12 wk)	27.3 (16.5) (54 wk)
	G2	42.9 (13.1)	—	32.7 (16.8) (6 wk)	32.1 (16.0) (12 wk)	34.1 (18.4) (54 wk)
	Cervical flexion (°)					
	G1	39.7 (16.1)	—	39.2 (15.8) (6 wk)	41.7 (18.7) (12 wk)	42.5 (16.5) (54 wk)
	G2	39.7 (14.9)	—	41.2 (19.1) (6 wk)	39.6 (16.5) (12 wk)	44.3 (17.0) (54 wk)
	Cervical extension (°)					
	G1	33.3 (13.2)	—	39.9 (13.3) (6 wk)	39.8 (13.6) (12 wk)	42.3 (14.1) (54 wk)
	G2	36.3 (16.3)	—	41.8 (15.8) (6 wk)	40.8 (16.1) (12 wk)	46.1 (17.6) (54 wk)
Sterling et al., 2015 [27]	Right cervical rotation (°)					
	G1	45.8 (17.6)	—	51.6 (18.4) (6 wk)	52.0 (19.5) (12 wk)	54.0 (19.2) (54 wk)
	G2	42.0 (22.5)	—	52.5 (17.4) (6 wk)	48.8 (17.9) (12 wk)	55.7 (17.7) (54 wk)
	Left cervical rotation (°)					
	G1	43.6 (16.3)	—	49.5 (17.2) (6 wk)	49.7 (20.3) (12 wk)	51.3 (18.4) (54 wk)
	G2	46.3 (15.1)	—	48.8 (15.8) (6 wk)	46.4 (16.3) (12 wk)	51.4 (18.6) (54 wk)
	Cervical rotation (mean calculated)					
	G1	44.7 (16.95)	—	50.55 (17.8) (6 wk)	50.85 (19.9) (12 wk)	52.65 (18.8) (54 wk)
	G2	44.15 (18.8)	—	50.65 (16.6) (6 wk)	47.6 (17.1) (12 wk)	53.55 (18.15) (54 wk)
	PPT (kPa)					
	G1	153.8 (100.4)	—	191.8 (79.1) (6 wk)	213.2 (137.0) (12 wk)	193.9 (112.1) (54 wk)
	G2	174.7 (108.5)	—	199.4 (122.1) (6 wk)	181.1 (106.5) (12 wk)	200.2 (100.6) (54 wk)
	Pain catastrophizing (PCS)					
	G1	18.0 (11.3)	—	11.0 (9.5) (6 wk)	11.8 (11.0) (12 wk)	8.0 (10.8) (54 wk)
	G2	20.4 (13.8)	—	17.6 (13.6) (6 wk)	16.7 (12.3) (12 wk)	12.6 (11.8) (54 wk)
Cerezo Tellez et al., 2016 [29]	Pain (VAS, 0–10)					
	G1	5.1 (1.6)	—	0.29 (0.88) (2 wk)	—	1.02 (2) (24 wk)
	G2	5.1 (1.4)	—	3.53 (1.6) (2 wk)	—	3.5 (2.16) (24 wk)
	PPT (kPa) right trapezius					
	G1	205.93 (68.64)	—	480.51 (172.64) (2 wk)	—	429.52 (212.08) (24 wk)
	G2	196.13 (58.83)	—	292.23 (86.32) (2 wk)	—	304.98 (125.52) (24 wk)
	PPT (kPa) left trapezius					
	G1	205.93 (78.45)	—	462.86 (160) (2 wk)	—	413.82 (224) (24 wk)
	G2	205.93 (78.45)	—	297.13 (80) (2 wk)	—	306.93 (88) (24 wk)
	PPT (kPa) mean calculated					
	G1	205.93 (73.54)	—	471.68 (166.32) (2 wk)	—	421.67 (218.04)
	G2	201.03 (68.64)	—	294.68 (83.16) (2 wk)	—	305.95 (106.76)
Cerezo Tellez et al., 2016 [29]	Cervical rotation (°)					
	G1	53.9 (11.25)	—	61.95 (7.04) (2 wk)	—	62.8 (7.12) (24 wk)
	G2	53.3 (9.05)	—	55.31 (5.84) (2 wk)	—	55.29 (4.76) (24 wk)
	Cervical lateral-flexion (°)					
	G1	31.55 (8.1)	—	38.09 (6.56) (2 wk)	—	38.3 (6.76) (24 wk)
	G2	29.95 (6.75)	—	31.96 (4.16) (2 wk)	—	32.41 (5.72) (24 wk)
	Cervical flexion-extension (°)					
	G1	49.9 (9.45)	—	58.45 (6.56) (2 wk)	—	59.55 (7.2) (24 wk)
	G2	51 (8.3)	—	52.89 (5.84) (2 wk)	—	53.49 (9.08) (24 wk)
	Disability (NDI)					
	G1	30.5 (16)	—	13.2 (16.48) (2 wk)	—	12 (18.16) (24 wk)
	G2	31 (12)	—	24.53 (14.16) (2 wk)	—	22.57 (14.72) (24 wk)

Table 3: Continued.

Study	Outcome/Group	Baseline mean (SD)	Immediate, less than one week after a single session	Short-term, 1–12 weeks, mean (SD)	Midterm, 12–24 weeks, mean (SD)	Long-term, >24 weeks, mean (SD)
			Pain (VAS, 0–10)[+]			
	G1	5.8 (0.79)	—	0.10 (0.23) (2 wk)	—	—
	G2	5.0 (1.34)	—	3.35 (0.95) (2 wk)	—	—
			PPT (kPa)			
	G1	186.32 (68.64)	—	421.68 (147.09) (2 wk)	—	—
	G2	186.32 (68.64)	—	274.58 (137.29) (2 wk)	—	—
			Cervical flexion-extension (°)			
Cerezo-Tellez et al., 2016 [30]	G1	47.55 (12.2)	—	59.8 (6.95) (2 wk)	—	—
	G2	52.2 (7.5)	—	50.35 (11.35) (2 wk)	—	—
			Cervical rotation (°)			
	G1	56.6 (13)	—	66.8 (2.8) (2 wk)	—	—
	G2	55.4 (11.9)	—	60.8 (2.65) (2 wk)	—	—
			Cervical lateral flexion (°)			
	G1	32.95 (10.65)	—	43.45 (7.8) (2 wk)	—	—
	G2	36.8 (10.5)	—	33.55 (9.2) (2 wk)	—	—
			Pain (NPRS, 0–10)			
	G1	6.31 (0.72)	—	2.17 (0.81) (4 wk)	2.98 (0.63) (12 wk)	3.26 (0.74) (24 wk)
	G2	6.18 (1.07)	—	3.37 (1.22) (4 wk)	3.52 (0.95) (12 wk)	3.60 (0.56) (24 wk)
			Disability (NDI, %)			
Stieven et al., 2020 [31]	G1	26.52 (9.72)	—	22.94 (8.891) (4 wk)	23.08 (11.1) (12 wk)	24.99 (9.04) (24 wk)
	G2	27.13 (6.42)	—	20.94 (10.4) (4 wk)	23.66 (8.91) (12 wk)	22.86 (7.28) (24 wk)
			Pain catastrophizing (PCS)			
	G1	23.67 (9.51)	—	22.17 (6.04) (4 wk)	19.07 (7.89) (12 wk)	19.18 (6.47) (24 wk)
	G2	20.97 (8.56)	—	21.08 (8.83) (4 wk)	21.26 (9.41) (12 wk)	18.94 (8.06) (24 wk)
			Pain (VAS, 0–10)			
	G1	6.66 (1.4)	3.19 (1.6)	1.77 (1.4) (4 wk)	—	—
	G2	6.17 (1.6)	4.15 (1.9)	3.34 (1.2) (4 wk)	—	—
			PPT (kPa)			
	G1	171.61 (39.22)	303.02 (78.45)	355.97 (98.06) (4 wk)	—	—
	G2	184.36 (49.033)	253.01 (78.45)	219.66 (68.64) (4 wk)	—	—
			Disability (NDI)			
	G1	28.95 (10.2)	76.81 (12.1)	4.61 (6.2) (4 wk)	—	—
	G2	23.69 (9.8)	73.13 (10.5)	11.52 (7.3) (4 wk)	—	—
			Cervical flexion (°)			
Gallego-Sendarrubias et al., 2020 [28]	G1	67.89 (13.5)	64.19 (12.0)	78.38 (9.5) (4 wk)	—	—
	G2	69.25 (11.1)	61.92 (11.5)	70.58 (9.4) (4 wk)	—	—
			Cervical extension (°)			
	G1	52.32 (14.6)	82.60 (14.5)	69.09 (11.3) (4 wk)	—	—
	G2	55.68 (11.5)	79.11 (13.2)	62.40 (10.4) (4 wk)	—	—
			Right rotation (°)			
	G1	74.28 (18.1)	81.45 (13.7)	87.55 (8.1) (4 wk)	—	—
	G2	74.60 (15.3)	79.13 (11.5)	78.79 (10.9) (4 wk)	—	—
			Left rotation (°)			
	G1	71.79 (17.7)	82.02 (14.1)	87.19 (8.4) (4 wk)	—	—
	G2	73.81 (11.8)	79.12 (12.35)	78.89 (10.1) (4 wk)	—	—
			Cervical rotation (°) (mean calculated)			
	G1	73.03 (17.9)	59.60 (11.9)	87.37 (8.25) (4 wk)	—	—
	G2	74.2 (13.55)	56.28 (11.9)	78.84 (10.5) (4 wk)	—	—
			Right cervical lateral flexion (°)			
	G1	47.72 (14.3)	62.51 (10.5)	68.45 (12.5) (4 wk)	—	—
	G2	49.04 (13.1)	59.87 (10.6)	56.25 (13.0) (4 wk)	—	—
Gallego-Sendarrubias et al., 2020 [28]			Left cervical lateral flexion (°)			
	G1	53.64 (10.8)	61.05 (11.2)	70.11 (10.8) (4 wk)	—	—
	G2	55.43 (11.0)	58.07 (11.25)	59.77 (9.9) (4 wk)	—	—
			Cervical lateral flexion (mean calculated)			
	G1	50.68 (12.55)	—	69.28 (11.65) (4 wk)	—	—
	G2	52.23 (12.05)	—	58.01 (11.45) (4 wk)	—	—

Table 3: Continued.

Study	Outcome/Group	Baseline mean (SD)	Immediate, less than one week after a single session	Short-term, 1–12 weeks, mean (SD)	Midterm, 12–24 weeks, mean (SD)	Long-term, >24 weeks, mean (SD)
Dry needling combined with other interventions vs. dry needling alone						
			Pain (VAS, 0–10)+			
	G1	5.00 (4.00–6.00)	2.50 (1.00–4.00)	—	—	—
	G2	5.00 (3.50–6.00)	2.00 (1.00–5.00)	—	—	—
			Disability (NDI)+			
	G1	9.50 (8.00–13.00)	6.50 (3.25–10.00)	—	—	—
	G2	11.00 (7.00–14.50)	6.00 (4.00–14.00)	—	—	—
León-Hernández et al., 2016 [24]			Cervical flexion (°)			
	G1	52.05 (12.24)	53.76 (12.07)	—	—	—
	G2	52.42 (11.72)	51.07 (12.21)	—	—	—
			Cervical extension (°)			
	G1	58.62 (11.80)	62.98 (10.90)	—	—	—
	G2	58.11 (12.44)	60.26 (13.73)	—	—	—
			Cervical left lateral flexion (°)			
	G1	38.16 (9.36)	41.80 (9.63)	—	—	—
	G2	39.05 (8.01)	39.77 (9.18)	—	—	—
			Cervical right lateral flexion (°)			
	G1	37.55 (9.11)	40.75 (9.91)	—	—	—
	G2	38.77 (10.46)	40.59 (9.67)	—	—	—
			Cervical lateral flexion (mean calculated)			
	G1	37.85 (9.23)	41.27 (9.77)	—	—	—
	G2	38.91 (9.23)	40.18 (9.42)	—	—	—
León-Hernández et al., 2016 [24]			Cervical left rotation (°)			
	G1	59.31 (13.72)	59.59 (11.98)	—	—	—
	G2	61.40 (12.82)	64.33 (8.58)	—	—	—
			Cervical right rotation (°)			
	G1	60.50 (10.73)	61.18 (10.9)	—	—	—
	G2	60.36 (10.24)	62.22 (7.42)	—	—	—
			Cervical rotation (mean calculated)			
	G1	59.90 (12.22)	60.38 (11.44)	—	—	—
	G2	60.88 (11.53)	63.27 (8)	—	—	—
			Pain (VAS, 0–10)			
	G1	5.79 (1.89)	—	2.38 (1.85) (4 wk)	3.00 (1.73) (12 wk)	—
	G2	5.52 (1.80)	—	1.17 (1.12) (4 wk)	2.47 (2.31) (12 wk)	—
	G3 (N/A)	5.26 (1.46)	—	3.85 (2.38) (4 wk)	3.91 (2.50) (12 wk)	—
			Disability (NDI)			
	G1	17.45 (4.94)	—	12.00 (5.68) (4 wk)	11.0 (6.06) (12 wk)	—
Valiente-Castrillo et al., 2020 [25]	G2	15.80 (4.62)	—	7.19 (6.56) (4 wk)	7.57 (5.33) (12 wk)	—
	G3 (N/A)	16.78 (5.32)	—	13.21 (7.26) (4 wk)	13.78 (8.78) (12 wk)	—
			Pain catastrophizing (PCS)			
	G1	16.95 (11.39)	—	12.10 (11.01) (4 wk)	11.75 (10.48) (12 wk)	—
	G2	16.55 (12.36)	—	7.33 (7.90) (4 wk)	6.61 (7.86) (12 wk)	—
	G3 (N/A)	19.41 (11.37)	—	12.70 (10.95) (4 wk)	14.70 (10.26) (12 wk)	—

[+]Data are expressed as median and interquartile range. They were converted to mean and standard deviation in the forest plots.

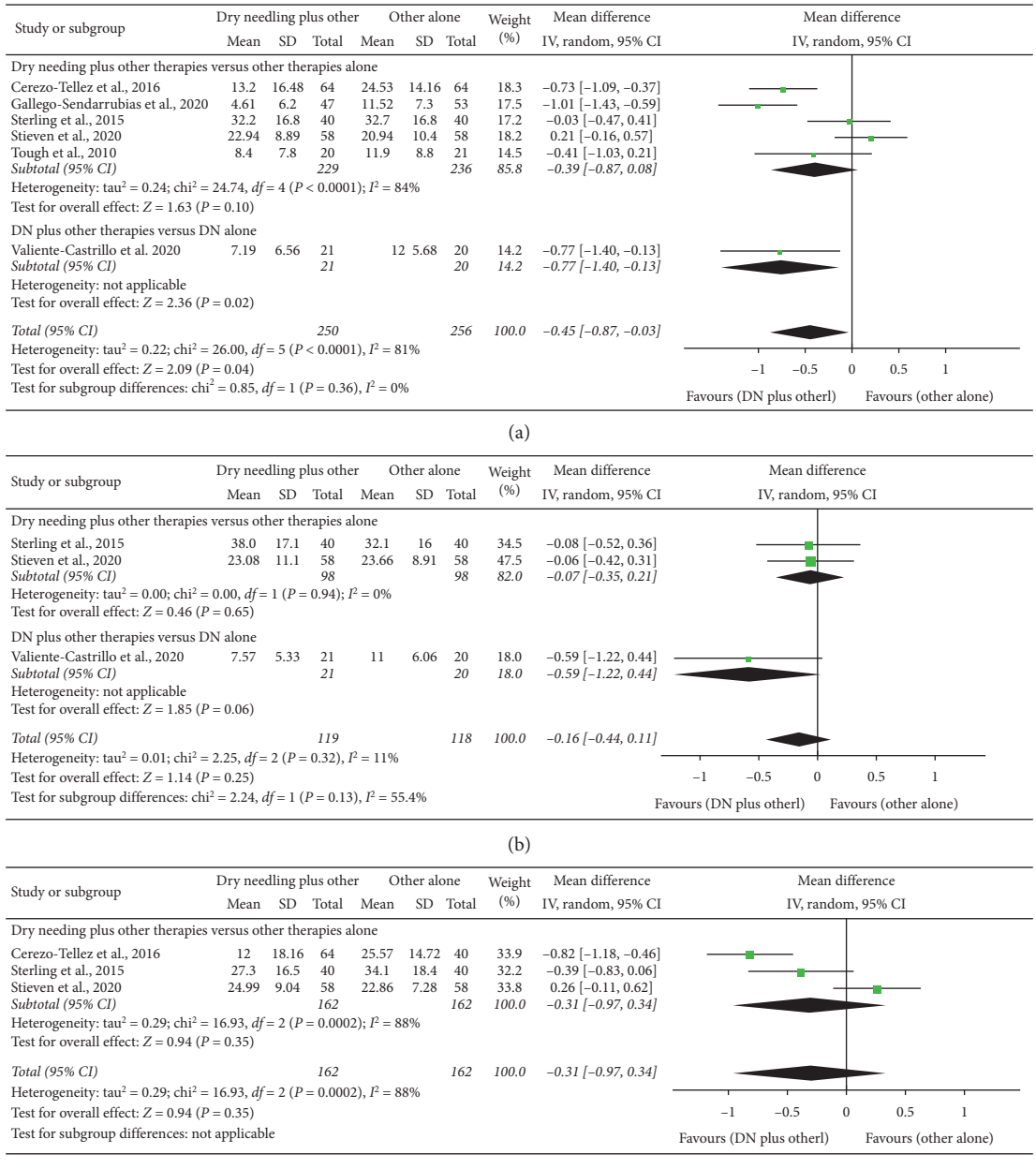


Figure 4: Comparison (standardized mean differences) between the effects of dry needling combined with other interventions against other interventions on pain-related disability (a) at short-term, (b) at midterm, and (c) at long-term.

$P = 0.30$, Figure 6(c). 3) for the combination of dry needling and other interventions. A significant effect at long-term was seen for lateral-flexion (MD 5.89, 95% CI 3.72 to 8.06, $n = 128$, $Z = 5.32$, $P < 0.001$, Figure 6(c). 3), although this analysis was based on just one study.

The meta-analysis observed a significant small short-term effect of dry needling combined with other interventions on the cervical range of motion: flexion (MD 6.01, 95% CI 2.86 to 9.16, $n = 352$, $Z = 3.74$, $P < 0.001$, Figure 6(a). 2); extension (MD 5.36, 95% CI 2.00 to 8.72, $n = 352$, $Z = 3.13$, $P = 0.002$, Figure 6(b). 2); rotation (MD 6.34, 95% CI 4.661 to 8.03, $n = 352$; $Z = 7.38$, $P < 0.001$, Figure 6(c). 2); lateral-flexion (MD 8.55, 95% CI 5.01 to 12.10, $n = 272$, $Z = 4.73$, $P < 0.001$, Figure 6(d). 2). All analyses had moderate heterogeneity. Table 3 summarizes main results and raw data of the included studies.

4.6. Dry Needling Combined with Other Therapies on Pain Catastrophizing. The combination of dry needling with other therapies exhibits a significant small effect on pain catastrophism at midterm (MD −1.71, 95% CI −6.36 to 2.94; SMD -0.36, 95% CI −0.61 to −0.10, $n = 237$; $Z = 2.69$; $P = 0.007$, Figure 7(b)) but not at short-term (MD −3.01, 95% CI −8.33 to 2.30, $n = 237$; $Z = 1.11$; $P = 0.27$, Figure 7(a)) and long-term (MD −3.34, 95% CI −5.77 to −0.91; $n = 196$; $Z = 0.72$; $P = 0.47$, Figure 7(c)).

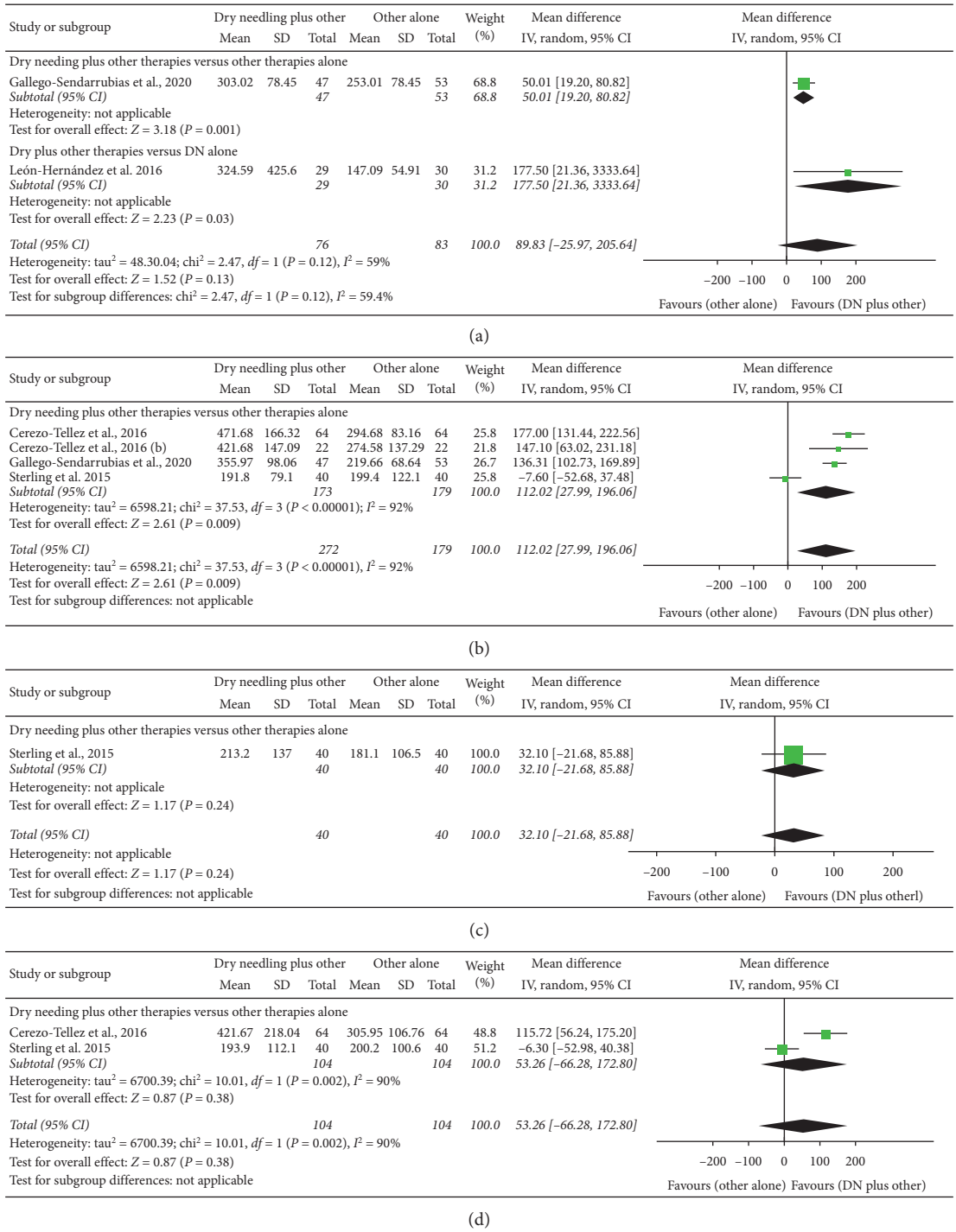


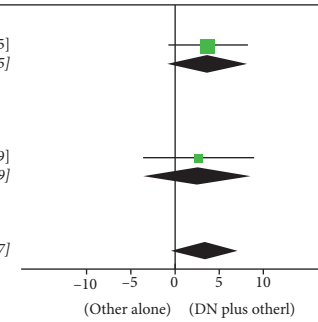
Figure 5: Comparison (mean differences) between the effects of dry needling combined with other interventions against other interventions on pressure pain thresholds (a) immediately after, (b) at short-term, (c) at midterm, and (d) at long-term.

4.7. Quality of Evidence (GRADE). Table 4 displays the details of GRADE assessment showing RoB, inconsistency of the results, indirectness of evidence, imprecision of results, and high probability of publication bias. The serious/very serious inconsistency of the results (heterogeneity) and the serious/very serious impression downgraded the evidence level of dry needling to low or very low.

4.8. Adverse Events. Seven trials (87.5%) reported information about adverse effects with all of them reporting just minor events and none reported any serious adverse effects. Postneedling soreness was the most common adverse event in all trials and resolved spontaneously in 24–48 h without further treatment (Supplementary Table 3).

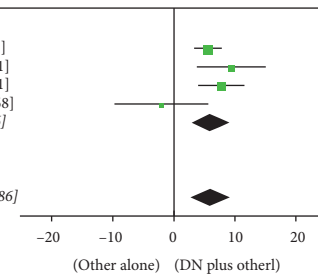
A.1 Immediate

Study or subgroup	Dry needling plus other Mean	SD	Total	Other alone Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Dry needing plus other therapies versus other therapies alone								
Gallego-Sendarrubias et al., 2020	76.81	12.1	47	73.13	10.5	53	64.8	3.68 [−0.79, 8.15]
Subtotal (95% CI)			*47*			*53*	*64.8*	*3.68 [−0.79, 8.15]*
Heterogeneity: not applicable								
Test for overall effect: $Z = 1.61$ ($P = 0.11$)								
Dry plus other therapies versus DN alone								
León-Hernández et al., 2016	53.76	12.07	29	51.07	12.21	30	34.2	2.69 [−3.51, 8.89]
Subtotal (95% CI)			*29*			*30*	*34.2*	*2.69 [−3.51, 8.89]*
Heterogeneity: not applicable								
Test for overall effect: $Z = 0.85$ ($P = 0.39$)								
Total (95% CI)			*76*			*83*	*100.0*	*3.34 [−0.28, 6.97]*
Heterogeneity: $tau^2 = 0.00$; $chi^2 = 0.06$, $df = 1$ ($P = 0.80$), $I^2 = 0\%$								
Test for overall effect: $Z = 0.98$ ($P = 0.33$)								
Test for subgroup differences: $chi^2 = 0.06$, $df = 1$ ($P = 0.80$), $I^2 = 0\%$								



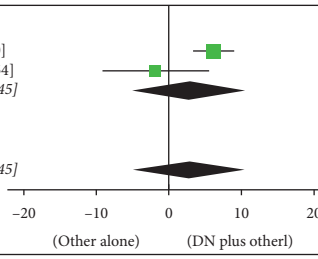
A.2 Short-term

Study or subgroup	Dry needling plus other Mean	SD	Total	Other alone Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Dry needing plus other therapies versus other therapies alone								
Cerezo-Tellez et al., 2016	58.45	6.56	64	52.89	5.84	64	39.4	5.56 [3.41, 7.71]
Cerezo-Tellez et al., 2016 (b)	59.8	6.95	22	50.35	11.35	22	19.3	9.45 [3.89, 15.01]
Gallego-Sendarrubias et al., 2020	78.38	9.5	47	70.58	9.4	53	28.9	7.80 [4.09, 11.51]
Sterling et al. 2015	39.2	15.8	40	41.2	19.1	40	12.5	−2.00 [−9.68, 5.68]
Subtotal (95% CI)			*173*			*258*	*100.0*	*6.01 [2.86, 9.16]*
Heterogeneity: $tau^2 = 5.35$; $chi^2 = 16.71$, $df = 3$ ($P = 0.08$), $I^2 = 55\%$								
Test for overall effect: $Z = 3.74$ ($P = 0.0002$)								
Total (95% CI)			*173*			*179*	*100.0*	*−1.76 [−2.66, −0.86]*
Heterogeneity: $tau^2 = 5.35$; $chi^2 = 6.71$, $df = 3$ ($P = 0.08$), $I^2 = 55\%$								
Test for overall effect: $Z = 3.74$ ($P = 0.0002$)								
Test for subgroup differences: not applicable								



A.3 Long-term

Study or subgroup	Dry needling plus other Mean	SD	Total	Other alone Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Dry needing plus other therapies versus other therapies alone								
Cerezo-Tellez et al., 2016	59.55	7.2	64	53.49	9.08	64	59.7	6.06 [3.22, 8.90]
Sterling et al. 2015	42.5	16.5	40	44.3	17	40	40.3	−1.80 [−9.14, 5.54]
Subtotal (95% CI)			*104*			*104*	*100.0*	*−2.89 [−4.67, 10.45]*
Heterogeneity: $tau^2 = 22.83$; $chi^2 = 3.83$, $df = 1$ ($P = 0.05$), $I^2 = 74\%$								
Test for overall effect: $Z = 0.75$ ($P = 0.45$)								
Total (95% CI)			*104*			*104*	*100.0*	*2.89 [−4.67, −10.45]*
Heterogeneity: $tau^2 = 22.83$; $chi^2 = 3.83$, $df = 1$ ($P = 0.05$), $I^2 = 74\%$								
Test for overall effect: $Z = 0.75$ ($P = 0.45$)								
Test for subgroup differences: not applicable								

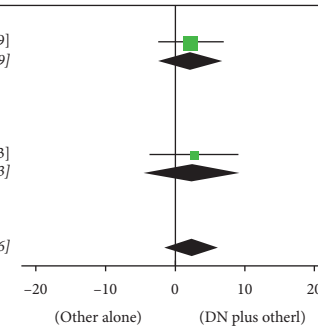


(a)

Figure 6: Continued.

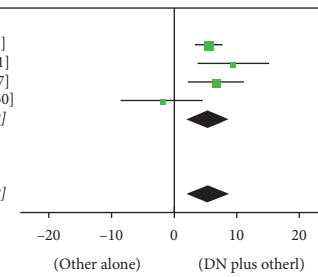
B.1 Immediate

Study or subgroup	Dry needling plus other Mean	SD	Total	Other alone Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Dry needing plus other therapies versus other therapies alone								
Gallego-Sendarrubias et al., 2020	64.19	12	47	61.92	11.5	53	65.1	2.27 [−2.35, 6.89]
Subtotal (95% CI)			*47*			*53*	*65.1*	*2.27 [−2.35, 6.89]*
Heterogeneity: not applicable								
Test for overall effect: $Z = 0.96$ ($P = 0.34$)								
Dry plus other therapies versus DN alone								
León-Hernández et al., 2016	62.98	10.9	29	60.26	13.73	30	34.9	2.72 [−3.59, 9.03]
Subtotal (95% CI)			*29*			*30*	*34.9*	*2.72 [−3.59, 9.03]*
Heterogeneity: not applicable								
Test for overall effect: $Z = 0.84$ ($P = 0.40$)								
Total (95% CI)			*76*			*83*	*100.0%*	*2.43 [−1.30, 6.16]*
Heterogeneity: tau² = 0.00; chi² = 0.01, $df = 1$ ($P = 0.91$), $I^2 = 0\%$								
Test for overall effect: $Z = 1.28$ ($P = 0.20$)								
Test for subgroup differences: chi² = 0.01, $df = 1$ ($P = 0.91$), $I^2 = 0\%$								



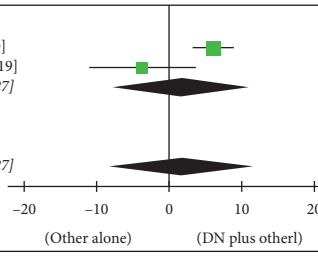
B.2 Short-term

Study or subgroup	Dry needling plus other Mean	SD	Total	Other alone Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Dry needing plus other therapies versus other therapies alone								
Cerezo-Tellez et al,. 2016	58.45	6.56	64	52.89	5.84	64	37.4	5.56 [3.41, 7.71]
Cerezo-Tellez et al., 2016 (b)	59.8	6.95	22	50.35	11.35	22	20.0	9.45 [3.89, 15.01]
Gallego-Sendarrubias et al., 2020	69.09	11.3	47	62.4	10.4	53	25.7	6.69 [2.41, 10.97]
Sterling et al., 2015	39.9	13.3	40	41.8	15.8	40	17.0	−1.90 [−8.30, 4.50]
Subtotal (95% CI)			*173*			*179*	*100.0*	*5.36 [2.00, 8.72]*
Heterogeneity: tau² = 6.65; chi² = 7.37, $df = 3$ ($P = 0.06$), $I^2 = 59\%$								
Test for overall effect: $Z = 3.13$ ($P = 0.0002$)								
Total (95% CI)			*173*			*179*	*100.0%*	*5.36 [2.00, 8.72]*
Heterogeneity: tau² = 6.65; chi² = 7.37, $df = 3$ ($P = 0.06$), $I^2 = 59\%$								
Test for overall effect: $Z = 3.13$ ($P = 0.002$)								
Test for subgroup differences: not applicable								



B.3 Long-term

Study or subgroup	Dry needling plus other Mean	SD	Total	Other alone Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Dry needing plus other therapies versus other therapies alone					9.08			
Cerezo-Tellez et al., 2016	59.55	7.2	64	53.49		64	55.5	6.06 [3.22, 8.90]
Sterling et al., 2015	42.3	14.1	40	46.1	17.6	40	44.5	−3.80 [−19.79, 3.19]
Subtotal (95% CI)			*104*			*104*	*100.0*	*1.67 [−7.94, 11.27]*
Heterogeneity: tau² = 41.20; chi² = 6.56, $df = 1$ ($P = 0.01$), $I^2 = 85\%$								
Test for overall effect: $Z = 0.34$ ($P = 0.73$)								
Total (95% CI)			*104*			*104*	*100.0*	*1.67 [−7.94, 11.27]*
Heterogeneity: tau² = 41.20; chi² = 6.56, $df = 1$ ($P = 0.01$), $I^2 = 85\%$								
Test for overall effect: $Z = 0.34$ ($P = 0.73$)								
Test for subgroup differences: not applicable								

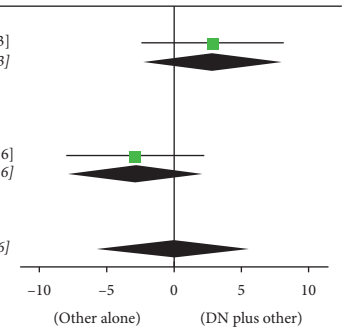


(b)

Figure 6: Continued.

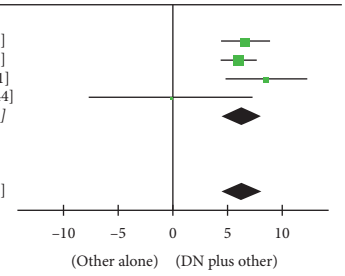
C.1 Immediate

Study or subgroup	Dry needling plus other Mean	SD	Total	Other alone Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Dry needing plus other therapies versus other therapies alone								
Gallego-Sendarrubias et al., 2020	62.02	14.1	47	79.12	12.35	53	49.3	2.90 [−2.35, 8.13]
Subtotal (95% CI)			*47*			*53*	*49.3*	*2.90 [−2.35, 8.13]*
Heterogeneity: not applicable								
Test for overall effect: $Z = 1.09$ ($P = 0.28$)								
Dry plus other therapies versus DN alone								
León-Hernández et al., 2016	60.38	11.44	29	63.27	8	30	50.7	−2.89 [−7.94, 2.16]
Subtotal (95% CI)			*29*			*30*	*50.7*	*−2.89 [−7.94, 2.16]*
Heterogeneity: not applicable								
Test for overall effect: $Z = 1.12$ ($P = 0.26$)								
Total (95% CI)			*76*			*83*	*100.0*	*2.43 [−1.30, 6.16]*
Heterogeneity: $\text{tau}^2 = 9.89$; $\text{chi}^2 = 2.44$, $df = 1$ ($P = 0.12$), $I^2 = 59\%$								
Test for overall effect: $Z = 0.01$ ($P = 0.99$)								
Test for subgroup differences: $\text{chi}^2 = 2.44$, $df = 1$ ($P = 0.12$), $I^2 = 59.0\%$								



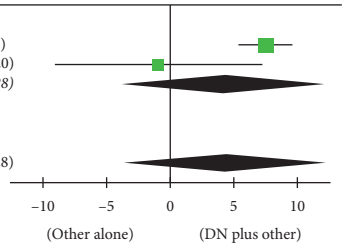
C.2 Short-term

Study or subgroup	Dry needling plus other Mean	SD	Total	Other alone Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Dry needing plus other therapies versus other therapies alone								
Cerezo-Tellez et al., 2016	61.95	7.04	64	55.31	5.84	64	32.9	6.64 [4.40, 8.88]
Cerezo-Tellez et al., 2016 (b)	66.8	2.8	22	60.8	2.65	22	45.9	6.00 [4.39, 7.61]
Gallego-Sendarrubias et al., 2020	67.37	8.25	47	78.84	10.5	53	16.5	8.53 [4.85, 12.21]
Sterling et al., 2015	50.55	17.8	40	50.65	16.6	40	4.7	−0.10 [−7.64, 7.44]
Subtotal (95% CI)			*173*			*179*	*100.0*	*6.34 [4.66, 8.03]*
Heterogeneity: $\text{tau}^2 = 0.93$; $\text{chi}^2 = 4.40$, $df = 3$ ($P = 0.22$), $I^2 = 32\%$								
Test for overall effect: $Z = 7.38$ ($P = 0.00001$)								
Total (95% CI)			173			179	100.0	6.34 [4.66, 8.03]
Heterogeneity: $\text{tau}^2 = 0.93$; $\text{chi}^2 = 4.40$, $df = 3$ ($P = 0.22$), $I^2 = 32\%$								
Test for overall effect: $Z = 7.38$ ($P < 0.00001$)								
Test for subgroup differences: not applicable								



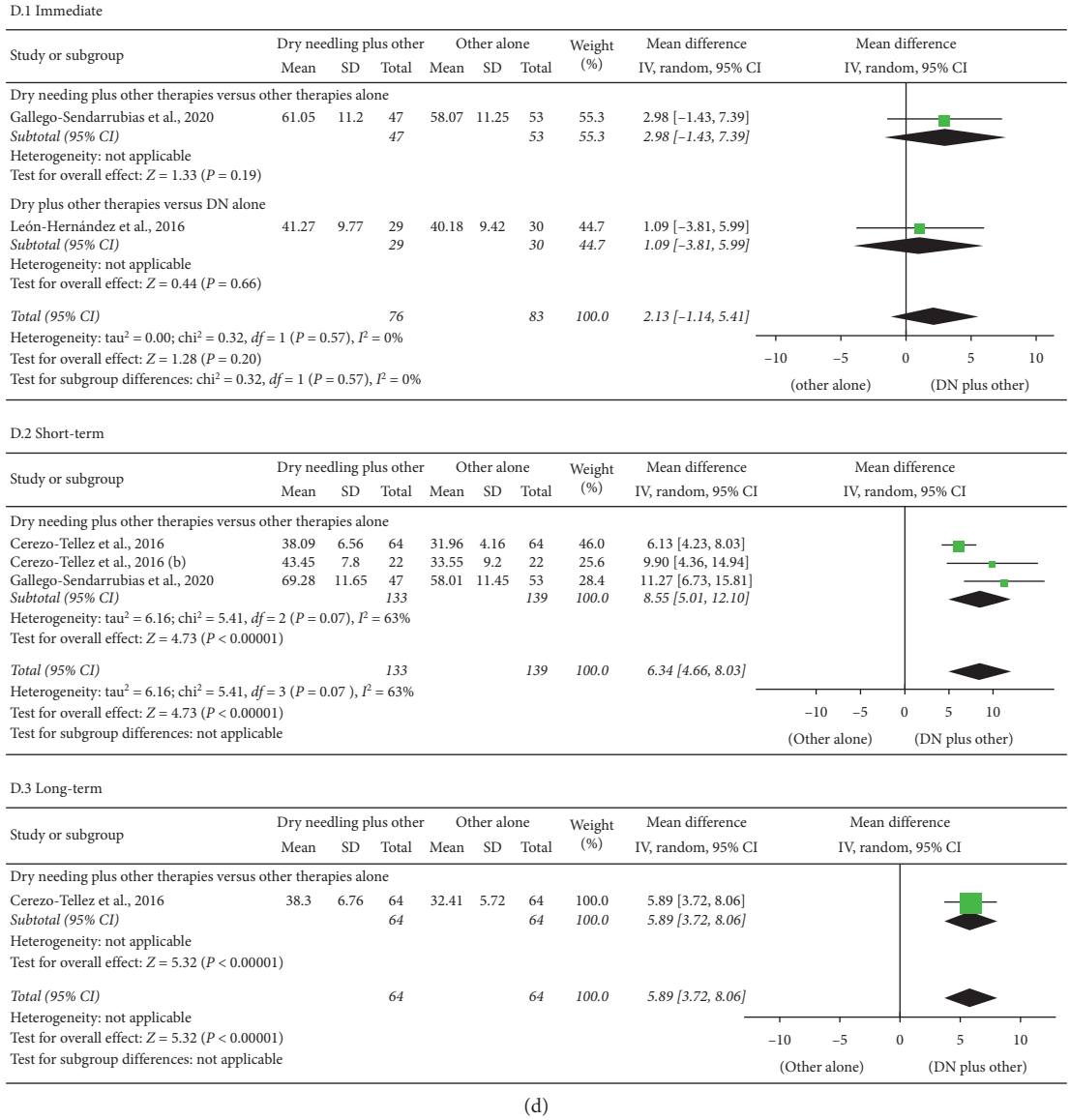
C.3 Long-term

Study or subgroup	Dry needling plus other Mean	SD	Total	Other alone Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Dry needing plus other therapies versus other therapies alone								
Cerezo-Tellez et al., 2016	62.8	7.12	64	53.29	4.76	64	61.3	7.51 (5.41, 8.61)
Sterling et al., 2015	52.65	18.8	40	53.55	18.15	40	38.7	−0.90 (−9.00, 7.20)
Subtotal (95% CI)			*104*			*104*	*100.0*	*4.25 (−3.78, 12.28)*
Heterogeneity: $\text{tau}^2 = 26.26$; $\text{chi}^2 = 3.88$, $df = 1$ ($P = 0.05$); $I^2 = 74\%$								
Test for overall effect: $Z = 1.04$ ($P = 0.30$)								
Total (95% CI)			104			104	100.0	4.25 (−3.78, 12.28)
Heterogeneity: $\text{tau}^2 = 26.26$; $\text{chi}^2 = 3.88$, $df = 1$ ($P = 0.05$), $I^2 = 74\%$								
Test for overall effect: $Z = 1.04$ ($P = 0.30$)								
Test for subgroup differences: not applicable								



(c)

Figure 6: Continued.



(d)

Figure 6: Comparison (mean differences) between the effects of dry needling combined with other interventions against other interventions on cervical range of motion in flexion (a), extension (b), rotation (c), and lateral-flexion (d) motion (1) immediately after, (2) at short-term, and (3) at long-term.

5. Discussion

5.1. Trigger Point Dry Needling Combined with Other Therapies. The objective of this meta-analysis was to compare the effects of the application of dry needling combined with other interventions against an intervention alone or dry needling alone applied over cervical TrPs associated with neck pain symptoms. We found low-to-moderate evidence suggesting a positive effect of including dry needling into physical therapy treatment for improving pain intensity at short-term and midterm and for improving pain-related disability at short-term as compared with the physical therapy intervention alone. Additionally, adding dry needling to a physical therapy intervention was also effective at short-term but not midterm and long-term, for increasing pressure pain thresholds and cervical range of motion. A small effect on pain catastrophism at midterm was found. The RoB of the clinical trials included in this study was generally low, but the inconsistency (heterogeneity) and imprecision of the results downgraded the level of evidence (GRADE).

The current meta-analysis is the first one investigating the impact of dry needling combined other interventions versus another intervention alone on pain intensity, related-disability, pressure pain sensitivity, cervical range of motion, and pain catastrophism in patients with TrPs associated with neck pain symptoms. Liu et al. [7] investigated the effects of the isolated application of dry needling and found low evidence supporting its effects immediately after and at 4 weeks when compared with control or sham. We found low-

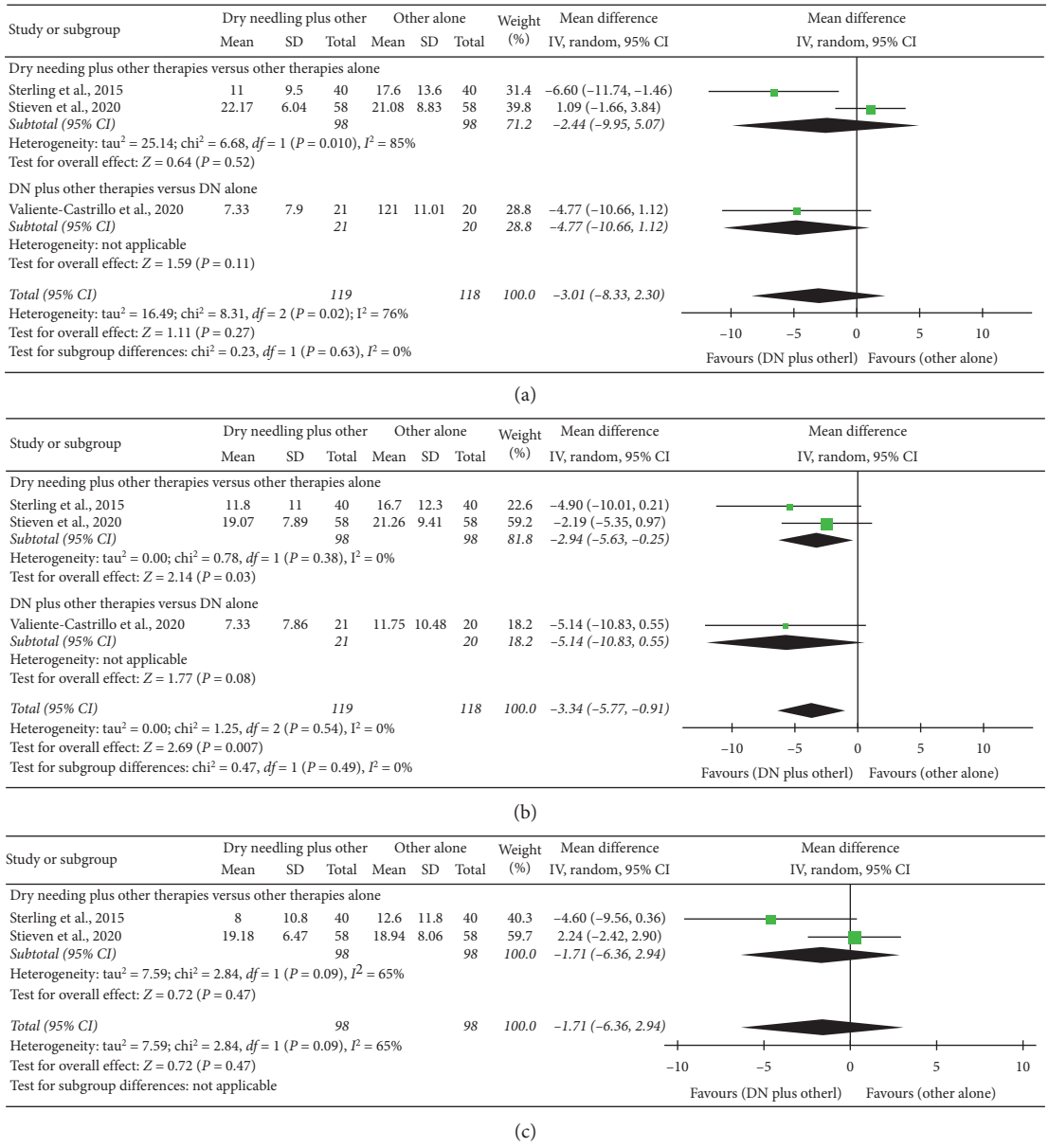


Figure 7: Comparison (mean differences) between the effects of dry needling combined with other interventions against other interventions on pain catastrophism (a) at short-term, (b) at midterm, and (c) at long-term.

quality evidence supporting a small positive effect of the inclusion of dry needling into a physical therapy treatment for improving pain intensity and pain-related disability when compared with the physical therapy treatment approach alone; however, the effects were observed mostly at short-term and at midterm only for pain intensity. The decrease on pain of −0.96 points (95% CI −1.61 to −0.31) at short-term and of −1.84 points (95% CI −2.83 to −0.85) at midterm did not reach the minimal clinically important difference (MCID) of 2.1 points described for people with mechanical neck pain [32], although changes at midterm were slightly superior to the general MCID of 1.4 points determined by Bijur et al. [33]. Nevertheless, we should recognize that the lower bound estimate of the confidence intervals did not surpass the MCID in either case, limiting the clinical relevance of these results. It is possible that some patients with TrPs associated with neck pain symptoms exhibit more benefits to dry needling than others. Based on current evidence, it seems that including dry needling into a physical therapy treatment approach could have only small effects at short-term and midterm follow-up periods for the treatment of neck pain associated to TrPs (low-to-moderate evidence); however, more studies are clearly needed.

We also found that adding dry needling into a physical therapy intervention has a moderate effect (low evidence) at short-term for decreasing pressure pain sensitivity (by increasing the pressure pain thresholds) and small effects for increasing cervical range of motion. These results agree with current theories supporting a potential hypoalgesic effect of dry needling [34], although differences were only significant

Table 4: Level of evidence (GRADE) for dry needling on pain intensity, pressure pain sensitivity, and cervical range of motion in patients with neck pain.

Number of studies	Risk of bias	Inconsistency	Indirectness of evidence	Imprecision	Publication bias	Quality of evidence	MD or SMD (95% CI)
Effects of the inclusion of dry needling on neck pain intensity							
Immediate follow-up (less than 1 week after single session)							
Overall effect ($n = 2$)	No	Serious ($I^2 = 54\%$)	No	Very serious	No	Very low	MD −0.55 (−1.64 to 0.55)
DN plus other therapy vs. others (n = 1)	No	No	No	Serious	No	Low	MD −0.96 (−1.61 to −0.31)*
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Very serious	No	Low	MD 0.21 (−1.20 to 1.62)
Short-term follow-up (1–12 weeks after intervention)							
Overall effect ($n = 7$)	No	Very serious ($I^2 = 94\%$)	No	No	No	Low	MD −1.76 (−2.66 to −0.86)*
DN plus other therapy vs. other ($n = 6$)	No	Very serious ($I^2 = 95\%$)	No	No	No	Low	MD −1.84 (−2.83 to −0.85)*
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Very serious	No	Low	MD −1.21 (−2.15 to −0.27)*
Midterm follow-up (12–24 weeks after intervention)							
Overall effect ($n = 3$)	No	No ($I^2 = 0\%$)	No	Serious	No	Moderate	MD −0.52 (−0.79 to −0.25)*
DN plus other therapy vs. others ($n = 2$)	No	No ($I^2 = 0\%$)	No	Serious	No	Moderate	MD −0.52 (−0.80 to −0.24)*
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Serious	No	Moderate	MD −0.53 (−1.78 to 0.72)
Long-term follow-up (more than 24 weeks after intervention)							
Overall effect ($n = 3$)	No	Very serious ($I^2 = 98\%$)	No	No	No	Low	MD −1.11 (−2.56 to 0.35)
DN plus other therapy vs. others ($n = 3$)	No	Very serious ($I^2 = 98\%$)	No	No	No	Low	MD −1.11 (−2.56 to 0.35)
Effects of the inclusion of dry needling on pain-related disability							
Short-term follow-up (1–12 weeks after intervention)							
Overall effect ($n = 6$)	No	Very serious ($I^2 = 81\%$)	No	No	No	Low	SMD −0.45 (−0.87 to −0.03)*
DN plus other therapy vs. others ($n = 5$)	No	Very serious ($I^2 = 84\%$)	No	No	No	Low	SMD −0.39 (−0.87 to 0.08)
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Serious	No	Moderate	SMD −0.77 (−1.40 to −0.13)*
Midterm follow-up (12–24 weeks after intervention)							
Overall effect ($n = 3$)	No	No ($I^2 = 11\%$)	No	Very serious	No	Low	SMD −0.16 (−0.44 to 0.11)
DN plus other therapy vs. others ($n = 2$)	No	No ($I^2 = 0\%$)	No	Very serious	No	Low	SMD −0.07 (−0.35 to 0.21)
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Very serious	No	Low	SMD −0.59 (−1.22 to 0.04)
Long-term follow-up (more than 24 weeks after intervention)							
Overall effect ($n = 3$)	No	Very serious ($I^2 = 88\%$)	No	No	No	Low	SMD −0.32 (−0.97 to 0.29)

Table 4: Continued.

Number of studies	Risk of bias	Inconsistency	Indirectness of evidence	Imprecision	Publication bias	Quality of evidence	MD or SMD (95% CI)
DN plus other therapy vs. others ($n = 3$)	No	Very serious ($I^2 = 88\%$)	No	No	No	Low	SMD −0.32 (−0.97 to 0.29)
Effects of the inclusion of dry needling on pressure pain thresholds							
Immediate follow-up (less than 1 week after single session)							
Overall effect ($n = 3$)	No	Serious ($I^2 = 79\%$)	No	Serious	No	Low	MD 40.26 (−20.42 to 100.94)
DN plus other therapy vs. others ($n = 1$)	No	No	No	Serious	No	Moderate	MD 50.01 (19.20 to 80.82)*
DN plus other therapy vs. DN alone ($n = 2$)	No	Very serious ($I^2 = 80\%$)	No	Very serious	No	Very low	MD 69.18 (−107.93 to 246.28)
Short-term follow-up (1–12 weeks after intervention)							
Overall effect ($n = 4$)	No	Very serious ($I^2 = 91\%$)	No	No	No	Low	MD 110.43 (26.71 to 194.15)*
DN plus other therapy vs. others ($n = 4$)	No	Very serious ($I^2 = 91\%$)	No	No	No	Low	MD 110.43 (26.71 to 194.15)*
Midterm follow-up (12–24 weeks after intervention)							
Overall effect ($n = 1$)	No	No	No	Very serious	No	Low	MD 32.10 (−21.68 to 85.88)
DN plus other therapy vs. others ($n = 1$)	No	No	No	Very serious	No	Low	MD 32.10 (−21.68 to 85.88)
Long-term follow-up (more than 24 weeks after intervention)							
Overall effect ($n = 2$)	No	Very serious ($I^2 = 88\%$)	No	Very serious	No	Very low	MD 50.09 (−64.61 to 164.78)
DN plus other therapy vs. others ($n = 2$)	No	Very serious ($I^2 = 88\%$)	No	Very serious	No	Very low	MD 50.09 (−64.61 to 164.78)
Effects of the inclusion of dry needling on cervical flexion range of motion							
Immediate follow-up (less than 1 week after single session)							
Overall effect ($n = 2$)	No	No ($I^2 = 0\%$)	No	Very serious	No	Low	MD 3.34 (−0.28 to 6.97)
DN plus other therapy vs. others ($n = 1$)	No	No	No	Very serious	No	Low	MD 3.68 (−0.79 to 8.15)
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Very serious	No	Low	MD 2.69 (−3.51 to 8.89)
Short-term follow-up (1–12 weeks after intervention							
Overall effect ($n = 4$)	No	Serious ($I^2 = 55\%$)	No	No	No	Moderate	MD 6.01 (2.86 to 9.16)*
DN plus other therapy vs. others ($n = 4$)	No	Serious ($I^2 = 55\%$)	No	No	No	Moderate	MD 6.01 (2.86 to 9.16)*
Long-term follow-up (more than 24 weeks after intervention)							
Overall effect ($n = 2$)	No	Serious ($I^2 = 74\%$)	No	Serious	No	Low	MD 2.89 (−4.67 to 10.45)
DN plus other therapy vs. others ($n = 2$)	No	Serious ($I^2 = 74\%$)	No	Serious	No	Low	MD 2.89 (−4.67 to 10.45)

Table 4: Continued.

Number of studies	Risk of bias	Inconsistency	Indirectness of evidence	Imprecision	Publication bias	Quality of evidence	MD or SMD (95% CI)
Effects of the inclusion of dry needling on cervical extension range of motion							
Immediate follow-up (less than 1 week after single session)							
Overall effect ($n = 2$)	No	No ($I^2 = 0\%$)	No	Very serious	No	Low	MD 2.43 (−1.30 to 6.16)
DN plus other therapy vs. others ($n = 1$)	No	No	No	Very serious	No	Low	MD 2.27 (−2.35 to 6.89)
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Very serious	No	Low	MD 2.72 (−3.59 to 9.03)
Short-term follow-up (1–12 weeks after intervention)							
Overall effect ($n = 4$)	No	Serious ($I^2 = 59\%$)	No	No	No	Moderate	MD 5.36 (2.00 to 8.72)*
DN plus other therapy vs. others ($n = 4$)	No	Serious ($I^2 = 59\%$)	No	No	No	Moderate	MD 5.36 (2.00 to 8.72)*
Long-term follow-up (more than 24 weeks after intervention)							
Overall effect ($n = 2$)	No	Very serious ($I^2 = 85\%$)	No	Serious	No	Very low	MD 1.67 (−7.94 to 11.27)
DN plus other therapy vs. others ($n = 2$)	No	Very serious ($I^2 = 85\%$)	No	Serious	No	Very low	MD 1.67 (−7.94 to 11.27)
Effects of the inclusion of dry needling on cervical rotation range of motion							
Immediate follow-up (less than 1 week after single session)							
Overall effect ($n = 2$)	No	Serious ($I^2 = 59\%$)	No	Very serious	No	Very low	MD −0.03 (−5.71 to 5.64)
DN plus other therapy vs. others ($n = 1$)	No	No	No	Very serious	No	Low	MD 2.90 (−2.33 to 8.13)
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Very serious	No	Low	MD −2.89 (−7.94 to 2.16)
Short-term follow-up (1–12 weeks after intervention)							
Overall effect ($n = 4$)	No	No ($I^2 = 32\%$)	No	No	No	High	MD 6.34 (4.66 to 8.03)*
DN plus other therapy vs. others ($n = 4$)	No	No ($I^2 = 32\%$)	No	No	No	High	MD 6.34 (4.66 to 8.03)*
Long-term follow-up (more than 24 weeks after intervention)							
Overall effect ($n = 2$)	No	Serious ($I^2 = 74\%$)	No	Serious	No	Low	MD 4.25 (−3.78 to 12.28)
DN plus other therapy vs. others ($n = 2$)	No	Serious ($I^2 = 74\%$)	No	Serious	No	Low	MD 4.25 (−3.78 to 12.28)
Effects of the inclusion of dry needling on cervical lateral flexion range of motion							
Immediate follow-up (less than 1 week after single session)							
Overall effect ($n = 2$)	No	No ($I^2 = 0\%$)	No	Very serious	No	Low	MD 2.13 (−1.14 to 5.41)
DN plus other therapy vs. others ($n = 1$)	No	No	No	Very serious	No	Low	MD 2.98 (−1.43 to 7.39)
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Very serious	No	Low	MD 1.09 (−1.14 to 5.41)
Short-term follow-up (1–12 weeks after intervention)							
Overall effect ($n = 3$)	No	Serious ($I^2 = 63\%$)	No	Serious	No	Low	MD 8.55 (5.01 to 12.10)*

Table 4: Continued.

Number of studies	Risk of bias	Inconsistency	Indirectness of evidence	Imprecision	Publication bias	Quality of evidence	MD or SMD (95% CI)
DN plus other therapy vs. others ($n = 3$)	No	Serious ($I^2 = 63\%$)	No	Serious	No	Low	MD 8.55 (5.01 to 12.10)*
Long-term follow-up (more than 24 weeks after intervention)							
Overall effect ($n = 1$)	No	No	No	Very serious	No	Low	MD 5.89 (3.72 to 8.06)*
DN plus other therapy vs. others ($n = 1$)	No	No	No	Very serious	No	Low	MD 5.89 (3.72 to 8.06)*
Effects of the inclusion of dry needling on pain catastrophizing							
Short-term follow-up (1–12 weeks after intervention)							
Overall effect ($n = 3$)	No	Serious ($I^2 = 76\%$)	No	Very serious	No	Very low	MD −3.01 (−8.33 to 2.30)
DN plus other therapy vs. others ($n = 2$)	No	Very serious ($I^2 = 85\%$)	No	Very serious	No	Very low	MD −2.44 (−9.95 to 5.07)
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Very serious	No	Low	MD −4.77 (−10.66 to 1.12)
Midterm follow-up (12–24 weeks after intervention)							
Overall effect ($n = 3$)	No	No ($I^2 = 0\%$)	No	Serious	No	Moderate	MD −3.34 (−5.77 to −0.91)*
DN plus other therapy vs. others ($n = 2$)	No	No ($I^2 = 0\%$)	No	Serious	No	Moderate	MD −2.94 (5.63 to −0.25)*
DN plus other therapy vs. DN alone ($n = 1$)	No	No	No	Very serious	No	Low	MD −5.14 (−10.83 to 0.55)
Long-term follow-up (more than 24 weeks after intervention)							
Overall effect ($n = 2$)	No	Serious ($I^2 = 65\%$)	No	Very serious	No	Very low	MD −1.71 (−6.36 to 2.94)
DN plus other therapy vs. others ($n = 2$)	No	Serious ($I^2 = 65\%$)	No	Very serious	No	Very low	MD −1.71 (−6.36 to 2.94)

*Statistically significant ($P < 0.05$). Risk of bias: No, most information is from results at low risk of bias; Serious, crucial limitation for one criterion or some limitations for multiple criteria, sufficient to lower confidence in the estimate of the effect; Very serious, crucial limitation for one or more criteria sufficient to substantially lower confidence in the estimate of the effect. Inconsistency: Serious, $I^2 > 40\%$; Very serious, $I^2 > 80\%$. Indirectness of evidence, no indirectness of evidence was found in any study. Imprecision (based on sample size): Serious, $n < 250$ subjects; Very serious, $n < 250$, and the estimated effect is little or absent. Publication bias (based on funnel plots), no publication bias was found. Funnel plots are not shown because of the small number of trials.

for short-term. It is possible that this neurophysiological effect is short-lasting. On the contrary, the effects of adding dry needling on cervical range of motion were small and should not be considered as clinically relevant. These results may be related to the fact that most trials included in the current meta-analysis have shown positive effects on these outcomes, and the inclusion of another intervention does not lead to better results, which has been also found when combining manual therapy with exercise for the management of neck pain [12]. This can be also related to the fact that manual therapy approaches [35] and dry needling interventions [34] share common neurophysiological mechanisms, and they only potentiate their effects on a subgroup of patients. Future studies should investigate this.

5.2. Safety of Trigger Point Needling. Since dry needling is an invasive intervention, clinicians should monitor the presence of adverse events. Carlesso et al. [36] defined an adverse event "as a sequela of medium-term duration with any symptom perceived as unacceptable to the patient and requiring further treatment." Adverse events can be categorized as minor, moderate, or major. Previous studies have found that most events occurring after application of dry needling, such as bleeding or postneedling soreness, can be categorized as minor adverse events [37, 38]. Most studies included in this meta-analysis monitored the presence of adverse events during the study and reported the presence of postneedling soreness as the most common adverse event, supporting that dry needling seems to be a potentially safe intervention. Nevertheless, major adverse events, e.g., pneumothorax, have been also reported in the literature when applied dry needling to the cervical and thoracic spine, although their rate is less than 0.1% (1 per 1,024 needling treatments) and depend on the anatomical location. In fact, case reports describing pneumothorax after dry needling treatment have applied the intervention over thoracic

musculature [39, 40]. Although dry needling seems to be a safe intervention if properly applied, therapists need to be aware of the potential risks associated with its application on each body area where it is applied.

5.3. Strengths and Limitations. The results of the current meta-analysis should be generalized within the context of its potential strengths and limitations. The strengths include a comprehensive literature search, methodological rigor, exhaustive data extraction, rigorous statistical analysis, and the inclusion of randomized controlled trials of high methodological quality. Among the limitations, we recognized that dry needling was applied with different dosages, that is, sessions, frequency of application, and combined with a variety of interventions exhibiting different evidence (e.g., manual therapy, stretching, and exercise). Second, the heterogeneity and imprecision of the results of the trials was serious; therefore, current results should be taken with caution. Third, the number of trials in some comparisons was small ($n = 3$) which limits the extrapolation of the results. It is possible that a greater number of high-quality clinical trials investigating midterm and long-term effects of dry needling combined with more detailed physical therapy interventions would lead to different results.

5.4. Clinical and Research Implications. Although this is the first meta-analysis investigating the effects of adding dry needling to other physical therapy interventions in patients with neck pain associated to myofascial TrPs, several questions remain to be elucidated. First, just few studies investigating long-term follow-up periods are available in the literature. Second, trials in this meta-analysis investigated different physiotherapy approaches in heterogeneous populations (traumatic vs. insidious onset). Third, since neck pain is characterized by motor control disturbances, the inclusion of dry needling could lead to changes in muscle strength outcomes in this population. A recent meta-analysis reported medium effect sizes for dry needling to enhance force production in individuals with neck pain (moderate evidence), although this analysis was just based on two studies [41]. In fact, these two studies were included in the current meta-analysis, but we did not pool data from strength outcomes due to the heterogeneous interventions applied in them. It is probable that the combination of dry needling would be not as effective as it can be with any physical therapy intervention. Proper understanding of the clinical presentation of each individual patient and the underlying mechanisms of each intervention could lead to better clinical outcomes.

6. Conclusion

The current meta-analysis found low-to-moderate evidence suggesting a positive effect of adding dry needling into a physical therapy approach for improving pain intensity at short-term and midterm and for improving pain-related disability at short-term as compared with the same intervention applied alone. Additionally, adding dry needling was effective at short-term for increasing pressure pain thresholds and cervical range of motion and on pain catastrophism at midterm. Although the methodological quality of the included trials was high, the inconsistency (heterogeneity) and imprecision of the results downgraded the overall levels of evidence.

Data Availability

No data are publicly available since this is a systematic review and meta-analysis.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

CFdlP, GPM, MNS, JSI, GGC, and JLAB conducted literature review and did the statistical analysis. CFdlP, ILdUV, and JAC contributed to drafting the paper. All authors contributed to the study concept and design, contributed to interpretation of data, revised the text for intellectual content, and have read and approved the final version of the manuscript.

Supplementary Materials

Supplementary Table 1: database formulas during literature search; Supplementary Table 2: characteristics of the dry needling intervention of the included studies; Supplementary Table 3: adverse events described in the included studies. (*Supplementary Materials*)

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