Does Syndrome Differentiation Matter? A Meta-Analysis of Randomized Controlled Trials in Cochrane Reviews of Acupuncture

Huijuan Cao, PhD,¹ Suzannah Bouchier, BAppSc,² and Jianping Liu, PhD, MD¹

ABSTRACT

Background: One of the basic and important principles of Traditional Chinese Medicine theory is syndrome differentiation, which is widely utilized for individual diagnosis and in the application of acupuncture treatment. However, the impact of syndrome differentiation on therapeutic effect is unclear because of insufficient supportive clinical evidence.

Objective: The aim of this study was to analyze current Cochrane Database systematic reviews of acupuncture and to evaluate differences in therapeutic effects of acupuncture treatment when syndrome differentiation is utilized, compared to when this approach is not utilized.

Methods: Cochrane Database systematic reviews of acupuncture were included if the reviews had sufficient data to perform subgroup analyses by syndrome differentiation applied during acupoints' selection. Searching was conducted across all available articles of the Cochrane Library, and the search concluded in July 2011.

Results: Forty-four trials from five Cochrane reviews were included in 10 subgroup meta-analyses. Seven meta-analyses showed that there were no differences between trials using fixed acupoints prescriptions and trials using individualized treatment based on relevant symptom improvements in cases of acute stroke, depression, epilepsy, migraine, and peripheral joint osteoarthritis (OA). The remaining 3 meta-analyses showed that acupuncture with fixed prescriptions was superior to individualized acupuncture for pain relief of peripheral joint OA, compared to sham control.

Conclusions: The available evidence showed no significant difference between acupuncture treatment with or without syndrome differentiation. Large, well-designed trials are warranted to address the use of syndrome differentiation for specific diseases or conditions in order to confirm if there are any advantages of using syndrome differentiation to achieve better therapeutic effects with acupuncture.

Key Words: Syndrome Differentiation, Acupuncture, Traditional Chinese Medicine, Meta-Analysis, Cochrane Review

INTRODUCTION

SYNDROME DIFFERENTIATION (Bian Zheng Lun Zhi) is one of the most important principles of diagnosis and treatment approaches, according to Traditional Chinese

Medicine (TCM) theory. TCM diagnosis is not focused on disease but on Zheng (the pattern of the syndrome), an approach that differs from Western medicine. Syndrome is a way of classifying pathological symptoms and signs to determine basic disharmony in the body. Each syndrome has a

¹Center for Evidence-Based Chinese Medicine of Beijing University of Chinese Medicine, Beijing, China.

²Centre for Complementary Medicine Research, University of Western Sydney, Sydney, New South Wales, Australia.

Professor, Director of Center for Evidence-Based Chinese Medicine of Beijing University of Chinese Medicine, Beijing, China.

set of signs and symptoms that identify the origin, location, and nature of the condition.¹ The name of a condition suggests its entire course of pathological changes, whereas the determination of a syndrome reflects the pathology of a disease at a certain stage. The condition of the body is constantly changing as pathogenic and antipathogenic factors confront each other. The body struggles to maintain a dynamic equilibrium between its internal condition and the external environment. Accordingly, the symptoms and signs of an illness will change as it proceeds, and so must the diagnosis of the patient's syndrome. The TCM theory for syndrome differentiation includes eight principles, Zang-fu, meridians, Qi and Blood, or Triple-Energizer.² Differentiation analyzes the characteristics of Zheng and disease according to different parameters, such as Zang-fu's function, connection of Yin and Yang meridians, and transportation of Qi and Blood.

The principles of acupuncture treatment include regulating Yin and Yang, strengthening the body's resistance, eliminating pathogens, and distinguishing between the presenting symptoms and the syndrome. In TCM, acupoints are selected from twelve regular meridians that correlate to individual organs. The meridians are the pathways through which Qi and Blood flow. Disorders of the meridians may affect corresponding organs; likewise, disorders of the organs will be reflected in the meridians. In acupuncture practice, points are selected depending on the meridian syndrome differentiation, which includes the following aspects^{3,4}:

- (1) Observation of any small changes on the surfaces of specific meridians or acupoints. Any localized changes to the skin may reflect the pathological state of Zheng and disease. Syndromes can be diagnosed by identifying certain signs and symptoms that emerge along the course of a particular meridian pathway. This can assist practitioners when they are designing individualized treatment protocols for patients.
- (2) Zheng may result from disharmony of an individual organ or from an interaction between organs. It is important to understand the unique physiological function of organs in TCM theory. Acupuncture can be administered according to TCM theory regarding syndrome differentiation, but this may also combined with modern medical diagnosis techniques.⁵
- (3) When applying acupuncture prescriptions, syndrome differentiation should be considered for selection of meridians, actions of acupoints, using appropriate acupuncture techniques and equipment, stimulation intensity, and application of combined therapies, such as moxibustion, cupping, and herbal medicine.

Acupuncture application based on clinical syndrome differentiation using meridian theories also addresses the whole body system, which reflects the unique character of TCM, thus ensuring the efficacy of acupuncture treatment.⁶

Although syndrome differentiation is widely accepted in individual diagnosis and treatment using acupuncture, there remains insufficient clinical evidence regarding the impact of syndrome differentiation on therapeutic effect. This review aims to evaluate the difference of therapeutic effect between acupuncture treatments with or without syndrome differentiation as shown in Cochrane acupuncture reviews.

METHODS

Inclusion Criteria

Cochrane systematic reviews evaluating the therapeutic effect of acupuncture, compared with no treatment, placebo, or conventional medication, which had meta-analysis with more than 4 included trials (at least 2 trials using syndrome differentiation for point selection and at least 2 trials that did not use this approach).

Identification and Selection of Reviews

All available Cochrane systematic reviews on acupuncture were searched from the Cochrane Library (the search ended in July 2011); search terms included acupuncture, electro-acupuncture, and meridian. Two authors (Cao and Liu) independently reviewed, identified, and checked the individual trials against the inclusion criteria.

Data Extraction and Quality Assessment

The data were independently extracted from the included reviews. These data included authors, title of study, year of publication, study size, assessment of risk of bias within studies, details of methodological information, number of trials which used/did not use syndrome differentiation, and outcomes (with risk ratio [RR], or mean difference [MD], and relative 95% confidence interval [CI] for each trial).

According to criteria in the Cochrane Reviewers' Handbook,⁷ the authors of all included reviews had already assessed the methodological quality of each included trial. The following characteristics were assessed: sequence generation; allocation concealment; blinding; incomplete data assessment; selective outcome reporting; and other sources of bias. There were three potential responses for these six items: "yes"; "no"; and "unclear." In all cases an answer of "yes" indicated a low risk of bias and an answer of "no" indicated a high risk of bias. If there was insufficient detail reported in the study the response was listed as "unclear."

Data Analysis and Statistical Methods

Data were extracted and summarized using RRs with 95% CIs for binary outcomes or MDs with 95% CIs for continuous outcomes. Revman 5.0.20 software was used for data analyses. Subgroup meta-analysis was performed,

looking at different methods of points' selection (whether syndrome differentiation was used) and if the trials had good homogeneity (which was assessed by examining I^2 , a quantity that describes approximately the proportion of variation in point estimates caused by heterogeneity rather than by sampling error), in study design, participants, interventions, control, and outcome measures. The conservative random-effects model (REM) was used unless the degree of heterogeneity was readily explainable, or when the measure of heterogeneity I^2 was $<25\%$, in which case, a fixed effect model (FEM) was used.

RESULTS

Description of Reviews

After primary searches of the Cochrane Library, 99 citations were identified, with the majority of these being excluded after reviewing their titles and abstracts; 32 full-text articles were retrieved, however; most of these were excluded because of insufficient data for subgroup meta-analysis. In total, five⁸⁻¹² reviews with a combined 12,851 participants were included in this current study (Fig. 1 and Table 1).

There were five conditions involved within the five review articles, including epilepsy, migraine prophylaxis,

peripheral joint osteoarthritis (OA), depression, and acute stroke. There were 93 RCTs originally included in these reviews. Because of the previous meta-analysis and characteristics for each trial, only 44 studies from the five reviews were subsequently included in the current subgroup meta-analysis. The subgroup was categorized by whether syndrome differentiation was used during acupoints' selection. All the trials that applied syndrome differentiation mentioned that acupoints were either standardized or individually selected "according to Traditional Chinese Medicine," or "depending on Chinese syndrome diagnosis" (Table 2).

Methodological Quality of Included Randomized Controlled Trials

Among the 44 included trials, only seven were assessed as having a "low risk of bias," with 26 trials listed as having a "high risk of bias" because of poor methodological quality, and 11 assessed as being "unclear" (Table 2).

Results of Subgroup Meta-Analyses

From the five included reviews, a subgroup analyses for each outcome measurement was conducted across each disease respectively according to whether syndrome differentiation was used for acupoints' selection. Overall, ten subgroup analyses were conducted, and seven showed no difference between trials using fixed prescriptions and individualized prescriptions with respect to symptom reduction for acute stroke, depression, epilepsy, migraine prophylaxis, and peripheral joint OA. (Table 3).

One meta-analyses (Table 3) showed acupuncture with a fixed prescription had significant therapeutic effect on pain relief of peripheral joint OA, compared to a sham control condition with respect to short-term effects (MD -2.24 , 95%CI -4.00 to -0.48 , $p=0.01$, 6 trials, REM), although individualized acupuncture produced no difference from sham control (MD -0.42 , 95% CI -1.68 to 0.84 , $p=0.51$, 3 trials, REM). Two subgroup analyses (Table 3) also found similar results for acupuncture versus sham acupuncture with respect to responses for migraine prophylaxis 8 weeks and 6 months following randomization. Acupuncture without syndrome differentiation (RR 4.83, 95% CI 1.81 to 12.89, $p=0.002$, 2 trials, FEM and RR 1.79, 95%CI 1.16 to 2.77, $p=0.008$, 2 trials, FEM) seemed superior to acupuncture with syndrome differentiation (RR 1.09, 95%CI 0.94 to 1.26, $p=0.28$, 5 trials, FEM and RR 1.07, 95%CI 0.92 to 1.25, $p=0.38$, 4 trials, FEM).

DISCUSSION

According to the ten subgroup analyses across 44 RCTs, applying syndrome differentiation in acupoints' selection was no more effective than using a fixed formula

FIG. 1. Flow chart of review inclusions and exclusions.

TABLE 1. CHARACTERISTICS OF FIVE INCLUDED REVIEWS

<i>First author & year</i>	<i># of included trials</i>	<i>Conditions</i>	<i># of participants</i>	<i>Main findings</i>
Cheuk 2008	11	Epilepsy	914	Two trials found that more children treated with needle acupuncture plus Chinese herbs had $\geq 75\%$ reduction in seizure frequency $\geq 50\%$ reduction in seizure duration, compared with children who were treated with Chinese herbs alone. Compared to phenytoin and valproate, the pooled results showed that patients who received needle acupuncture appeared to be more likely to have $\geq 75\%$ reduction in seizure frequency.
Linde 2009	22	Migraine prophylaxis	4419	Pooled analyses did not show a statistically significant superiority for true acupuncture, compared to sham or routine care, but acupuncture was associated with slightly better outcomes and fewer adverse effects than prophylactic drug treatment.
Manheimer 2010	16	Peripheral joint osteoarthritis	3498	Compared to a sham control, acupuncture showed statistically significant improvements in osteoarthritis (OA) pain and function; however, these pooled short-term benefits did not meet the current study's predefined thresholds for clinical relevance (i.e., 1.3 points for pain; 3.57 points for function) and there was substantial statistical heterogeneity. Compared to wait-list control, physician consultation, exercise, or education, acupuncture was associated with statistically significant, clinically relevant short-term reductions in OA pain and improvements in function. Acupuncture, as an adjuvant to an exercise-based physiotherapy program, did not result in any greater improvements than the exercise program alone. Information on safety was reported in only eight trials and, even in those trials, there was limited reporting and heterogeneous methods.
Smith 2010	30	Depression	2812	There was insufficient evidence of a consistent beneficial effect from acupuncture, compared with a wait-list control or sham acupuncture control. Two trials found that acupuncture may have an added benefit when combined with medication, compared with medication alone. The majority of trials compared manual and electro-acupuncture with medication and found no effect between groups.
Zhang 2005	14	Acute stroke	1208	There was a borderline significant trend toward lower patient morbidity or dependence and a reduction in global neurological deficit scores in an acupuncture group after 3 months or more compared with sham acupuncture or open control. Severe adverse events with acupuncture (dizziness, intolerable pain, and/or infection of acupoints) were rare (6/386; 1.55%).

for acupoints' selection, which seems inconsistent with TCM theory.

A possible explanation for these findings may include the relatively small number of trials assessed, with most resulting in a high risk of bias with respect to methodological quality (Table 2). According to a literature review conducted in 2005, syndrome differentiation was cited as being important in acupuncture application; however, insufficient attention is currently placed upon this in clinical practice.¹³ Researchers who conducted the review collected clinical reports of acupuncture and moxibustion published in three major Chinese acupuncture journals

from 2001 to 2003. Only 35 out 2864 studies reported that selection of acupoints was based on meridian differentiation. In addition, because the limitation of only including RCTs, a fixed prescription was more likely to be used as the standard treatment for easier assessment and control.

As a result of there being insufficient original studies directly comparing acupuncture with or without syndrome differentiation, only included trials from Cochrane reviews were included in the current subgroup meta-analysis. Data from each study were extracted using the existing analysis; this secondary analysis may have increased the potential of

TABLE 2. CHARACTERISTICS OF 44 INCLUDED TRIALS FROM 5 COCHRANE REVIEWS⁸⁻¹²

<i>First author & year</i>	<i>Conditions</i>	<i>Risk of bias</i>	<i>Acupuncture points' selection (and combined therapies)</i>	<i>Controls</i>	<i>Duration of treatments</i>
Alecrim, 2005	Migraine prophy/laxis	Unclear	Acupuncture points: Individualized selection according to TCM	Sham acupuncture	12 weeks
Alecrim, 2006	Migraine prophy/laxis	Low	Acupuncture points: Semi-standardized point selection (GB 12 20 & 21 and BL 10 in all patients + individualized additional points from a selection)	Sham acupuncture	12 weeks
Alecrim, 2008	Migraine prophy/laxis	Low	Acupuncture points: Individualized selection based on TCM principles	Very superficial insertion of 10–15 needles at acupuncture points considered irrelevant for headache	12 weeks
Baust, 1978	Migraine prophy/laxis	High	Acupuncture points: If pain mainly frontal, GB 14, Ex 3, LI 4; if temporal, Ex 9, GB 20, TE 5; if occipital, GV 15, BL 10, BL 60	Placebo points 2–3 cm distant from true points	12 days
Berman, 1999	Peripheral joint OA	High	Point selection: Formula Points stimulated: GB 34 & 39, Sp 6 & 9, St 35, 36, UB 60, KI 3, Ex 32 (Xiyian); electro-stimulation at St 35 and Ex 32	Standard of care—remain on current level of oral therapy (Western drugs)	8 weeks
Berman, 2004	Peripheral joint OA	Unclear	Point selection: Formula Points stimulated: GB 34 & 39, Sp 6 & 9, St 35 & 36, Ex 32 (Xiyian), UB 60, KI 3; electro stimulation at Ex 32 (Xiyian)	Control group A: Combined insertion/non-insertion procedure Control group B: Education	26 weeks
Cai, 2002	Acute stroke	Unclear	2 scalp acupoints + drug therapy	Drug therapy	14 days
Ceccherelli, 1992	Migraine prophy/laxis	Unclear	Acupuncture points: BL 2, 10 & 60, GB 3 & 20, GV 11 & 20, LR 3, CV 13, Ex-HN 1, St 8 (on non-painful side)	Placebo acupuncture	10 weeks
Diener, 2006	Migraine prophy/laxis	Low	Acupuncture points: Semi standardized depending on Chinese syndrome diagnosis	Control intervention 1: Sham acupuncture Control intervention 2: Guideline-based individualized standard treatment: (1) preference beta-blockers; (2) preference flunarizine; (3) preference valproic acid	5 weeks
Dowson, 1985	Migraine prophy/laxis	High	Acupuncture points: Point selection according to location of pain (modified after 2–3 sessions if no response)	Mock transcutaneous nerve stimulation	6 weeks
Duan, 1997	Acute stroke	Unclear	2 acupoints (DU 20, GB 7), manual twirling stimulation, 24 minutes/session, once/day for 30 days + routine drug therapy	Routine drug therapy	30 days
Fan, 2005	Depression	High	Acupuncture was applied to four acupoints points, DU 20, M-HN-3, four gates, ear seeds to auricular points for Liver and Heart	Control group A: Fluoxetine Control group B: Sham acupuncture	3 months
Fink, 2001	Peripheral joint OA	High	Point selection: Formula Number of points used: 12	Sham acupuncture	3 weeks
Foster, 2007	Peripheral joint OA	Low	Point selection: Flexible formula Local points were Sp 9 & 10; St 34, 35 & 36; Xiyian, GB 34, & trigger points; distal points were LI 4, TH 5, Sp 6, Liv 3, St 44, KI 3, BL 60, & GB 41	Control group A: Sham “non-penetrating acupuncture at the same points as the true acupuncture” Control group B: Advice Control group 1: Sham acupuncture + conventional stroke rehabilitation	3 weeks
Gosman, 1998	Acute stroke	Low	10 acupoints (DU 20, LI 11, ST 38, Ex-mob, SJ 5) + conventional stroke rehabilitation		12 months

(continued)

TABLE 2. (CONTINUED)

<i>First author & year</i>	<i>Conditions</i>	<i>Risk of bias</i>	<i>Acupuncture points' selection (and combined therapies)</i>	<i>Controls</i>	<i>Duration of treatments</i>
He, 2005	Depression	High	Acupuncture points DU 26, PC 6, Liv 3, HT; additional acupuncture points added according to diagnosis	Control group 2: Conventional stroke rehabilitation	8 weeks
Henry, 1985	Migraine prophylaxis	High	Acupuncture points: LI 4, St 36, BL 2, BL 10 & 60, LR 3 needling with electro-stimulation	Fluoxetine, 20 mg/day, taken in the morning	3.5 months
Huang, 2002	Acute stroke	Unclear	4–6 acupoints, pricking Blood therapy, once/day for 7 days + drug therapy, including ligustrazine and dextran	Needling 1 cm distant from points used in acupuncture group	7 days
Khang, 2002	Depression	High	Electro-acupuncture group received stimulation to points DU 20, 17 & 21, & M-HN-3; secondary points were added based on a differential diagnosis	Drug therapy including, ligustrazine and dextran	6 weeks
Kloster, 1999	Epilepsy	Unclear	Needle acupuncture, at LR 3, LI 4, GV 20 + acupoints chosen according to TCM diagnosis	Amitriptyline, 150–300 mg/d according to severity, medication was administered twice/day, for 6 weeks	7.5 weeks
Li 2004	Depression	High	Acupuncture points DU 20, 16, & 26, M-HN-1 and –3, Liv 3, & UB 18 used	Sham acupuncture	6 weeks
Linde K, 2005	Migraine prophylaxis	Low	Acupuncture points in all patients recommended GB 20 & 40 or 41 or 42, DU 20, Liv 3, SJ 3 or Taiyang; additional optional points recommended according to individual symptoms	Fluoxetine	8 weeks
Linde M, 2005	Migraine prophylaxis	Unclear	Acupuncture points in all patients GB 8 & 20, LI 4, LR 3, Sp 6 + either GB 14 or UB 10, depending on site of maximum pain	Control intervention: Minimal acupunctureControl 2: Wait-list	3 months
Luo, 1985	Depression	High	Two acupuncture points were stimulated: DU 20 and M-HN-3	Non-penetrating sham needles at the same points	6 weeks
Luo, 1988	Depression	High	Two acupuncture points were stimulated: DU 20 and M-HN-3	Amitriptyline	6 weeks
Luo, 1998	Depression	High	Two acupuncture points were stimulated: DU20 and M-HN-3	Amitriptyline	6 weeks
Ma, 2001	Epilepsy	High	Acupuncture at 6 points + Xi Feng capsule; additional acupuncture at 1 or 2 acupoints depending on TCM diagnosis	amitriptyline Xi Feng capsule alone	6 months
Sangdee, 2002	Peripheral joint OA	High	Point selection: Formula Points stimulated: St 35, LR 8, Ex 32 (Xiyan) + 1 trigger point	Control group A: Sham procedure + placebo diclofenac Control group B: Sham procedure + diclofenac Control group C: Electro- acupuncture + diclofenac	4 weeks
Scharf, 2006	Peripheral joint OA	Unclear	Point selection: Flexible formula Points stimulated: according to TCM: 1–2 of 16 defined distant points	Control group A: Sham acupuncture with 10 points total	6 weeks
Si, 1998	Acute stroke	High	8 acupoints (DU 20, DU 24, LI 4, LI 11, St 36, PC 6, LR 3, Sp6), plus routine drug therapy	Control group B: Conservative therapy Routine drug therapy	37 days
Takeda, 1994	Peripheral joint OA	High	Point selection: Formula Points stimulated: GB 34, St 35, Sp 9, Ex-31 (Heding), Ex-32 (Xiyan)	Superficial needling one inch from the acupuncture points	3 weeks

(continued)

TABLE 2. (CONTINUED)

<i>First author & year</i>	<i>Conditions</i>	<i>Risk of bias</i>	<i>Acupuncture points' selection (and combined therapies)</i>	<i>Controls</i>	<i>Duration of treatments</i>
Tukmachi, 2004	Peripheral joint OA	High	Point selection: Formula Points stimulated: Electro-acupuncture at Sp 9, GB 34, BL 40 & 57, two Xiyao points; manual stimulation at GB 34; needle insertion only at St 36, LR 3 & LI4	Control group A: Symptomatic medicationControl group B: Acupuncture + continuance on medication	5 weeks
Vas, 2004	Peripheral joint OA	High	Point selection: Formula Points stimulated: Electro-acupuncture at GB 34, Sp 6 & 9, St 36 & 40, KI 3, LI 4, Ex-32 (Xiyao)	Retractable needles went into cylinders and were placed at true points + mock electro-stimulation	12 weeks
Vincent, 1989	Migraine prophylaxis	Unclear	Acupuncture points: Classical points chosen individually according to tenderness; 8 both local and distant points used	Superficial needling only	6 weeks
Weinschutz, 1993	Migraine prophylaxis	High	Acupuncture points: Up to 10 points chosen according to pain localization and modalities	Sham acupuncture	8 weeks
Weinschutz, 1994	Migraine prophylaxis	Unclear	Acupuncture points: Up to 10 points chosen according to pain localization and modalities	Sham acupuncture	8 weeks
Wenbin, 2002	Depression	High	Participants receiving acupuncture based on TCM syndrome differentiation	Fluoxetine hydrochloride	8 weeks
Williamson, 2007	Peripheral joint OA	High	Point selection: Flexible formula Points stimulated for all patients were: Sp 9, 10; St 35 & 36; GB 34; Xiyao; & Liv 3	Control group A: Physiotherapy Control group B: Advice and exercise	6 weeks
Witt, 2005	Peripheral joint OA	Low	Point selection: Flexible formula	Control group A: Sham acupuncture Control group B: Wait-list	8 weeks
Wu, 2002	Acute stroke	High	Points chosen according to principles of TCM 6 main acupoints and > 6 auxiliary acupoints + routine drug therapy	Routine drug therapy	25 days
Xiong, 2003	Epilepsy	High	Acupuncture + Chinese herb mixtures; acupuncture at 10 points for 30 minutes, daily	Control group 1: Chinese herb alone Control group 2: Carbamazepine	6 weeks
Yan, 2004	Depression	High	Electro-acupuncture on 2 acupoints: DU 20, and M-NH- 3	Amitriptyline	3 weeks
Zhang, 2003	Depression	High	Two primary groups of acupuncture points were needled alternatively to participants; additional combined points were added	Amitriptyline	3 weeks
Zhang, 2006	Epilepsy	High	Treatment group 1: Catgut implantation in 17 acupoints Treatment group 2: Needle acupuncture at same acupoints + valproate 200 mg t.i.d.	Valproate at 200 mg t.i.d.	3 months

TCM, Traditional Chinese Medicine; OA, osteoarthritis.

TABLE 3. EFFECT OF ESTIMATES OF SUBGROUPS META-ANALYSIS IN 44 INCLUDED TRIALS⁸⁻¹²

<i>Outcomes or subgroups</i>	<i># of studies</i>	<i># of participants</i>	<i>Statistical methods</i>	<i>Effect estimates</i>
1. Acupuncture for peripheral joint osteoarthritis				
Acupuncture versus sham control group on the pain outcome at the short-term measurement	9		MD (IV, random, 95% CI)	Subtotals only
Trials used syndrome differentiation	3	1119	MD (IV, random, 95% CI)	-0.42 [-1.68, 0.84]
Trials did not use syndrome differentiation	6	716	MD (IV, random, 95% CI)	-2.24 [-4.00, -0.48]
Acupuncture versus waiting list or other active treatment control group on the pain outcome at the short-term measurement point	6		MD (IV, random, 95% CI)	Subtotals only
Trials used syndrome differentiation	3	962	MD (IV, random, 95% CI)	-1.16 [-1.62, -0.71]
Trials did not use syndrome differentiation	3	387	MD (IV, random, 95% CI)	-4.28 [-7.53, -1.03]
2. Acupuncture for migraine prophylaxis				
Acupuncture versus sham interventions on response up to 8 weeks/2 months after randomization	7		RR (M-H, fixed, 95% CI)	Subtotals only
Trials used syndrome differentiation	5	1010	RR (M-H, fixed, 95% CI)	1.09 [0.94, 1.26]
Trials did not use syndrome differentiation	2	81	RR (M-H, fixed, 95% CI)	4.83 [1.81, 12.89]
Acupuncture versus sham interventions on response to 4 months after randomization	11		RR (M-H, fixed, 95% CI)	Subtotals only
Trials used syndrome differentiation	6	1041	RR (M-H, fixed, 95% CI)	1.08 [0.93, 1.25]
Trials did not use syndrome differentiation	5	184	RR (M-H, fixed, 95% CI)	1.38 [0.99, 1.92]
Acupuncture versus sham interventions on response to 6 months after randomization	6		RR (M-H, fixed, 95% CI)	Subtotals only
Trials used syndrome differentiation	4	973	RR (M-H, fixed, 95% CI)	1.07 [0.92, 1.25]
Trials did not use syndrome differentiation	2	81	RR (M-H, fixed, 95% CI)	1.79 [1.16, 2.77]
3. Acupuncture for epilepsy				
Acupuncture versus control on reduction in seizure frequency	4		RR (M-H, fixed, 95% CI)	Subtotals only
Trials used syndrome differentiation	2	94	RR (M-H, fixed, 95% CI)	1.01 [0.83, 1.23]
Trials did not use syndrome differentiation	2	120	RR (M-H, fixed, 95% CI)	1.08 [0.95, 1.23]
4. Acupuncture for depression				
Electro-acupuncture versus amitriptyline on improvement in depression	5		RR (M-H, fixed, 95% CI)	Subtotals only
Trials used syndrome differentiation	2	512	RR (M-H, fixed, 95% CI)	0.94 [0.85, 1.05]
Trials did not use syndrome differentiation	3	318	RR (M-H, fixed, 95% CI)	1.20 [0.96, 1.50]
Electro-acupuncture versus amitriptyline on reduction in severity of depression	6		MD (IV, random, 95% CI)	Subtotals only
Trials used syndrome differentiation	2	512	MD (IV, random, 95% CI)	-0.67 [-1.83, 0.50]
Trials did not use syndrome differentiation	4	341	MD (IV, random, 95% CI)	-0.40 [-2.91, 2.11]
Manual acupuncture versus SSRI on improvement in depression	4		RR (M-H, fixed, 95% CI)	Subtotals only
Trials used syndrome differentiation	2	234	RR (M-H, fixed, 95% CI)	1.24 [0.98, 1.57]
Trials did not use syndrome differentiation	2	127	RR (M-H, fixed, 95% CI)	1.20 [1.00, 1.44]
5. Acupuncture for acute stroke				
Acupuncture versus control on changes of global neurological deficit score at the end of treatment period	6		MD (IV, random, 95% CI)	Subtotals only
Trials used syndrome differentiation	2	137	MD (IV, random, 95% CI)	2.53 [2.22, 2.84]
Trials did not use syndrome differentiation	4	281	MD (IV, random, 95% CI)	3.51 [1.40, 5.63]

MD, mean difference; CI, confidence interval; RR, risk ratio; SSRI, selective serotonin, reuptake inhibitor.

bias on data synthesis or selective reporting. Another limitation of this review was how point selection was identified when creating standardized treatment. Given that this information was not always reported, it was impossible to know if syndrome differentiation was used.

It is well-known that acupuncture is especially useful for promoting and regulating Qi and Blood, and for dredging meridians to stop pain. Acupuncture syndrome differentiation is not only determined by acupoint prescription, but also relies on point stimulation. The majority of the trials did

not report the skill levels and experience of the acupuncture practitioners, which may make an impact on the therapeutic effect of individualized acupuncture.

Correct treatment is based on analysis of each individual and disease. The main goal in differentiating among syndromes is to identify changes in the functioning of the body and to understand the characteristics of the disease. It is imperative to remember that different symptoms can occur in the same disease, and different diseases sometimes produce the same symptoms.¹⁴ One advantage of applying syndrome differentiation is to create individualized treatment.¹⁵ However, it is necessary to be aware that, although syndrome differentiation is the key to diagnosis and treatment according to TCM theory, current clinical evidence is insufficient to support a beneficial effect of syndrome differentiation.

CONCLUSIONS

The available evidence showed no significant difference between acupuncture treatment with or without syndrome differentiation. Because of the above limitations of the current study, further searching of clinical trials outside of Cochrane reviews could potentially provide further data regarding the effectiveness of syndrome differentiation. However, a large number of well-designed pragmatic RCTs to support the potential benefit of syndrome differentiation with respect to therapeutic effects of acupuncture for specific diseases are still warranted. More attention to syndrome differentiation when applying acupuncture should be reported in clinical research in the future.

ACKNOWLEDGMENTS

Drs. Cao and Liu were supported a grant from an international cooperation project (No. 2009DFA31460) and the basic operational funding for scientific research from Beijing University of Chinese Medicine, both in China. Dr. Liu was also partially supported by Grant Number R24 AT001293 from the National Center for Complementary and Alternative Medicine of the U.S. National Institutes of Health. Ms. Bouchier was supported by the Centre for Complementary Medicine Research at the University of Western Sydney, Australia.

DISCLOSURE STATEMENT

No competing financial interests exist.

REFERENCES

1. Liu YC. *The Essential book of Traditional Chinese Medicine: Volume 1. Theory*. New York: Columbia University Press; 1988:227–232.
2. Li XJ. Application of concept of holism and syndrome differentiation in acupuncture and moxibustion [in Chinese]. *Shanxi J Trad Chinese Med*. 2000;21(7):313–314.
3. Liu ZW, Liu L, Fan W, et al. *Essentials of Chinese Medicine: Volume 2. Clinical Fundamentals in Chinese Medicine*. London & New York: Springer Dordrecht Heidelberg; 2009: 171–183.
4. Liu WL, Zhu WF. Characteristics of syndrome differentiation in acupuncture application [in Chinese]. *J Clin Acupunct*. 1998;14(10):3–6.
5. He JS. Consideration on [sic] diagnosis and treatment based on an overall analysis of symptoms and signs in [sic] acupuncture clinic. *World J Acupunct Moxibustion*. 2009;19(2):1–4.
6. Liang FR, Zeng F, Tang Y. Thinking about building a clinical syndrome differentiation system of acupuncture and moxibustion [in Chinese]. *Zhong Guo Zhen Jiu*. 2008;28(8): 551–553.
7. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions* (version 5.0.2). The Cochrane Collaboration London: John Wiley & Sons; 2009.
8. Zhang S, Liu M, Asplund K, Li L. Acupuncture for acute stroke. *Cochrane Database Syst Rev*. 2005;2:CD003317.
9. Smith CA, Hay PPI, MacPherson H. Acupuncture for depression. *Cochrane Database Syst Rev*. 2010;1:CD004046.
10. Cheuk DKL, Wong V. Acupuncture for epilepsy. *Cochrane Database Syst Rev*. 2008;4:CD005062.
11. Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. Acupuncture for migraine prophylaxis. *Cochrane Database Syst Rev*. 2009;1:CD001218.
12. Manheimer E, Cheng K, Linde K, Lao L, et al. Acupuncture for peripheral joint osteoarthritis. *Cochrane Database Syst Rev*. 2010;1:CD001977.
13. Zhou EH, Deng BY, Su SY, Li YF. Analysis on literature about syndrome differentiation and treatment of meridians in clinical acupuncture and moxibustion in recent 3 years [in Chinese]. *Zhong Guo Zhen Jiu* 2005;25(1):41–42.
14. Liu YC. *The Essential book of Traditional Chinese Medicine: Volume 2. Clinical Practice*. New York: Columbia University Press; 1988:1–14.
15. He J, Chen WT. Advantages and limitations of syndrome differentiation. *Trad Chinese Med Res*. 2011;24(4):5–6.

Address correspondence to:

Jianping Liu, PhD, MD
Beijing University of Chinese Medicine
Bei San Huan Dong Lu 11, 88# mail box
Chaoyang District, Beijing 100029
China

E-mail: jianping_1@hotmail.com