Sham Electroacupuncture Methods in Randomized Controlled Trials

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Sham electroacupuncture (EA) control is commonly used to evaluate the specific effects of EA in randomized-controlled trials (RCTs). However, establishing an inert and concealable sham EA control remains methodologically challenging. Here, we aimed to systematically investigate the sham EA methods. Eight electronic databases were searched from their inception to April 2015. Ten out of the 17 sham EA methods were identified from 94 RCTs involving 6134 participants according to three aspects: needle location, depth of needle insertion and electrical stimulation. The top three most frequently used types were sham EA type A, type L and type O ordinally. Only 24 out of the 94 trials reported credibility tests in six types of sham EA methods and the results were mainly as follows: sham EA type A (10/24), type B (5/24) and type Q (5/24). Compared with sham EA controls, EA therapy in 56.2% trials reported the specific effects, of which the highest positive rate was observed in type N (3/4), type F (5/7), type D (4/6) and type M (2/3). In conclusion, several sham EA types were identified as a promising candidate for further application in RCTs. Nonetheless, more evidence for inert and concealable sham EA control methods is needed.

A randomized controlled trial (RCT) has been the cornerstone of medical clinical research since the first RCT paper entitled “Streptomycin treatment of pulmonary tuberculosis: a Medical Research Council investigation” was published in 1948. By the late 20th century, RCT was recognized as the gold standard for a clinical trial. To improve the quality of clinical research, the methodology has been refined to avoid any bias over the past several decades. The most important design techniques for avoiding bias in clinical trials are randomization and blinding. Blinding is intended to limit the occurrence of conscious and unconscious bias in clinical trials (performance bias) and interpretation of outcomes (ascertainment bias). Blinding is crucial for treatment evaluation because lack of blinding can bias the reliable assessment of treatment effects. For RCTs, placebo is a standard control method to blind the participants and health care providers. The purpose of placebo group is to account for the placebo effect, i.e., effects from treatment that do not depend on the treatment itself. However, blinding is difficult to ensure in non-pharmacological treatment trials because fabrication of placebo such as placebo/sham acupuncture controls requires the placebo to be both inert and indistinguishable, which is relatively difficult.

RCTs for acupuncture appeared in 1970s. Since then, a number of RCTs on acupuncture have been published. The “sham” acupuncture is identified as the procedure controlling for the acupuncture treatment components with the aim to blind the participants and control for non-specific placebo effects. Since participants are to a large extent ignorant of the components of acupuncture such as needle location, depth of needle insertion, needle stimulation and patient/practitioner interactions, sham acupuncture can be considered to be therapeutically inactive. However, it is difficult to design a standard method for sham acupuncture avoiding all therapeutically active components. Thus, the methodological difficulties in designing appropriate sham acupuncture controls for RCTs remained challenging.

Electroacupuncture (EA) is an extension technique based on traditional acupuncture combined with modern electrotherapy. Owing to its accurate, reproducible and standardized intensity and duration of stimulation with simple, verifiable electrical parameters, EA has been widely used in clinical studies and basic research into underlying mechanisms of acupuncture treatment. Currently, EA is being used extensively in China and elsewhere around the world. However, no systematic analyses have yet been published to describe the sham EA procedures. Thus, the objective of this study is to investigate the sham EA methods utilized in EA RCTs.
Methods

Search strategy. Eight electronic databases, including Cochrane Controlled Trials Register, PubMed, EMBASE, AMED, China National Knowledge Infrastructure (CNKI), VIP Journals Database, Wanfang database, and Chinese Biomedical Database (CBM) were searched from their inceptions to April 2015. The search terms were confined to “Electroacupuncture” AND “sham acupuncture OR placebo acupuncture” AND “randomized controlled trial (RCT)”. All searches were limited to studies on human.

Eligibility Criteria. RCTs concerning the effects of EA on any kind of diseases with at least one control group receiving sham EA were included, regardless of publication status and languages. Quasi-RCTs and non-RCTs were excluded.

The studies were eligible if EA therapy alone or adjunct therapy were given in treatment group and secondly, if sham EA or any type of faked manipulation mimicking real EA in aspects of acupoint, penetration and electro-stimulation were given in control group. There were no restrictions on needle parameters or intensity, frequency and mode of stimulation. Studies that compared EA with transcutaneous nerve electrical stimulation (TENs), another acupuncture plus sham EA or placebo medications were excluded. If three or more groups were designed in one study, only real EA versus sham EA groups were included.

Study selection and data extraction. Two authors (ZXC, YL) reviewed the titles and abstracts of the potential references independently. All the potentially relevant studies were marked and their full articles were retrieved. Further examinations were carried out to make a final selection decision. The same two authors performed the data extraction independently for the predefined items: author, year, country, EA indications, sample size, the characteristics of interventions, outcome measures, results and dropouts. The disagreements were resolved through consulting a third part (GQZ).

Risk of bias assessment. Two authors (ZXC and YL) performed the methodological quality assessment of each included trial independently based on the Cochrane Collaboration’s tool for assessing risk of bias14. The criteria consisted of the following: adequate sequence generation, allocation concealment, blinding of participants, blinding of personnel, blinding of outcome assessor, free of incomplete outcome data, free of selective reporting and free of other bias.

Description of sham EA methods. The sham EA methods used in each control group were examined and the details were extracted according to three respects: needle location, depth of needle insertion and electrical stimulation. Partially based on the previous sham acupuncture type I–V classification published by Dincer et al.8 we summarized seventeen kinds of sham EA methods: (1) Sham EA on therapeutic acupoints plus no skin penetration plus no electrical stimulation (Sham EA type A); (2) Sham EA on therapeutic acupoints plus skin penetration plus no electrical stimulation (Sham EA type B); (3) Sham EA on therapeutic acupoints plus the same depth plus no electrical stimulation (Sham EA type C); (4) Sham EA on therapeutic acupoints plus superficial insertion plus no electrical stimulation (Sham EA type D); (5) Sham EA on therapeutic acupoints plus superficial insertion plus electrical stimulation (Sham EA type E); (6) Sham EA on nonspecific acupuncture points plus the same depth plus electrical stimulation (Sham EA type F); (7) Sham EA on nonspecific acupuncture points plus the same depth plus no electrical stimulation (Sham EA type G); (8) Sham EA on nonspecific acupuncture points plus superficial insertion plus electrical stimulation (Sham EA type H); (9) Sham EA on nonspecific acupuncture points plus superficial insertion plus no electrical stimulation (Sham EA type I); (10) Sham EA on nonspecific acupuncture points plus no skin penetration plus electrical stimulation (Sham EA type J); (11) Sham EA on non-specific acupuncture points plus no skin penetration plus no electrical stimulation (Sham EA type K); (12) Sham EA on non-acupuncture points plus the same depth plus electrical stimulation (Sham EA type L); (13) Sham EA on non-acupuncture points plus the same depth plus no electrical stimulation (Sham EA type M); (14) Sham EA on non-acupuncture points plus superficial insertion plus electrical stimulation (Sham EA type N); (15) Sham EA on non-acupuncture points plus superficial insertion plus no electrical stimulation (Sham EA type O); (16) Sham EA on non-acupuncture points plus no skin penetration plus electrical stimulation (Sham EA type P); (17) Sham EA on non-acupuncture points plus no skin penetration plus no electrical stimulation (Sham EA type Q).

Assessment of the effectiveness. Considering wildly varying outcome measures across different disease conditions, treatment efficacy was evaluated for each study according to the modified method based on a previous publication16. The results of each trial were presented by using the following primary outcome measures: “T > C” meaning that real EA treatment group was significantly superior to sham EA control group; “ND” meaning no difference between EA and sham EA groups; “T < C” meaning that real EA group was significantly inferior to sham EA group. If the efficacy of a trial was reported as “T > C” or “T < C” without between-groups comparison having been conducted, we collected the original data by reviewing the articles or contacting the corresponding author. If the original data were available, an effect-size analysis was conducted to reconfirm the between-groups difference. If the original data were not available, the efficacy results were presented as “T > C?” or “T < C?”.

The credibility of blinding. The credibility test was formally performed in validation studies to assess the blinding effect of sham acupuncture based on credibility questionnaire and statistical analysis15–17. The information on the credibility test was extracted to explore the relationship between the credibility of blinding and the type of sham EA method.

Results

Study selection. A total of 679 potentially relevant articles were identified. By reviewing titles and abstracts, 374 papers were excluded for at least one of following reasons: (1) not clinical trials; (2) case report, comment,
review, letter, news or editorial; (3) not in contrast with sham EA; (4) lack of EA intervention. After examining the full content of the remaining 305 articles, we removed 211 records, of which 127 articles were due to lack of sham EA controls, including electro-acupuncture (14 studies), manual acupuncture (13 studies), TNES (7 studies), other treatment (69 studies) or no treatment (24 studies); 49 articles removed for lack of real EA groups, with their target intervention designed as manual acupuncture (10 studies), TNES (38 studies) or periosteal stimulation therapy (PST) (1 study); 10 articles were not RCTs; 13 articles were double publications; 12 articles were cross-over design. Ultimately, 94 studies involving 6134 participants were selected (Fig. 1).

**Characteristics of included studies.** The 94 included articles were published from 1992 to 2015. Among them, 5 studies were published between 1992 and 1999; 33 studies were published between 2000 and 2010; the remaining 56 studies were published between 2010 and 2015 (Fig. 2). Indications for EA included pain (32 studies), anesthesia (8 studies), stroke (7 studies), depression (6 studies), obesity (4 studies), primary dysmenorrhea (4 studies), and menstrual pain (4 studies).

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**Figure 1. Flow diagram.**

**Figure 2. The time distribution of the included articles.**
substance abuse (heroin or smoking) (3 studies)44,95,107; osteoarthritis (2 studies)22,104; migraine (2 studies)38,78; nausea and vomiting (2 studies)35,37; postoperative ileus (2 studies)35,38; insomnia (2 studies)35,81; benign prostate hyperplasia (2 studies)79,82; diabetic mellitus related diseases (2 studies)93,109; carpal tunnel syndrome (1 study)100; rheumatoid arthritis (1 study)90; whiplash-associated disorders (1 study)89; constipation (1 study)89; multiple sclerosis (1 study)44; tinnitus (1 study)26; auditory hallucination (1 study)30; attention deficit hyperactivity disorder (1 study)102; postpartum insufficient lactation (1 study)71; hot flushes (1 study)58; postpartum insufficient lactation (1 study)71; cardiac ischemia-reperfusion injury (1 study)75; stress-related symptoms (1 study)108. The rest three studies43,77,85 reported the effects of EA on healthy subjects.

EA treatment alone was adopted in 55 trials18–25,28–31,34–39,42,43,53,55,58,60,61,66,68,69,71,72,75,77–80,83–91,98–101,103,104,107–109,110,111, while the interventions of the remaining 39 trials were a combination of EA and western conventional medicine (WCM). Four trials18,47,54,100 were designed as two groups of EA, and seven trials38,43,61,63,98,99,101 were conducted with two groups of sham EA. Compared with sham EA group, real EA group in 83 studies selected the same number of acupoints; nine studies25,46,66,89,105,106,108,111 used more number of acupoints; one study26 used less number of acupoints; one study24 did not report the number of acupoints. Eight studies26,49,54,76,95–97,110 identified acupoints by using a point detector. The “deep” sensation was required in 65 real EA groups18–25,28–31,34–39,42,43,44,46,47,48,50,56–58,60–62,64–66,68,71,75–77,83–85,87–90,95,98–102,104–106,109,111 and 3 sham EA groups selected nonspecific acupoints41,78,101. Eight studies utilized pricking sensation to mimic needle sensation and blind participants in control group20,21,23,52,60,63,67,81. Forty-two studies18–22,25,28–38,40–45,47,49,51,55,59–62,64–66,68,71,75–77,79–83,85,89,92,100,106–111 did not provide any information on the total duration of treatment. The characteristics of the studies were listed in Table 1.

**Characteristics of sham EA.** Ten different types of sham EA methods used in the trials were identified as follows: (1) sham EA type A were used in twenty-six control groups18–22,23,32,35,37,39,40,42–44,46,47,48,50,51,55,59–62,64–66,68,71,75–77,79–83,85,89,92,100,106–111; (2) sham EA type B were used in seven control groups23,24,39,45,50,63,76; (3) sham EA type C were used in seven control groups28,44,47,49,51,58,61; (4) sham EA type D were used in six control groups24,43,62,72,92; (5) sham EA type E were used in seven control groups38,61,71,98,99,101; (6) sham EA type E were used in seventeen control groups26,27,36,43,46,48,50,53,54,61,77,79–83,98,99,101; (7) sham EA type M were used in three control groups72,88,89; (8) sham EA type N were used in four control groups83,89,90; (9) sham EA type O were used in fourteen control groups80,93,102,103,105,106,108,109,110,111; (10) sham EA type Q were used in ten control groups25,34,36,58,59,63,100,101,111. For the needle location, 48 sham EA groups24,27,30,32–34,36,38,41–43,45,46,48,50–52,56,61,63–68,70,71,75–77,79–83,87–89,95,98–102,107,111 chose non-acupoints that were either away from the therapeutic acupoints with a distance ranging from 1 cm to 40 cm or devised in advance to avoid any known meridian or extra-point. Seven sham EA groups25,46,66,89,92,105,106 used a combination of acupoints which were thought to be ineffective for treating the diseases. For the depth of needle insertion, 34 sham EA groups26–28,38,39,42–44,51,53,64,68,69,71,75–77,79–83,85,87–90,95,98–102,107,111 conducted the needle insertion to the same depth as corresponding real EA groups. Twenty-four sham EA groups29,30,32,35,41,43,45,56–58,62–64,70,72,80,83,86,87,90–93,95 performed either superficial or subcutaneous needle insertion with depth varying from 0.5 mm to 2 cm, whereas one study35 retracted the needle after superficial penetration. The remaining 43 sham EA groups had sham EA without skin penetration. Forty-one out of 43 trials did not apply any needle insertion by using Streitberger needles21,23,25,31,35,59,63,65,66,81; contractible placebo needles with dull tips and tubes24,35,52; placebo needles with blunt tips19,20,40,66,67,100; verum needles fixed by tapes or rings without piercing18,23,34, leading wires alone without needles13,38,76,93 and mock laser pen103 or electrode38,74,94,96,102–104,111. Two sham EA groups84,88 did not describe any details on the sham needles. For electrical stimulation, 35 sham EA groups23,24,26,27,38,39,43,46,48,50,53,54,59,61,63,65,71,77–79,83–85,88–90,95,98,100,101,103 used electrical stimulation, whereas two sham EA groups stimulated with current just at the beginning of sham procedure. The other five sham EA groups18–22,25,28–38,40,45,47,49,51,52,55–58,60–62,64–66,70–72,80–82,86,87,91–94,96,97,100,102–104,111 did not receive any electrical stimulation through inactivated EA device or disconnected cables. The details of sham EA were described in Table S1.

**Risk of bias assessment.** The number of items complied with the criteria varied from 3/8 to 7/8 with the average of 5.2. All 94 studies declared randomization and 63 studies reported the details. Among them, 49 sham control groups72,98,100,107,108,111 described a computer-generated randomization; 11 studies34,40,41,50,52,57,69,73,74,84,86 were based on random number Table; 3 studies34,87,101 used the lot. Adequate allocation concealment was found in 43 studies18–20,23,25,29,30,35–37,43–45,55,57,58,60,63,67–69,71,72,76,79,81,84,86,88,91,93,95,98,99,105–107,109–111 with sequencially numbered, opaque, sealed envelopes or independent administrator. The remaining 51 studies did not provide the details on allocation concealment. Blinding of participant was described in 59 studies. Among these, 23 studies23,25,34,46,47,52,57,59,63,65,72,81,88,97,102,103,105–108,110 proved their success of blinding by credibility test, while one study66 failed in blinding of participant after testing by statistical analysis. No study mentioned blinding of acupuncturists. Ninety-two out of the 94 studies reported blinding of assessor, whereas one study103 did not contain any information on assessor blinding and another study106 was sorted as “no” due to its unsuccessful assessor blinding. Eighteen studies25,30,40,50,60,65,69,79,80,91–93,97–99,103,105–107 conducted intention-to-treat analysis. Seventy-five studies18–22,24–41,43,44,46,47,49,68–70,79–81,92–94,97–100,105–107 were free of incomplete outcome data; eleven studies23,42,45,48,89,90,93,99,106,107 assessed as “no” due to high dropout rate or statistically significant
| Reference (author, year and country) | Diseases | No. of acupuncture point (T/C) | Sample size (T/C) | dropout (T/C) | Primary outcome measures | Difference between groups | Characteristic of sham electro-acupuncture (EA) methods |
|-------------------------------------|----------|-------------------------------|-----------------|--------------|--------------------------|--------------------------|--------------------------|
| Nittisou et al. 2014 USA10          | Stroke   | 4/4                           | 37/33           | 5/2/3        | NRS and SF, MPQ scores   | T > C                    | Therapeutic acupuncture no penetration no electrical stimulation Sham EA type A |
| Chu et al. 2012 Hong Kong19         | Pain perception in Irritable Bowel Syndrome | 6/6            | 15/15          | 0/0/0        | FMRI                     | T > C                    | Therapeutic acupuncture no penetration no electrical stimulation Sham EA type A |
| Wang et al. 2010 Denmark20         | Tinnitus | 4/14                          | 20/20           | 9/4/5        | The frequency of tinnitus occurrence and the tinnitus loudness | ND                     | Therapeutic acupuncture no penetration no electrical stimulation Sham EA type A |
| Zyloneky et al. 2010 USA21         | Pain     | 2/2                           | N/N             | 29(N/N)      | FIMRI and MASS ratings   | T > C                    | Therapeutic acupuncture no penetration no electrical stimulation Sham EA type A |
| Jubb et al. 2008 UK22              | Osteoarthritis | 6/6            | 34/34           | 4/2/2        | WOMAC pain score         | T > C                    | Therapeutic acupuncture no penetration no electrical stimulation Sham EA type A |
| Chung et al. 2012 Hong Kong23      | Postpartum Depression | 18/18           | 10/10           | 6/5/1        | EPDS, HADS, HDRS, and CGI scores | ND                     | Therapeutic acupuncture no penetration electrical stimulation Sham EA type B |
| Barlas et al. 2006 UK24            | Pain     | 4/4                           | 12/12           | N/N(N/N)     | Pressure pain threshold  | T > C                    | Therapeutic acupuncture no penetration electrical stimulation Sham EA type B |
| Barlas et al. 2006 UK24            | Pain     | 4/4                           | 12/12           | N/N(N/N)     | Pressure pain threshold  | ND                     | Therapeutic acupuncture no penetration electrical stimulation Sham EA type B |
| Wayne et al. 2005 US25             | Stroke Rehabilitation | 14–22/1–3       | 16/17           | 9/3/6        | FMA score                | ND                     | Non-acupuncture points no penetration no electrical stimulation Sham EA type Q |
| Sahin et al. 2010 Turkey26         | Pain     | 14/14                        | 15/16           | 2/2/0        | VAS scores               | ND                     | Non-acupuncture points the same depth electrical stimulation Sham EA type L |
| Fanti et al. 2003 Italy27          | Pain     | 10/10                        | 10/10           | 0/0/0        | VAS scores               | ND                     | Non-acupuncture points the same depth Electrical stimulation Sham EA type L |
| Hsing et al. 2012 Brazil28         | Stroke recovery | 11–14/11–14             | 31/31           | 0/0/0        | NIHSS, Barthel Index and modified Rankin scales scores | T > C                    | Therapeutic acupuncture the same depth no electrical stimulation Sham EA type C |
| Gorman-Hedestrom et al. 1998 Sweden29 | Stroke  | 4/4                           | 37/33           | 3/2/1        | The neurological score and the Barthel and Sunnaas index scores | ND                     | Therapeutic acupuncture superficial penetration no electrical stimulation Sham EA type D |
| Jing et al. 2009 China29           | Auditory Hallucination | 6/6            | 30/30           | 7/4/3        | The Psychotic Symptom Rating Scales and Auditory Hallucination Subscale total score | T > C                    | Non-acupuncture points superficial penetration no electrical stimulation Sham EA type O |
| Kong et al. 2009 USA30             | Pain     | 2/2                           | N/N             | 29(N/N)      | Gracely Sensory and Affective scales scores and IMRI | ND                     | Therapeutic acupuncture no penetration no electrical stimulation Sham EA type A |
| Darbandi et al. 2013 Iran31        | Obesity  | 4/4                           | 47/47           | 8/5/3        | BW, BMI and BFM          | ND                     | Non-acupuncture points superficial penetration no electrical stimulation Sham EA type O |
| Yang et al. 2012 China32           | Pain     | 12/12                        | 40/40           | 0/0/0        | the consumption of sevoflurane and the recovery profile | T > C                    | Therapeutic acupuncture no penetration no electrical stimulation Sham EA type A |
| Liu et al. 2013 China33            | Post-stroke detrusor overactivity | 10/10           | 35/36           | 5/2/3        | maximum cystometric capacity and bladder compliance | T > C                    | Non-acupuncture points no penetration no electrical stimulation Sham EA type Q |
| Zhang et al. 2014 China34          | Postoperative ileus | 2/2            | 20/20           | 1/1/0        | Time of the first bowel sounds and passage of flatus | T > C                    | Non-acupuncture points superficial penetration no electrical stimulation Sham EA type O |
| Mao et al. 2014 USA36              | Aromatase Inhibitor-Related Arthralgia | 4/4            | 22/22           | 6/3/3        | BPI                      | ND                     | Non-acupuncture points no penetration no electrical stimulation Sham EA type Q |
| Leung et al. 2011 Hong Kong37      | Pain     | 3/3                           | 20/20           | 0/0/0        | the maximum tolerable pressure, VAS score and beta-endorphin level | T > C                    | Therapeutic acupuncture no penetration no electrical stimulation Sham EA type A |
| Rusy et al. 2002 USA38a            | Postoperative Nausea and Vomiting | 1/1            | 40/40           | 0/0/0        | occurrence of nausea and vomiting and use of antiemetic rescue medication | T > C                    | Non-specific acupuncture points the same depth Sham EA type F |
| Rusy et al. 2002 USA38b            | Postoperative Nausea and Vomiting | 1/1            | 40/40           | 0/0/0        | occurrence of nausea and vomiting and use of antiemetic rescue medication | T > C                    | Non-acupuncture points no penetration no electrical stimulation Sham EA type Q |
| Yang et al. 2014 China39           | Migraine | 3/3                           | 10/10           | 0/0/0        | VAS scores               | ND                     | Non-acupuncture points the same depth Electrical stimulation Sham EA type L |

Continued
| Reference (author, year and country) | Diseases | No. of acupuncture (T/C) | Sample size (T/C) | dropout (T/C) | Primary outcome measures | Characteristic of sham electro-acupuncture (EA) methods | Needle location | Degree of needle insertion | Electrical stimulation | The type of sham EA method |
|-------------------------------------|----------|--------------------------|-------------------|--------------|--------------------------|------------------------------------------------------|---------------|--------------------------|----------------------|--------------------------|
| Chen et al. 2013 China[l]           | Pancreatic cancer pain | 10/10                                                                 | 30/30             | 1(0/1)       | NRS                      | T > C therapeutical acupuncture no penetration no electrical stimulation Sham EA type A |
| Quispe-Cabanillas et al. 2012 Brazil[l] | Multiple sclerosis | 9/9                                                                 | 16/15             | 0(0/0)       | EDSS, pain VAS score and quality of life TAMS          | T > C non-acupuncture points superficial penetration no electrical stimulation Sham EA type O |
| Aranha et al. 2015 Brazil[l]       | Pain      | 7/8–7/8                  | 24/23             | 17(7/10)     | VAS scores and cervical movements                     | T > C non-acupuncture points the same depth no electrical stimulation Sham EA type M |
| Yu et al. 2013 Hong Kong[l]        | Postoperative pain | 2/2                                                                 | 12/12             | 0(0/0)       | C-MMASS and HR, MAP                                      | ND non-acupuncture points the same depth Electrical stimulation Sham EA type L |
| Yu et al. 2013 Hong Kong[l]        | Postoperative pain | 2/2                                                                 | 12/12             | 0(0/0)       | C-MMASS and HR, MAP                                      | T > C therapeutic acupuncture superficial penetration no electrical stimulation Sham EA type D |
| Li et al. 2010 China[l]            | Attention deficit hyperactivity disorder | 15–16/15–16                                                                 | 92/88             | 10(6/4)       | relapse rate                                             | T > C therapeutic acupuncture the same depth no electrical stimulation Sham EA type C |
| Zheng et al. 2007 Australia[l]     | Chronic pain | 4/4                                                                 | 17/18             | 12(8/4)      | the dosage reduction of OLM, the incidence of side effect, and VAS score | ND non-acupuncture points superficial penetration no electrical stimulation Sham EA type O |
| Li et al. 2013 China[l]            | General anesthesia | 10/6                                                                 | 9/10              | 0(0/0)       | the levels of TNF-α, IL-8 and IL-10                     | ND non-acupuncture points the same depth Electrical stimulation Sham EA type L |
| Lin et al. 2002 Taiwan[l]          | Postoperative pain | 2/2                                                                 | 25/25             | 0(0/0)       | VAS score                                              | ND therapeutic acupuncture the same depth no electrical stimulation Sham EA type C |
| Lin et al. 2002 Taiwan[l]          | Postoperative pain | 2/2                                                                 | 25/25             | 0(0/0)       | VAS score                                              | ND therapeutic acupuncture the same depth no electrical stimulation Sham EA type C |
| Chen et al. 2013 Taiwan[l]         | Constipation | 6/6                                                                 | 30/30             | 30 (16/14)   | the defecation rate                                     | T > C non-acupuncture points the same depth Electrical stimulation Sham EA type L |
| Schulz et al. 2014 Austria[l]      | Obesity     | 3/3                                                                 | 28/24             | 14(7/7)      | the relative reduction of body weight                  | T > C therapeutic acupuncture the same depth no electrical stimulation Sham EA type C |
| Yu et al. 2014 China[l]            | General anesthesia | 2/2                                                                 | 20/20             | 0(0/0)       | The serum cortisol and ACTH                           | T > C? non-acupuncture points the same depth Electrical stimulation Sham EA type L |
| Xie et al. 2014 China[l]           | Postoperative pain | 2/2                                                                 | 20/20             | 0(0/0)       | VAS score, Total Doses of Sufentanil and Desocin        | T > C therapeutic acupuncture the same depth no electrical stimulation Sham EA type C |
| Sim et al. 2002 Singapore[l]       | Intraoperative pain | N/N                                                                  | 30/30             | 0(0/0)       | The total intraoperative usage of alfentanil, The total morphine consumption and VAS score | ND non-acupuncture points no penetration no electrical stimulation Sham EA type Q |
| Song et al. 2009 China[l]          | Depression   | 2/2                                                                 | 31/32             | 10(3/7)      | HDRS and CGI                                           | T > C non-acupuncture points the same depth Electrical stimulation Sham EA type L |
| Shafshak 1995 Egypt[l]             | Obesity     | 2/2                                                                 | 10/10             | N(N/N)       | the success rate of going on the diet trigenmen          | T > C non-acupuncture points the same depth Electrical stimulation Sham EA type L |
| Shafshak 1995 Egypt[l]             | Obesity     | 2/2                                                                 | 10/10             | N(N/N)       | the success rate of going on the diet trigenmen          | T > C non-acupuncture points the same depth Electrical stimulation Sham EA type L |
| Franasiak et al. 2012 USA[l]      | Polycystic Ovary Syndrome | 8/8                                                                  | 46/50             | 16(9/7)      | Serum LH and FSH, The monthly rates of ovulation        | ND non-acupuncture points no penetration no electrical stimulation Sham EA type Q |
| Naslund et al. 2002 Sweden[l]      | Idiopathic anterior knee pain | 6/6                                                                 | 30/28             | 1(0/1)       | one leg vertical jump, functional score, daily VAS recording and skin temperature | ND non-acupuncture points superficial penetration no electrical stimulation Sham EA type O |
| Shen et al. 2000 US[l]             | Chemotherapy-Induced Emeis | 4/4                                                                 | 37/33             | 1(1/1)       | Total number of emesis episodes occurring               | T > C non-acupuncture points superficial penetration no electrical stimulation Sham EA type O |
| Woyon et al. 2004 Sweden[l]       | Hot flushes in postmenopausal women. | 6/6                                                                 | 15/15             | 7(4/3)       | The number of flushes/24 h                             | ND non-acupuncture points superficial penetration no electrical stimulation Sham EA type O |
| Zhang et al. 2012 Hong Kong[l]     | Depression   | 12/12                                                                | 38/35             | 10(7/3)      | score of HAMD-17 and SDS                               | T > C therapeutic acupuncture no penetration electrical stimulation Sham EA type B |
| Zheng et al. 2010 Australia[l]     | Pain         | 2/2                                                                 | 12/12             | 0(0/0)       | SPT and TST                                            | T > C therapeutic acupuncture no penetration no electrical stimulation Sham EA type A |
| Ma et al. 2010 China[l]            | Menstrual Pain | 2/2                                                                 | 13/14             | 1(1/0)       | VAS scores                                              | T > C nonspecific acupuncture points the same depth electrical stimulation Sham EA type F |
| Ma et al. 2010 China[l]            | Menstrual Pain | 2/2                                                                 | 13/12             | 1(1/0)       | VA S scores                                            | T > C non-acupuncture points the same depth Electrical stimulation Sham EA type L |

Continued...
| Reference (author, year and country) | Diseases | No. of acupuncture (T/C) | Sample size (T/C) | dropout (T/C) | Primary outcome measures | Difference between groups | Characteristic of sham electro-acupuncture (EA) methods |
|-------------------------------------|----------|--------------------------|-------------------|--------------|--------------------------|--------------------------|---------------------------------------------------|
| Wang et al. 2014 Taiwan85           | Chronic stroke | 4/4                      | 10/10             | 5/1(4)       | R1, R2 and R2–R1         | T > C                       | therapeutic acupuncture, superficial penetration, No electrical stimulation, Sham EA type D |
| Yeung et al. 2011 Hong Kong86 a     | Insomnia  | 8/8                      | 26/26             | 7(4/3)       | ISI and PSQI             | ND                        | non-acupuncture points, superficial penetration, electrical stimulation, Sham EA type N |
| Yeung et al. 2011 Hong Kong86 b     | Insomnia  | 8/8                      | 26/26             | 7(4/3)       | ISI and PSQI             | T > C                       | non-acupuncture points, No penetration, No electrical stimulation, Sham EA type Q |
| Chan et al. 2014 Taiwan88           | Heroin Addicts | 4/4                      | 30/30             | 2(1/1)       | the daily consumption of methadone | T > C                       | therapeutic acupuncture, superficial penetration, No electrical stimulation, Sham EA type D |
| Man et al. 2014 Hong Kong88         | Post-stroke depression | 20/20                  | 23/20             | 10(4/6)      | HAMD-17 and CGI-S        | T > C                       | therapeutic acupuncture, No penetration, electrical stimulation, Sham EA type B |
| Oh et al. 2013 Australia87          | Pain      | 16/12                    | 16/16             | 3(2/1)       | WOMAC, BPI-SF and FACT-G instrument | ND                        | therapeutic acupuncture, No penetration, No electrical stimulation, Sham EA type A |
| Song et al. 2007 USA88              | Depression | 2/2                      | N/N               | N(N/N)       | 24-item HAMD and the level of G protein α-subtypes in the platelet membrane | ND                        | non-acupuncture points, the same depth, No electrical stimulation, Sham EA type M |
| Cameron et al. 2011 Australia89     | Whiplash-associated Disorders | 8/8                    | 64/60             | 8(0/8)       | VAS                      | T > C                       | non-acupuncture points, the same depth, No electrical stimulation, Sham EA type M |
| Darbandi et al. 2014 Iran88         | Obesity   | 4/4                      | 20/20             | 0(0/0)       | BMI, TFM, WC and HC      | T > C                       | non-acupuncture points, superficial penetration, No electrical stimulation, Sham EA type O |
| Wei et al. 2008 China83             | Postpartum Insufficient Lactation | 2/2                   | 46/46             | 0(0/0)       | total therapeutic effect, 24-hour milk secretion quantity, prolactin level | T > C                       | nonspecific acupuncture points, the same depth, electrical stimulation, Sham EA type F |
| Wang et al. 2007 USA86              | Pain      | 4/4                      | 29/27             | 0(0/0)       | intraoperative allantul consumption, VAS score | T > C                       | therapeutic acupuncture, superficial penetration, No electrical stimulation, Sham EA type D |
| Kvorning et al. 2003 Sweden87       | Anaesthesia | 12/12                    | 23/23             | 1(1/0)       | Physiological reactions to skin incision | T > C                       | therapeutic acupuncture, No penetration, No electrical stimulation, Sham EA type A |
| Kvorning et al. 2003 Sweden88       | Anaesthesia | 6/6                      | 23/23             | 0(0/0)       | The minimal alveolar concentration of sevoflurane | T < C                       | therapeutic acupuncture, No penetration, No electrical stimulation, Sham EA type A |
| Yang et al. 2010 China84            | Cardiac ischemia-reperfusion injury | 6/6                    | 30/30             | 0(0/0)       | levels of serum cardiac troponin I | T > C                       | therapeutic acupuncture, the same depth, No electrical stimulation, Sham EA type C |
| Sahmeddini et al. 2010 Iran85       | Perioperative Pain | 4/4                    | 45/45             | 0(0/0)       | score on VAS-100         | ND                         | therapeutic acupuncture, no penetration, No electrical stimulation, Sham EA type A |
| Wang et al. 2007 China85            | Anaesthesia | 1/1                      | 9/5               | 3(3/0)       | BOLD fMRI                | T > C                       | non-acupuncture points, the same depth, electrical stimulation, Sham EA type L |
| Jia et al. 2009 China87             | Migraine  | 2/2                      | 138/138           | 1(0/1)       | VAS score and the plasma 5-HT level | T > C                       | nonspecific acupuncture points, the same depth, electrical stimulation, Sham EA type F |
| Wang et al. 2013 China88            | Benign prostate hyperplasia | 2/2                    | 50/50             | 23(9/14)     | IPSS                      | T > C                       | non-acupuncture points, the same depth, electrical stimulation, Sham EA type L |
| Andreescu et al. 2011 Canada89     | Depression | 2/2                      | 28/29             | 11(4/7)      | HDRS score               | ND                         | non-acupuncture points, superficial penetration, No electrical stimulation, Sham EA type O |
| Yeung et al. 2009 Hong Kong85       | Insomnia  | 8/8                      | 30/30             | 3(1/2)       | ISI                      | ND                         | therapeutic acupuncture, no penetration, No electrical stimulation, Sham EA type A |
| Chen et al. 2014 Taiwan88           | Pain      | 1/1                      | 25/24             | 0(0/0)       | VAS scores and the dosage of opium derivative analgesic | ND                         | therapeutic acupuncture, the same depth, No electrical stimulation, Sham EA type C |
| Wang et al. 2008 China88            | Diabetic Gastroparesis | 4/4                    | 11/12             | 4(2/2)       | GCSI score               | T > C                       | non-acupuncture points, superficial penetration, electrical stimulation, Sham EA type N |
| Meissner et al. 2004 Germany89      | Pain      | 6/6                      | 8/8               | 0(0/0)       | SEPs                     | T > C                       | therapeutic acupuncture, no penetration, electrical stimulation, Sham EA type B |
| Zhou et al. 2012 China88            | Benign Prostate Hyperplasia | 2/2                    | 11/11             | 0(0/0)       | MVC strength              | ND                         | non-acupuncture points, the same depth, electrical stimulation, Sham EA type L |
| Yeh et al. 2012 Taiwan88            | Shivering during regional anesthesia | 4/4                    | 40/40             | 0(0/0)       | Shivering score and tympanic temperature | T > C                       | non-acupuncture points, superficial penetration, No electrical stimulation, Sham EA type O |
| Yu et al. 2011 Taiwan88             | Benign Prostate Hyperplasia | 6/6                    | 21/21             | 5(3/2)       | The change of the maximum flow rate, average flow rate, void volume | T > C                       | non-acupuncture points, superficial penetration, No electrical stimulation, Sham EA type O |

Continued
| Reference (author, year and country) | Diseases | No. of acupuncture (T/C) | Sample size (T/C) | dropout (T/C) | Primary outcome measures | Difference between groups | Characteristic of sham electro-acupuncture (EA) methods |
|--------------------------------------|----------|--------------------------|------------------|--------------|-------------------------|-------------------------|--------------------------------|
| Ma et al. 2011 China^88 | Pain | 2/2 | 116/117 | 0(0/0) |VAS score | T > C | therapeutic acupuncture, no penetration, no electrical stimulation | Sham EA type B |
| Li et al. 2013 China^89 | Intraoperative immunosuppression | 10/6 | 19/19 | 0(0/0) |the levels of TNFα, IL-8, IL-10, IgM, IgA, IgG and full blood count | ND | non-acupuncture points, the same depth | Sham EA type L |
| Deluze et al. 1992 Switzerland^90 | Fibromyalgia | 4-10/4 | 36/34 | 15(8/7) | Pain threshold, number of analgesic tablets used, VAS score | T > C | non-acupuncture points, superficial penetration | Sham EA type N |
| Ng et al. 2013 Hong Kong^91 | Postoperative ileus | 4/4 | 55/55 | 0(0/0) |Time to defecation | T > C | non-acupuncture points, superficial penetration, no electrical stimulation | Sham EA type O |
| Lee and Lee 2009 Republic of Korea^92 | Chronic Prostatitis / Chronic Pelvic Pain Syndrome | 6/6 | 13/13 | 5(2/3) | NIH-CPSI | Non-acupuncture points | superficial penetration, no electrical stimulation | Sham EA type O |
| Tam et al. 2007 Hong Kong^93 | Rheumatoid arthritis | 6/6 | 12/12 | 5(0/5) |VAS | ND | Therapeutic acupuncture, superficial penetration, no electrical stimulation | Sham EA type D |
| Kvorning and Akeson 2010 Sweden^94 | Anaesthesia | 12/12 | 22/23 | 0(0/0) |Plasma levels of adrenaline | T > C | Therapeutic acupuncture, no penetration | Sham EA type A |
| Waite and Clough 1998 UK^95 | Smoking cessation | 2/2 | 40/38 | 0(0/0) |Biochemically validated total cessation of smoking | T > C | Non-acupuncture points, superficial penetration | Sham EA type N |
| Holzer et al. 2011 Austria^96 | Postoperative pain | 3/3 | 20/20 | 0(0/0) |VAS scores and the consumption of piritramide | ND | Therapeutic acupuncture, no penetration, no electrical stimulation | Sham EA type A |
| Sator-Katzenschlager et al. 2006 Austria^97 | Perioperative pain | 3/3 | 32/30 | 1(0/1) |VAS scores, adverse event and analgesic drug consumption | T > C | Therapeutic acupuncture, no penetration | Sham EA type A |
| Liu et al. 2011 China^98 a | Primary dysmenorrhea | 1/1 | 50/50 | 5(3/2) |VAS scores | ND | Nonspecific acupuncture points, The same depth | Sham EA type F |
| Liu et al. 2011 China^98 b | Primary dysmenorrhea | 1/1 | 50/46 | 6(3/3) |VAS scores | ND | Nonspecific acupuncture points, The same depth | Sham EA type L |
| Liu et al. 2014 China^99 a | Primary dysmenorrhea | 2/2 | 167/167 | 6(4/2) |VAS scores | T > C | Nonspecific acupuncture points, The same depth | Sham EA type F |
| Liu et al. 2014 China^99 b | Primary dysmenorrhea | 2/2 | 167/167 | 6(4/2) |VAS scores | T > C | Nonspecific acupuncture points, The same depth | Sham EA type L |
| Maeda et al. 2013 USA^100 1 | Carpal tunnel syndrome | 2/2 | 22/19 | 0(0/0) |functional MRI, VAS scores | T > C | Nonspecific acupuncture points, No penetration | Sham EA type F |
| Maeda et al. 2013 USA^100 2 | Carpal tunnel syndrome | 2/2 | 18/19 | 0(0/0) |functional MRI, VAS scores | T > C | Nonspecific acupuncture points, No penetration | Sham EA type F |
| Shi et al. 2011 China^101 a | Primary dysmenorrhea | 1/1 | 10/10 | 0(0/0) |VAS scores, The plasma PGE_{2α}, PGF_{2α}, TXB_{2α}, and 6-keto PGF_{1α}, levels | ND | Nonspecific acupuncture points, The same depth | Sham EA type F |
| Shi et al. 2011 China^101 b | Primary dysmenorrhea | 1/1 | 10/10 | 0(0/0) |VAS scores, The plasma PGE_{2α}, PGF_{2α}, TXB_{2α}, and 6-keto PGF_{1α}, levels | ND | Nonspecific acupuncture points, The same depth | Sham EA type L |
| Dias et al. 2010 Brazil^102 | Local anaesthesia | 8/8 | 16/17 | 0(0/0) |VAS scores | ND | Therapeutic acupuncture, no penetration, no electrical stimulation | Sham EA type A |
| Zhang et al. 2013 Hong Kong^103 | Chronic neck Pain | 5/5 | 103/103 | 46(19/27) |NPQ scores | ND | Therapeutic acupuncture, no penetration, no electrical stimulation | Sham EA type A |
| Sangdee et al. 2002 Thailand^104 | Osteoarthritis of the knee | 4/4 | 48/47 | 4(2/2) |VAS score, and Lequesne's functional index | T > C | Therapeutic acupuncture, no penetration, no electrical stimulation | Sham EA type B |
| Johansson et al. 2001 Sweden^105 | Stroke rehabilitation | 9–10/4 | 48/51 | 20(11/9) |The scores of Barthel Index, the Rivermead Mobility Index and NHP, the time needed to walk 10 meters | ND | Therapeutic acupuncture, no penetration, no electrical stimulation | Sham EA type B |
| Hopwood et al. 2008 UK^106 | Stroke recovery | 8–10/6 | 57/48 | 13(10/3) |The scores of Barthel Index | ND | Therapeutic acupuncture, no penetration, no electrical stimulation | Sham EA type A |

Continued
Table 1. Characteristics of 94 included studies. T, treatment group/real EA group; C, control group/sham EA group; NS, not stated; T > C, EA treatment group was significantly superior to sham EA control group; ND, no difference between EA and sham EA group; T < C, real EA group was significantly inferior to sham EA group; T > C?, the efficacy result of trial was reported as “T > C” without conducting the between-group analysis and with the original data not available; NRS, Numerical Rating Scale; SF_MPQ, Short-Form McGill Scale; FMRI, Functional magnetic resonance imaging; MASS, the Massachusetts General Hospital Acupuncture Sensation Scale; WOMAC, The Western Ontario and McMaster University Osteoarthritis Index; EPDS, Edinburgh Postnatal Depression Scale; HADS, Hospital Anxiety and Depression Scale; HDRS17, 17-item Hamilton Rating Scale for Depression; CGI, Clinical Global Impression; FMA, Fugl-Meyer Assessment; VAS, Visual Analog Scale; NIHSS, the National Institutes of Health Stroke Scale. BW, body weight; BMI, body mass index; BFM, body fat mass; BPI, Brief Pain Inventory; EDSS, Expanded Disability Status Scale; FAMS, Functional Assessment of multiple Sclerosis; C-MMAS, Modified Massachusetts General Hospital Acupuncture Sensation Scale – Chinese version; HR, Heart rate; MAP, mean arterial blood pressure; OLM, opioid-like medication; TNF-α, tumor necrosis factor-α; IL-8, interleukin-8; IL-10, interleukin-10; HDRS, Hamilton Depression Rating Scale; HAMD-17, the 17-item Hamilton Rating Scale for Depression; SSS, the Chinese version Self-Rating Depression Scale; SPT, single pain threshold; TST, temporal summation thresholds; R1, angle of muscle reaction; R2, passive range of motion; R2–R1, dynamic component; ISI, The Insomnia Severity Index; PSQI, the Pittsburgh Sleep Quality Index; CGI, Clinical Global Impression – Severity scale; BPI-SF, Brief Pain Inventory Short Form; FACT-G instrument, the Functional Assessment of Cancer Therapy-General instrument; 24-item HAMD, the 24-item Hamilton Depression Rating Scale; TFM, Trunk Fat Mass; WC, Waist Circumference; HC, Hip Circumference; VAS-100, a 100-mm visual analogue scale; BOLD fMRI, blood oxygen level dependent functional magnetic resonance imaging; IPSS, the International Prostate Symptom Score; GCSI, the Gastroparesis Cardinal Symptom Index; SEPs, somatosensory evoked potentials; MVC, maximal voluntary contraction; NPQ, the Northwick Park Neck Pain Questionnaire; NHP, the Nottingham Health Profile; MSQ, Mini-Sleep Questionnaire; MBI-SS, the Maslach Burnout Inventory—Student Survey. Note: Sham EA type A: sham EA on therapeutic acupoints plus no penetration plus no electrical stimulation; Sham EA type B: sham EA on therapeutic acupoints plus no penetration plus electrical stimulation; Sham EA type C: sham EA on therapeutic acupoints plus the same depth plus no electrical stimulation; Sham EA type D: sham EA on therapeutic acupoints plus superficial penetration plus no electrical stimulation; Sham EA type E: sham EA on nonspecific acupuncture points plus the same depth plus electrical stimulation; Sham EA type F: sham EA on nonspecific acupuncture points plus the same depth plus electrical stimulation; Sham EA type L: sham EA on non-acupuncture points plus the same depth plus electrical stimulation; Sham EA type M: sham EA on non-acupuncture points plus the same depth plus no electrical stimulation; Sham EA type N: sham EA on non-acupuncture points plus superficial penetration plus electrical stimulation; Sham EA type O: sham EA on non-acupuncture points plus superficial penetration plus no electrical stimulation; Sham EA type Q: sham EA on non-acupuncture points plus no penetration plus no electrical stimulation.
| Reference (author, year and country) | A | B | C | D | E | F | G | H |
|--------------------------------------|---|---|---|---|---|---|---|---|
| Nitrissou et al. 2014 USA44 | + | + | + | + | + | + | ? | + |
| Chu et al. 2012 Hong Kong43 | + | + | + | + | + | + | ? | + |
| Wang et al. 2010 Denmark45 | + | + | + | + | + | + | ? | + |
| Zyloney et al. 2010 USA46 | + | + | ? | ? | + | ? | + | + |
| Jubb et al. 2008 UK47 | + | + | + | + | + | + | ? | + |
| Chung et al. 2012 Hong Kong48 | + | + | + | + | + | + | ? | + |
| Barlas et al. 2006 UK49 | + | + | + | + | + | + | ? | + |
| Wayne et al. 2005 US50 | + | + | + | + | + | + | ? | + |
| Sahin et al. 2010 Turkey51 | + | + | + | + | + | + | ? | + |
| Fanti et al. 2003 Italy52 | + | + | + | + | + | + | ? | + |
| Huang et al. 2012 Brazil53 | + | + | + | + | + | + | ? | + |
| Gosman-Hedstrom et al. 1998 Sweden54 | + | + | + | + | + | + | ? | + |
| Jing et al. 2009 China55 | + | + | + | + | + | + | ? | + |
| Kong et al. 2009 USA56 | + | + | + | + | + | + | ? | + |
| Darbandi et al. 2013 Iran57 | + | + | + | + | + | + | ? | + |
| Yang et al. 2012 China58 | + | + | + | + | + | + | ? | + |
| Liu et al. 2013 China59 | + | + | + | + | + | + | ? | + |
| Zhang et al. 2014 China60 | + | + | + | + | + | + | ? | + |
| Mao et al. 2014 USA61 | + | + | + | + | + | + | ? | + |
| Leung et al. 2011 Hong Kong62 | + | + | + | + | + | + | ? | + |
| Rusy et al. 2002 USA63 | + | + | + | + | + | + | ? | + |
| Yang et al. 2014 China64 | + | + | + | + | + | + | ? | + |
| Chen et al. 2013 China65 | + | + | + | + | + | + | ? | + |
| Quispe-Cabanillas et al. 2012 Brazil66 | + | + | + | + | + | + | ? | + |
| Aranha et al. 2015 Brazil67 | + | + | + | + | + | + | ? | + |
| Yu et al. 2013 Hong Kong68 | + | + | + | + | + | + | ? | + |
| Li et al. 2010 China69 | + | + | + | + | + | + | ? | + |
| Zheng et al. 2007 Australia70 | + | + | + | + | + | + | ? | + |
| Li et al. 2013 China71 | + | + | + | + | + | + | ? | + |
| Lin et al. 2002 Taiwan72 | + | + | + | + | + | + | ? | + |
| Chen et al. 2013 Taiwan73 | + | + | + | + | + | + | ? | + |
| Schukro et al. 2014 Austria74 | + | + | + | + | + | + | ? | + |
| Yu et al. 2014 China75 | + | + | + | + | + | + | ? | + |
| Xie et al. 2014 China76 | + | + | + | + | + | + | ? | + |
| Sim et al. 2002 Singapore77 | + | + | + | + | + | + | ? | + |
| Song et al. 2009 China78 | + | + | + | + | + | + | ? | + |
| Shafiahk 1995 Egypt79 | + | + | + | + | + | + | ? | + |
| Franasik et al. 2012 USA80 | + | + | + | + | + | + | ? | + |
| Naslund et al. 2002 Sweden81 | + | + | + | + | + | + | ? | + |
| Shen et al. 2000 US82 | + | + | + | + | + | + | ? | + |
| Wyon et al. 2004 Sweden83 | + | + | + | + | + | + | ? | + |
| Zhang et al. 2012 Hong Kong84 | + | + | + | + | + | + | ? | + |
| Zheng et al. 2010 Australia85 | + | + | + | + | + | + | ? | + |
| Ma et al. 2010 China86 | + | + | + | + | + | + | ? | + |
| Wang et al. 2014 Taiwan87 | + | + | + | + | + | + | ? | + |
| Yeung et al. 2011 Hong Kong88 | + | + | + | + | + | + | ? | + |
| Chan et al. 2014 Taiwan89 | + | + | + | + | + | + | ? | + |
| Man et al. 2014 Hong Kong90 | + | + | + | + | + | + | ? | + |
| Oh et al. 2013 Australia91 | + | + | + | + | + | + | ? | + |
| Wong et al. 2006 Hong Kong92 | + | + | + | + | + | + | ? | + |
| Song et al. 2007 USA93 | + | + | + | + | + | + | ? | + |
| Cameron et al. 2011 Australia94 | + | + | + | + | + | + | ? | + |
| Darbandi et al. 2014 Iran95 | + | + | + | + | + | + | ? | + |
| Wei et al. 2008 China96 | + | + | + | + | + | + | ? | + |
| Wang et al. 2007 USA97 | + | + | + | + | + | + | ? | + |
| Kvorning et al. 2003 Sweden98 | + | + | + | + | + | + | ? | + |

Continued
Table 2. Risk of bias of included studies. Note: A, Adequate sequence generation; B, Allocation Concealment; C, Blinding (participants); D, Blinding (personnel); E, Blinding (outcome assessor); F, Incomplete outcome data addressed; G, Free of selective reporting; H, Free of other bias. +, Yes; −, No; ?, Unclear.

Credibility of blinding. Only 24 out of the 94 studies reported the credibility of blinding in participants by conducting the credibility test in six types of sham EA methods. Twenty-three studies proved to be successful and one study proved to be failure. All six types of sham EA methods were claimed to be successful in blinding. They are sham EA type A (10/24 with 1 failure)22,23,25,34,36,45,52,57,59,63,65,72,81,88,97,102,103,105–108,110 reported significant superiority over corresponding sham EA groups; forty-three real EA groups were not statistically better than sham EA groups; one study showed that sham EA group was superior to the real EA group; the remaining two studies109,111 lacked original data for between-groups analyses and were stated as “T > C?”. The efficacy results of the studies are listed in Table 1 and summarized in Table 3 according to different types of sham EA methods and EA indications.

Compared with sham EA controls, EA therapy in about 56.2% (59/105 comparisons) of comparisons reported the specific effect. Correspondingly, the real EA was superior to sham EA for type N (75%, 3/4 comparisons), type
| electroacupuncture (EA) indications | Sham EA type A 26 control groups | Sham EA type B 7 control groups | Sham EA type C 7 control groups | Sham EA type D 6 control groups | Sham EA type E 7 control groups | Sham EA type L 17 control groups | Sham EA type M 3 control groups | Sham EA type N 4 control groups | Sham EA type O 14 control groups | Sham EA type Q 10 control groups | The NO. of reference included |
|-----------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|-------------------------------|
| Pain 32 RCTs                      | T > C 8 comparisons ND 7 comparisons | T > C 3 comparisons ND 1 comparison | T > C 1 comparison ND 3 comparisons | T > C 1 comparison | ND 2 comparisons | T > C 1 comparison | T > C 1 comparison | T > C 1 comparison ND 2 comparisons | ND 2 comparisons | T > C 17 ND 17 T > C 1 |
| Obesity 4 RCTs                    |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 comparison | T > C 1 comparison | T > C 4 ND 1 |
| Anesthesia 8 RCTs                 | T > C 2 comparisons ND 1 comparison | T < C 1 comparison |                                |                                | ND 2 comparisons | T > C 1 comparison |                                | T > C 1 comparison | T > C 3 ND 3T < C 1T > C 1 |
| Stroke 7 RCTs                     | ND 1 comparison | ND 1 comparison | T > C 1 comparison | T > C 1 comparison | ND 1 comparison | ND 1 comparison | T > C 1 comparison ND 1 comparison | T > C 3 ND 4 |
| Depression 6 RCTs                 |                                |                                | T > C 2 comparisons ND 1 comparison | T > C 1 comparison | ND 1 comparison | ND 1 comparison | T > C 1 comparison ND 1 comparison | T > C 3 ND 3 |
| Primary dysmenorrhea and (or) Menstrual Pain 4 RCTs |                                |                                | T > C 2 comparisons ND 2 comparisons | T > C 2 comparisons ND 2 comparisons | ND 2 comparisons | T > C 1 comparison |                                | T > C 4 ND 4 |
| Substance abuse 3 RCTs            |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 comparison | ND 1 comparison | T > C 2 ND 1 |
| Healthy 3 RCTs                    |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 comparison | T > C 2 ND 2 |
| Osteoarthritis 2 RCTs             | T > C 2 comparisons |                                |                                |                                |                                |                                |                                 |                                |                                | T > C 2 |
| Migraine 2 RCTs                   |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 ND 1 |
| Nausea and Vomiting 2 RCTs        |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 comparison | T > C 3 |
| Postoperative ileus 2 RCTs        |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 2 |
| Insomnia 2 RCTs                   | ND 1 comparison |                                |                                |                                |                                |                                |                                 | T > C 1 ND 2 |
| benign prostate hyperplasia 2 RCTs |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 2 |
| Diabetic mellitus 2 RCTs          |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 ND 1 |
| Carpal tunnel syndrome 1 RCTs     |                                |                                | T > C 2 comparisons |                                |                                |                                |                                 | T > C 2 |
| Rheumatoid arthritis 1 RCTs       |                                |                                | ND 1 comparison |                                |                                |                                |                                 | ND 1 |
| Whiplash-associated disorders 1 RCTs |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 |
| Constipation 1 RCTs               | T > C 1 comparison |                                |                                |                                |                                |                                |                                 | T > C 1 |
| Multiple sclerosis 1 RCTs         |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 |
| Tinnitus 1 RCTs                   | ND 1 comparison |                                |                                |                                |                                |                                |                                 | ND 1 |
| Auditory hallucination 1 RCTs     |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 |
| ADHD (Attention deficit hyperactivity disorder) 1 RCTs |                                |                                | T > C 1 comparison |                                |                                |                                |                                 | T > C 1 |

Continued
| electro-acupuncture (EA) indications | The type of sham EA method | The NO. of reference included |
|-------------------------------------|---------------------------|-------------------------------|
| PCOS (Polycystic Ovary Syndrome) 1 RCTs | | |
| hot flushes in postmenopausal women 1 RCTs | Sham EA type A 26 control groups | ND 1 comparison |
| Postpartum Insufficient Lactation 1 RCTs | Sham EA type B 7 control groups | ND 1 comparison |
| Cardiac ischemia-reperfusion injury 1 RCTs | Sham EA type C 7 control groups | T > C 1 comparison |
| Stress-related symptoms 1 RCTs | Sham EA type D 6 control groups | T > C 1 comparison |
| The positive rate of efficacy result | Sham EA type E F 17 control groups | T > C 1 comparison |
| | Sham EA type F 3 control groups | T > C 1 comparison |
| | Sham EA type G 3 control groups | T > C 1 comparison |
| | Sham EA type H 1 control groups | T > C 1 comparison |
| | Sham EA type I 1 control groups | T > C 1 comparison |
| | Sham EA type J 1 control groups | T > C 1 comparison |
| | Sham EA type K 1 control groups | T > C 1 comparison |
| | Sham EA type L 1 control groups | T > C 1 comparison |
| | Sham EA type M 1 control groups | T > C 1 comparison |
| | Sham EA type N 1 control groups | T > C 1 comparison |
| | Sham EA type O 1 control groups | T > C 1 comparison |
| | Sham EA type Q 1 control groups | T > C 1 comparison |

Table 3. Summary of effect result within different type of sham electro-acupuncture methods and electro-acupuncture indications. NOTE: T > C, EA treatment group was significantly superior to sham EA control group; ND, no difference between EA and sham EA group; T < C, real EA group was significantly inferior to sham EA group; T = C, the efficacy result of trial was reported as “T > C” without conducting the between-group analysis and with the original data not available.

F (71.4%, 5/7 comparisons), type D (66.7%, 4/6 comparisons) and type M (66.7%, 2/3 comparisons). The lowest percentage of positive efficacy result was 44.4% (8/18 comparisons) in sham EA type L. The positive rate of efficacy for the three most often used sham EA methods were 50% (13/26 comparisons) for sham EA type A, 44.4% (8/18 comparisons) for sham EA type L and 64.3% (9/14 comparisons) for sham EA type O.

The type of sham EA methods varied across different EA indications. The sham EA type A was most commonly used in RCTs for pain, anesthesia and osteoarthritis. The sham EA type D and sham EA type Q were applied mainly in stroke studies. The sham EA type B was commonly applied to RCTs on depression. The sham EA type L and sham EA type O were commonly performed in trials on obesity. The sham EA type F and sham EA type L were commonly used in studies on primary dysmenorrhea.

**Discussion**

To our knowledge, this is the first systematic analysis to address sham EA methods in RCTs. The numbers of publications and sham EA methods have been increasing every decade. We summarized seventeen kinds of sham EA methods according to three aspects as needle location, depth of needle insertion and electrical stimulation, whereas only ten types of sham EA methods were identified from 94 included RCTs involving 6134 participants. The three predominant types of sham EA methods used were sham EA type A, type L and type O Ordinally. Only 24 out of 94 trials reported credibility test with the results of 23 success and 1 failure using six types of sham EA methods mainly as follows: sham EA type A (10/24 with 1 failure), type B (5/24) and type Q (5/24). The remaining 3 sham EA methods were only tested in 4 trials. About 56.2% of comparisons provided the evidence of specific effect of EA therapy, and the four types of Sham EA controls with highest positive rate of efficacy result were type A (59.5%, 60/105 comparisons), type B (59.2%, 57/97 comparisons), type C (59.5%, 53/89 comparisons) and type D (59.2%, 60/103 comparisons).

The ideal design of sham acupuncture method remains methodologically challenging. Consequently, a great variety of emerging sham acupuncture methods have found their ways into present RCTs by using non-traditional Chinese medicine acupuncture, no or superficial penetration and no or suboptimal stimulation. The sham procedures in acupuncture RCTs were previously summarized by He et al. as seven types. A previous review by Dincer et al. reported the classification of sham acupuncture as sham type I–V based on three respects as needle location, insertion and stimulation. In the present study, we focused on the sham EA methods according to three aspects as needle location, depth of needle insertion and electrical stimulation, and summarized seventeen types of sham EA methods. Ten types of sham EA methods were actually used in the included RCTs.

The main purpose of RCTs on EA is to evaluate its specific effect. An optimal sham acupuncture technique must be biologically inactive and psychologically credible. A lot of practice has been done to make the sham
components of EA less perceptually and operationally distinguishable from real EA intervention for the purpose of keeping the blinding status of the participants. Streitberger needles, blunted needles and verum needles were frequently used with foam, tape or tube for hiding acupuncture loci from subjects. Furthermore, a pricking sensation was elicited by dull tips for concealing the perceptual differences. The sham EA device was often accompanied by indicator light or with sound signals for confusing the participants. In the present study, six types of sham EA method were tested as concealable control in terms of blinding of participants.

The top three types of sham EA methods used were sham EA type A, type L and type O. The most frequently applied sham EA method was type A, accounting for a popular belief in its inertness based on its absence of key EA components as needle stimulation and electrical stimulation as well as its indistinguishable manipulation on same therapeutic acupoints. In the present study, the validation of credible participant blinding of this sham EA type was reported by most credibility tests. The debate emerged over the past decades over the inertness of non-penetrating procedure since the slight acupressure effects and physiological activity might be evoked by the tactile stimulation from blunt needle tips even without skin penetration. Takayama et al. argued that non-penetrating placebo needle is at least clinically inert for pain alleviation based on their cross-over study reporting no analgesic effects of the skin-touch placebo needle over that of the no-touch placebo or that of the no-treatment control. However, conclusive evidence are out of our awareness up to now whether non-penetrating but skin-touch placebo needle plays a specific therapeutic role in other medical condition. Thus, the sham EA type A may be an promising candidate control for further RCTs on analgesic effects of EA and relative further researches are called for in aspect of any other conditions.

Sham EA type Q is deemed to be the most inert type of sham EA control because it avoids all therapeutic components, which also probably makes this sham method perceptually and operationally distinguishable from real EA intervention and to some extent results in participant blinding. In the present study, the credibility of participant blinding of this sham EA type was endorsed by five studies with credibility test. However, mechanical non-penetration can evoke brain responses in healthy subjects. Thus, controversy raised regarding whether this type of sham EA method is physiologically inert control. Moreover, four-fifth of the studies were conducted on acupuncture naïve participants. There is a possibility that previous experience of acupuncture treatments might have an impact on present perception of verum and sham EA intervention, which should be rigorously controlled in EA RCTs to avoid bias from unblinding. With the informed consent lack of explicit information on the sham method, debates emerged over ethical acceptability of the study.

The second commonly used sham EA method was type L. It was found that the differential effects of real EA and sham EA, which were attributed to point location, was not consistent across studies and conditions within this sham EA type, suggesting that EA on non-acupoints might be efficacious as EA on therapeutic acupoints. Furthermore, the improvements from baseline were also observed by Sahin et al., Li et al. and Yu et al. The similar findings were previously presented by Moffet et al. showing that sham acupuncture at non-acupoints was as efficacious as true acupuncture. It seemed that in the above studies the specificity of acupoints does not exist and to some extent were in violation of traditional acupuncture theories. Li et al. stated that the specificity of acupoints was not present in EA treatment. However, Wang et al. argued for the specificity of acupoints in EA treatment based on the better effects of EA at acupoints than that at non-acupoints on certain clinical outcomes. From the heterogeneous evidence of acupoint specificity, no definitive conclusion could be drawn based on the paucity of available high-quality clinical trials. The main issue in this sham EA type might lie in the accurate identification of non-acupoint rather than a rough location nearby traditional acupoint that might be responsible for specific effects, which rises the challenge of conducting appropriate sham control in EA clinical trials especially in the presence or absence of the mechanism of acupoint specificity and the consistency in finding actual point across the different practitioners. Nevertheless, it is unclear whether this type is a concealable control for participant blinding since this sham EA tested credibility in the present study. Therefore, it demonstrates that sham EA type L might not be adequately controlled from inert or concealable perspective only if the mechanisms of acupoints were explicitly explored or the validation of so-called non-acupoint was verified by further researches. Cautions should be taken for eliminating bias from this sham EA control type.

The third commonly used sham EA method was type O. During the procedure, the shallow insertion was applied to simulate deep skin penetration and to ensure the blinding of participant. In the present study, the validation of participant blinding of this sham EA type was endorsed by two studies. As for the issue of inertness, few studies reported that sham EA control improved baseline in certain clinical parameters compared with conventional group. Moffet et al. stated that shallow needling at non-acupoints might be as efficacious as real acupuncture. Lund et al. reported that minimal acupuncture based on superficial insertion was not a valid control from a physiological perspective. Hrbjartsson et al. held the view that sham EA type was not inert control from Chinese medicine perspective. A sham EA procedure with superficial needling at non-acupoints might have subliminal effects since the locations of points was nearby true acupoints or myotome. Moreover, it is likely that the superficial insertion was not consistently applied since the needling depth varied across different acupoints. The sham EA on different body parts and the relatively deep insertions might be conducted for taking the weight of the attached electrodes. Thus, this sham EA type may be concealable control but far from inert control in RCTs for EA, unless the extent to which the sham procedure could be regarded as physiologically inert has been clarified.

In the present study, six types of sham EA method were reported as successful in blinding. However, further investigations are needed for confirmation, since half of the tested types of sham EA controls were reported in a small number of trials. It should be noted that studies included did not provide sufficient evidence of blinding in acupuncturist. Vase et al. stated that it was hard to get acupuncture intervention fully double-blinded. Although non-penetrating needle was previously reported as potential sham control to mask both participants and practitioners in acupuncture research, a previous review demonstrated that the acupuncture intervention was not fully double-blinded. New strategies should be implemented for the development of double-bind sham EA control in terms of both participants and acupuncturists.
RCTs are generally recognized as the gold standard for the efficacy of clinical interventions by excluding the non-specific effect via a placebo control. However, one study reported that the effect of EA therapy was merely the non-specific effect. In the present study, the number of real EA group with superiority to, no difference from, and inferiority to corresponding sham EA group was 59, 43 and 1, respectively. Thus, more than half comparisons demonstrated that EA therapy existed specific effects. Within all types of sham EA methods, the highest effective rate were type N (75% 3/4 comparisons), type F (71.4%, 5/7 comparisons), type D (66.7%, 4/6 comparisons) and type M (66.7%, 2/3 comparisons) successively. Considering the small number of included studies within corresponding sham EA type, the evidence are still insufficient to recommend any type of sham EA control despite of the high positive rate.

In the present study, 43/105 comparisons reported that EA has no specific effects compared with sham EA control. For a reason, the extent to which the individual component of EA intervention plays its therapeutic influences on the final outcomes is not clear during clinical treatment. The debate consequently emerges regarding the therapeutic inactivity of sham EA control which is partially comprised of real EA components, such as suboptimal manual or electrical stimulation. The probability in the specific effects of EA may be reduced by the potential activity produced by sham EA control. On the other hand, EA is a complex intervention method. Its therapeutic effects consist of specific effects from needling and stimulation components as well as moderately large nonspecific effects, which means that the efficacy results of RCTs for EA are more likely to be influenced by a variety of factors, such as patient/practitioner interaction and patient expectations. In the clinical use, EA may be more effective than manual acupuncture in some situations such as when strong, continued stimulation is required, and when treating pain, anesthesia, stroke, depression, obesity and primary dysmenorrhea/period pain, suggesting that further RCTs with appropriate sham EA control are in need to verify the specific effects on above conditions.

There are several weaknesses in the present study. Firstly, the search and screen procedure were limited to randomized, parallel-controlled trials published in English. Thus, those trials with cross-over design or published in other than English language were omitted. Secondly, with the aim of evaluating the sham method in RCTs on EA, a generous criterion was established to select eligible studies. Therefore, it was not easy to examine the specific effect of EA by data synthesis from different outcomes and indications because of the heterogeneity of trials. Finally, the reported credibility test addressed blinding effects in participant rather than in both participant and acupuncturist. The credibility tests were not reported in all studies and the number of studies using sham EA types was small, and therefore the conclusion should be interpreted with cautions.

Conclusion
Ten types of sham EA methods were identified based on our scheme classification. Generally, sham EA type A, type L and type O were frequently used. Yet, further clinical trials are recommended to maintain standard methodology of concealable and inert placebo EA techniques. Only 24 out of 94 trials were reported as positive credibility test in six types of sham EA methods, where sham EA type A, type B and type Q were highly practiced. It is worthy to study further about the importance of concealable sham EA types. EA therapy in approximately, 56.2% of comparisons provided the specific effects. The four types of sham EA (N, F, D and M respectively) represented the highest positive rate of efficacy results. However, progressive evidences on specific effects are mandatory. The sham EA control was observed frequently in pain, anesthesia, stroke, depression, obesity and primary dysmenorrhea RCTs. Also, broader studies in these predominant diseases are advised.

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**Author Contributions**

Z.-X.C., Y.L., X.-G.Z., S.C., W.-T.Y., X.-W.Z. and G.-Q.Z. participated in its design, searched databases, extracted and assessed studies and drafted the manuscript. Z.-X.C., Y.L., X.-G.Z., S.C., W.-T.Y., and X.-W.Z. analyzed
data and carried out the statistical analysis. G.-Q.Z. acted as an arbitrator in the review. G.-Q.Z. conceived and designed the article, supervised the study and contributed to finalize the manuscript. All authors reviewed the manuscript.

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