



Analysis of the Choice of Control in Acupuncture Clinical Trials Involving Patients with Breast Cancer

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Control group selection in clinical trials is challenging, especially in acupuncture studies. A PubMed literature review of control groups in breast cancer acupuncture studies was performed and identified 67 studies for analysis. Although the types of acupuncture controls varied, sham acupuncture was the most common type of control. The rationale and specification of the sham procedures, however, were incomplete and not standardized, despite the availability of guidelines. This may impact the interpretation and replicability of the study findings. A standardized and complete description and rationale for all acupuncture controls are necessary.

Keywords: Acupuncture; Breast neoplasms; Control groups; Placebos; Randomized controlled trials

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INTRODUCTION

The use of an appropriate control group in research is important, but its selection can be challenging [1]. Control groups in randomized controlled trials (RCTs) minimize bias and control for confounding variables, thereby permitting the fair evaluation of an intervention. Thus, selecting an appropriate control group and ensuring its validity are essential for obtaining high-quality data.

Control group selection is especially difficult in acupuncture studies. The types of control groups vary between no treatment, waitlist, continuing usual care, placebo or sham control, or some other kind of specific intervention (e.g., relaxation technique) that differs from the experimental group [2]. Comparing acupuncture to the administration of a medication (e.g., an analgesic) is not likely appropriate, given the difference in mechanism and participant experience. “Sham” acupuncture varies in methodology. Some sham procedures use non-insertion techniques (e.g., blunted needles or retractable needles), some do use an acupuncture needle but not inserted at acupoints, and others vary in style or detail (e.g., time, duration, needle stimulation). The lack of standardization is problematic.

There exist technical standards for reporting acupuncture interventions in research based on the Standards for Reporting Interventions in Controlled Trials of Acupunc-

ture (STRICTA) [3] guidelines, an extension of the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines that set the standard for the presentation of RCTs, and its correlate, the Acupuncture Controls Guideline for Reporting Human Trials and Experiments (ACURATE) checklist [4]. However, these standards are not consistently or transparently adopted, thus making it difficult to assess the impact of the intervention, reproduce the study, and draw conclusions about whether a given acupuncture intervention is efficacious, particularly in comparison to other acupuncture procedures. Furthermore, there continues to be a debate about the optimal acupuncture control [5].

METHODOLOGY

We reviewed recent RCTs of breast cancer acupuncture studies to determine the range and adequacy of the control group choice and description in the reported literature. The following keywords were entered into the PubMed “search” function with a time interval of January 1, 2000, to May 19th, 2023 and restricted to publications in English: “acupuncture AND randomization AND breast cancer.” The search resulted in a total of 215 results (Fig. 1). Articles not describing an RCT or an acupuncture control were excluded, leaving 82 publications.

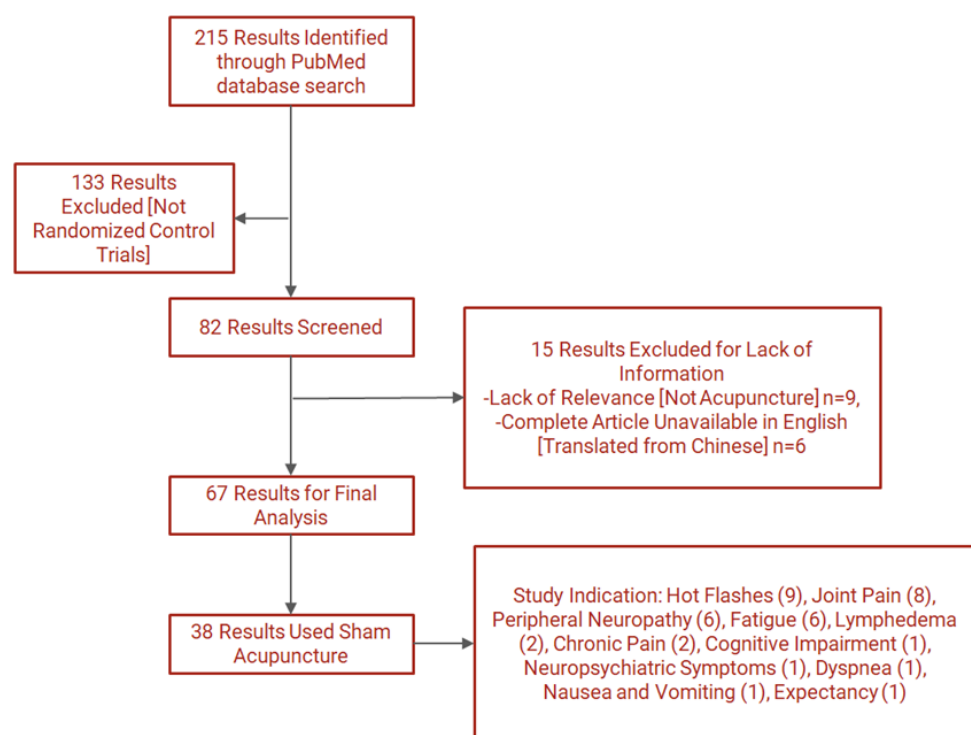


Fig. 1. PRISMA diagram of results identified through the PubMed search. PRISMA diagram of the results identified through the PubMed search. The literature search was conducted again in January 2024 to confirm that no randomized controlled trials were missed. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Of the 82 publications, nine failed to include any acupuncture-specific details (e.g., moxibustion-related trials), and six were written in Chinese and had no available English version of the publication. For the analysis, the remaining 67 publications were further coded as follows: status of the trial (completed or ongoing), number of participants enrolled, randomization status of the trial (RCT or not), type of acupuncture control, description of the acupuncture control extracted as text, whether a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram was included, and whether the choice of type of control was described or explained. Notably, a PubMed search, repeated on January 15, 2024 using the same criteria, confirmed that no additional RCTs were published in the intervening time.

RESULTS

Among the 67 publications, the most commonly used control was sham acupuncture alone without a waitlist control, followed by usual care (chemotherapy alone), and then a combination of sham and waitlist control (Table 1). The other types of controls were medication use, massage, psychoeducation, kinesiotherapy, hormone therapy, no treatment, enhanced self-care, applied relaxation, and circulation. None (0) of the search results included an ethical explanation for the control used; however, three results provide insight into the use of blinding to increase the validity of the RCT. A PRISMA diagram was included in the majority of reports (35/67, 52%).

Table 1 shows the types of acupuncture controls used in the RCTs of breast cancer treatments. Sham acupuncture was the most common, with 46% of trials ($n = 31$) using sham acupuncture as the control group; however,

Table 1. Types of acupuncture controls used in breast cancer treatment randomized controlled trials

Control type	Number of trials ($n = 67$)
Sham alone	31
Usual care (chemotherapy)	8
Sham + waitlist	7
Medication*	6
No treatment	4
Other [†]	11

*Gabapentin ($n = 5$) and flupentixol/melitracen ($n = 1$).

[†]Waitlist ($n = 3$), applied relaxation ($n = 2$), psychoeducation ($n = 2$), massage ($n = 1$), kinesiotherapy ($n = 1$), enhanced self-care ($n = 1$), and pneumatic circulation ($n = 1$).

12% of the trials ($n = 8$) described “usual care,” 10% ($n = 7$) used sham and waitlist control together, 9% ($n = 6$) used medication, 6% ($n = 4$) used “no treatment,” and 16% ($n = 11$) used other controls (e.g., massage, psychoeducation, kinesiotherapy, hormone therapy, no treatment, enhanced self-care, applied relaxation, and pneumatic circulation). There was no explicit justification or explanation for the choice of any control group.

Further analysis of sham acupuncture demonstrated that 42% of controls used a combination of non-acupoints and sham needles ($n = 16$), 26% used real needles on non-acupoints only ($n = 10$), 8% used sham needles only ($n = 3$), 11% used an alternative method, such as electrical stimulation of acupoints ($n = 4$), and 13% did not describe the sham acupuncture method ($n = 5$; see Table 2 and further specification therein).

DISCUSSION

Our findings show that sham acupuncture was selected as the control group in the majority of breast cancer acupuncture RCTs. No study explained or justified the choice of the control group, demonstrating a lack of rationale or justification for the specific choices made in the control type selection. It is possible that the specifics of the control procedures were more exhaustively defined in the contemporaneous written study protocols that were subject to ethical review and those informed study conduct and practice; if they exist, however, those protocol descriptions are generally unavailable in the literature and not described in the publications. We note

Table 2. The type of sham acupuncture used

Sham acupuncture type	Number of trials* ($n = 38$)
Combination (non-acupoints and sham needles) [†]	16
Non-acupoints only	10
Sham needles only [‡]	3
Alternate method	4
Not enough detail provided	5

* $N = 7$ of those sham + waitlist (combination [3], non-acupoints only [2], and sham needles only [2]).

[†]Of the 16 trials that used a combination of procedures, 15 did not penetrate the skin. Six used the Streitberger sham needle, five used the Park sham needle, and five did not specify. In one trial reporting a sham needle breaking the skin, they described “minimally invasive, shallow needles’ insertion at non-acupuncture points.”

[‡]The three trials utilizing only sham needles used Streitberger needles that did not penetrate the skin. This method inserts the sham needles at the correct acupoints.

that the publications evaluated in this report were restricted to RCTs of breast cancer treatment, to publications available in English, and to those indexed in PubMed. There is, therefore, possible language and publication bias.

Existing guidelines support the appropriate communication of acupuncture trials, including the methods, instruments, and procedures, and the selected control group. The STRICTA guidelines provide standards for reporting interventions in clinical trials of acupuncture [3]; the ACURATE checklist extends the STRICTA guidelines to provide details on sham acupuncture and thus support transparency, understanding, and replicability of the research [4]. Although some publications preceded the development of these guidelines, our review highlights the lack of adoption of either the STRICTA or ACURATE guidelines in most trials on the use of acupuncture in breast cancer.

CONCLUSION

Following the STRICTA and ACURATE guidelines will help with understanding the differences in the outcomes among various trials of acupuncture and may help with reproducibility. There are, however, other direct and indirect effects of acupuncture stimulation that will not be adequately captured by the guidelines but could be important to consider in the design of acupuncture studies. First, there is variability among practitioners—whether those practitioners are performing sham or standard acupuncture—and differences in patient responsiveness [6,7]. Second, any stimulation (e.g., at non-acupoints) from sham acupuncture may simulate acupuncture sufficiently to substantiate concerns that sham acupuncture is an inadequate control. In support of this concern, a systematic review by Kim et al. [8] demonstrated no significant difference in 36 out of 51 biomarkers between the sham and standard acupuncture. There are concerns about both the placebo effect [9-11] and the efficacy of participant blinding to the assigned treatment arm [12]. The lack of explanation as to why different sham acupuncture procedures were followed (e.g., sham needles versus non-acupoints) poses challenges to reproducibility and prevents fair comparisons among different treatments across acupuncture RCTs. Our data substantiate the need for standardization and specificity of not only the acupuncture procedure but also the control, whether sham acupuncture or others, to support the interpretation and replicability of the published literature.

AUTHOR CONTRIBUTIONS

Conceptualization: BEB. Data curation: MS. Funding acquisition: IHS, BEB. Investigation: MS. Methodology: MS, WL, TB. Project administration: SBK, BEB. Supervision: SBK, BEB. Writing - original draft: MS. Writing - review & editing: SBK, WL, IHS, TB, BEB.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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ETHICAL STATEMENT

This research did not involve any human or animal experiment.

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