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Insufficient evidence to determine the impact of patient preferences on clinical outcomes in acupuncture trials: a systematic review

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Abstract

Objective: To review reporting of preferences in acupuncture studies and their effect on clinical outcomes.

Study Design and Setting: Systematic review of published randomized and quasi-randomized controlled trials of acupuncture reporting participant preferences for randomization or treatment or using a preference design.

Results: Of the 31 included trials, 5 reported on randomization preference, 18 on treatment preference, and 1 reported on both. Seven used a preference design. Four out of seven trials noted that the group with preferences had different baseline characteristics (less education, worse baseline measure score, and greater or fewer years with pain). There was a tendency for greater attrition in nonpreference arms at 6 months but not earlier. Around three-quarters of participants turned down randomization in favor of nontrial treatment, and preference for acupuncture was around 20% when offered multiple treatments. Questions used to elicit preferences varied across trials and were poorly reported. Ten trials reported the effects of preferences on outcomes; only one detected a statistically (but not clinically) significant difference.

Conclusion: There is little evidence that preferences cause detectable effects on outcomes in acupuncture trials; however, trials use inconsistent methods and poorly report these data. Monitoring the level and effect of preferences in trials is recommended.

Keywords: Preferences; Preference design; Acupuncture; Systematic review; Randomized clinical trial; Randomization preference

1. Introduction

Patients participating in a clinical trial may have opinions about their preference to be randomized or their wish to be allocated to a particular treatment arm. Preferences could interact with outcomes in a trial when differences in characteristics of people with and without preferences are related to their prognosis, in which one treatment elicits a strong preference effect, and preference is related to outcome or through unseen deviations in trial fidelity through, for example, resentful demoralization from not being allocated a preferred treatment. Although preferences can be measured, the group effect of their strength and direction in a trial do not yet appear to be predictable [1]. For example, one trial may contain subsets of participants with strong and opposing preferences for treatment that may negate overall [1]. Participants in another similar trial that has an alternative slant in the informed consent documentation and a slightly different intervention might show a strong preference effect for that treatment.

Preferences can be counted or accounted for in several ways (Box 1). The trial can be designed so that baseline preferences for randomization (comprehensive cohort) [2] or treatment (preference design) are upheld. Preference designs seek to minimize the effect of preferences, and variations have been proposed [3,4]. Alternatively, the trial could run as usual with preferences for treatment noted yet not acted on (treatment preference elicitation or fully randomized preference trial).

The effect of preferences could be important because preferences for treatment are thought to influence outcomes [2,11,12], and differences in participants who are willing to be randomized could cause selection bias, threatening the trial's external validity [8,9]. Previous reviews have examined the effect of treatment preference elicitation in heterogeneous samples of trials, finding either equivocal [9] or detectable [5] evidence of effect on outcome. Others have

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What is new?

Key findings

- There are few visible effects of preferences on clinical outcomes in acupuncture trials, and acupuncture does not appear to be highly preferred over other treatment modalities.
- Reporting of preferences is poor, which hampers the interpretation of their effect, and the methods used to capture and analyze preferences appear suboptimal.

What this adds to what was known?

- Two previous reviews using summary data from a wide range of trials also found little evidence that preferences reported in trials interact with outcomes; however, one review using individual patient data did find evidence of effect.

What is the implication and what should change now?

- Continued monitoring of preferences in trials of other treatment areas is recommended using systematic methods of elicitation.

looked at one particular type of preference design (Zelen's) both in a range of trials [6] and studies of cancer treatments [7], with differing conclusions regarding desirability, bias, and impact.

To date, no comprehensive review has examined the spectrum of preference across one treatment modality. The number of trials of acupuncture for different conditions is increasing, but it is still a relatively novel treatment that might elicit strong preferences. Preferences are thought to particularly affect trials, in which: the participants are not blinded to treatment; one treatment is likely to be more popular than the other; trial participants are required to make participatory efforts; or the outcome is self-reported [11]. Many pragmatic acupuncture trials fall into this category, and blinded sham-controlled (usually nonpenetrated devices mimicking needles) acupuncture trials could also be vulnerable to preference effects if blinding failures occur at a rate greater than chance [11,12].

We aimed to conduct a systematic review of preferences in acupuncture studies in the following areas: the timing of preference elicitation; questions used to elicit preferences; strength of preference for randomization or treatment with acupuncture; and effect of preferences on baseline characteristics, attrition, and outcomes. Although we limited our topic area to acupuncture studies, it is anticipated that the data would be applicable to trials of complex interventions in other areas, such as physiotherapy or invasive procedures.

2. Methods

The search strategy was developed to identify abstracts and articles of randomized controlled trials (RCTs), quasi-randomized controlled trials (CCTs), and controlled cohort studies of acupuncture for the treatment of any medical or psychological condition in adults (aged $\geq$18 years). Other study designs (e.g., case–control) were excluded to improve comparability between trial arms. Studies of healthy volunteers or in which all participants were children (aged $<$18 years) were also excluded. The following databases were searched in November 2007: MEDLINE (1950 to November 2007), AMED (1985 to November 2007), CENTRAL (Cochrane Central Register of Controlled Trials), CINAHL (1982 to November 2007), EMBASE (1980 to November 2007), and the Science and Technology Proceedings with no language restriction (see web-only material Box W1 at www.jclinepi.com for search strategy). An initial screening was conducted by one reviewer (S.L.P.), and rejected titles and abstracts were rescreened by a second reviewer (J.B.). Because of resource limitations, we were not able to translate foreign language articles or contact authors for clarification of data.

Full articles were independently screened by two reviewers for including preferences. We defined this as any mention or implication of participant treatment preferences in that trial, use of a preference design, or comprehensive cohort. A citation search for authors' name of included studies was undertaken in MEDLINE in April 2010 to identify additional publications of expectation data arising from included articles dated post 2004. Data pertaining to preferences, general study data, and quality criteria were extracted by one reviewer and checked by another, resolving discrepancies by discussion. We evaluated studies on two items related to quality: the reporting and adequacy of allocation concealment [13] and blinding of outcome observer. We calculated Cohen's kappa statistic for agreement between screeners. Because of the heterogeneity across studies, a narrative synthesis is presented with central tendencies (means and medians) and variance estimates reported where available from the articles. Because of the potential differences between participants who consent to be randomized and those who do not, we present our results by study design (comprehensive cohorts, preference designs, and elicited treatment preferences in fully randomized trials).

3. Results

A total of 31 acupuncture trials (RCTs and CCTs) fulfilled the inclusion criteria (Fig. 1). Six were comprehensive cohorts (one also elicited postrandomization treatment preferences), 7 were preference designs, and 18 elicited treatment preferences only. Cohen's kappa for agreement between screeners was calculated at 0.44 (95% confidence interval: 0.23, 0.65), indicating ''moderate'' agreement [14].