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Methodological and Ethical Issues in Clinical Trials of Acupuncture

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ABSTRACT

In this review, controlled clinical trials of acupuncture are placed into five categories on the basis of the treatment with which acupuncture is compared. Methodological and ethical issues relevant to each category are discussed. *Wait list (or no treatment) controls*, which are ethically acceptable for stable, chronic conditions, assess the efficacy of acupuncture relative to the natural history of the condition but do not control for nonspecific treatment effects. *Placebo controls*, defined here as *noninvasive* procedures such as inactive transcutaneous electrical nerve stimulation (TENS) or mock needling, assess whether acupuncture has an effect beyond that of the therapeutic milieu. *Sham controls*, defined as invasive but inappropriate procedures such as shallow needling at nonacupoint sites, assess whether acupuncture efficacy depends on the style and location of needling. *Standard care comparisons* assess whether acupuncture performs at least as well as a medication, medical device, or physiotherapy. *Adjunctive care comparisons* assess the efficacy of acupuncture plus standard care relative to standard care alone. From an ethical perspective, active debate surrounds placebo and sham controls. Those who argue against these procedures consider withholding treatment to be improper. They favor the wait list and both standard care designs in which all patients receive treatment. Others argue that testing a treatment prior to demonstrating its efficacy against a placebo is equally improper. From a methodological perspective, it should also be considered that most clinical trials of acupuncture have assessed its efficacy by administering a fixed course of treatment based on biomedical diagnosis. The challenge for future trials is to design conditions that more closely mimic the delivery of acupuncture in clinical practice, as individualized treatment informed by its own diagnostic traditions.

INTRODUCTION

Methodology issues have been a major cause of the slow pace of acupuncture's acceptance by the biomedical community. The problem lies in the difficulty of creating generally acceptable models of clinical trial design for this traditional medical practice (Lewith and Vincent, 1996; Jobst, 1996; Ernst and White, 1997). This is not to say there has been a paucity of trials. There are well over a hundred controlled clinical trials of acupuncture in English-language journals alone (Eskinazi, 1996). Rather, the difficulties stem from the fact that acupuncture is rooted in a distinct physiology, with diagnostic and treatment procedures that differ strikingly from biomedicine.

As an example, it is often the case that Oriental medicine identifies several diagnostic

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subgroups for a given allopathically defined condition. A distinct set of acupuncture points is then used for treating each subgroup, with the option of further modifying the point selection to reflect an individual patient's diagnosis. In this light, it can be considered inappropriate to design acupuncture trials based solely on biomedical diagnoses, with protocols requiring all patients to be needled at the same points. Yet this is the approach that has been taken in the majority of clinical trials (Birch and Hammerschlag, 1996).

The formulaic approach to the testing of acupuncture can be seen as a logical consequence of applying Western scientific protocols initially designed for the rigorous testing of pharmaceuticals (placebo-controlled trials) or surgical techniques (sham-controlled trials). The approach aims to assess whether a certain "dosage" of acupuncture (based on number of needles, duration of treatment, and number of sessions) is therapeutic for a preestablished condition. Herein lies the dilemma. Clinical trial designs cannot easily accommodate individualized treatments, yet requiring all patients to be treated at the same set of acupuncture points may seriously underevaluate the efficacy of the treatment being assessed.

In the absence of a generally applicable trial design, a multiplicity of approaches has been attempted. Accordingly, an examination of the problems in acupuncture research needs to begin by placing clinical trials into design categories. Methodological and ethical issues relevant to each type of trial can then be addressed. Prior to beginning this analysis, it will be of interest to illustrate the current methodological state of affairs with two broad examples: one anecdotal, based on personal experience of acupuncture grants review; the other semiquantitative, based on an overview of published clinical trials of acupuncture.

In July 1993, the Office of Alternative Medicine (OAM) convened a panel to review the acupuncture research grants received in response to its initial call for proposals (Hammerschlag and Parfitt, 1994). Fifteen panel members, including Oriental medicine practitioners and researchers from within and outside the field, were assembled to review 55 grants in 3 days. Among only the first dozen grants considered were proposals to needle patients at (1) a uniform set of points based on treatment described in a standard Chinese text; (2) individualized sets of points based on trigger points; (3) individualized sets of points based on traditional Chinese medicine diagnosis; and (4) a single point based on previous experience of patients with similar symptoms. And this variation was only among the acupuncture *treatment* groups. An even greater variability was apparent from the protocols proposed for the *control* groups. Why?

First, like any treatment performed by a skilled practitioner, acupuncture can induce a placebo effect. But, unlike the readily camouflaged sugar pill, there is no similarly obvious means to disguise the intent of needling from the patient, let alone the practitioner—although, as described in a later section, there have been a number of creative attempts to solve these problems.

Second, the microtrauma resulting from piercing the skin induces a variety of physiological responses involving the microcirculation, local immune function, and neurally mediated analgesic effects (Kendall, 1989; Le Bars et al., 1991). As with the placebo effect, these nonspecific responses in *clinical practice* can significantly contribute to the healing effect produced by needling at prescribed, diagnosis-specific acupuncture points (Lewith and Vincent, 1996; Ernst and White, 1997). In contrast, in *clinical research,* the same nonspecific responses are considered as "noise," above which, especially if the sample size is small, it may be difficult to detect the "signal," with the possible result of type II errors. As will be discussed, there has been considerable debate, reflected in the use of numerous sham acupuncture procedures, as to how best to control for these nonspecific effects.

Needless to say, the large diversity of protocols outlined in the OAM research proposals led to spirited deliberations within the review panel. Because it took at least the first dozen grants to attain a reasonable degree of agreement on issues of research design, in fairness—after reviewing all 55 proposals—the panel returned to re-review the first 12.

A representative survey of published clinical

trials of acupuncture reveals that our experience in the review panel mirrored the at-large state of acupuncture research. In 1995, following the Food and Drug Administration (FDA) workshop to consider removing the "investigational" label from the acupuncture needle (Eskinazi et al., 1996), the National Academy of Acupuncture and Oriental Medicine (NAAOM) commissioned the Society for Acupuncture Research (SAR) to prepare a compendium of summaries of positive-outcome controlled clinical trials of acupuncture. A compilation of such information was envisioned as being useful for providing evidence-based credibility when promoting acupuncture to insurance companies, hospitals, and state lawmakers considering licensing legislation. Two SAR board members accepted the task, and last November, NAAOM published their summaries of 70 controlled clinical trials (Birch and Hammerschlag, 1996). As an exercise for the present article, these trials were assigned to categories defined by their research design (Table 1).

The studies were initially sorted into five categories on the basis of their control or comparison treatments. Use of an untreated control group through all ("no treatment") or part ("delayed treatment") of the study defined category 1. Remaining studies using control treatments were sorted according to whether these treatments were noninvasive (category 2) or invasive (category 3). This distinction was made because it seemed useful to apply the term *placebo* to noninvasive treatments, such as an inactive transcutaneous electrical nerve stimulation (TENS) electrode or the blunt end of an acupuncture needle, and the term *sham* to invasive treatments such as needling at shallow depths and at sites inappropriate to the treatment. Studies comparing acupuncture with a biomedical treatment, including medication, a medical device, or physiotherapy, were placed in category 4, while studies testing acupuncture as adjunctive to biomedical standard care comprised category 5.

Each of the five categories was then divided into subcategories based on variations of the control treatment. For example, four different styles of sham treatments were identified, depending on whether the needling was at the same depth as, or more superficial than the acupuncture treatment and whether the needling was performed at traditionally defined acupuncture points or at nonpoint locations. Each of the clinical trials was then assigned a place in the table on the basis of its control treatment subcategory as well as a further subtype determined by whether it used two groups (A vs. B design), two-group crossover, or more than two groups.

The diversity of control groups is readily apparent from Table 1. Within the major subtype, the A vs. B design, 43 trials were distributed among 13 subcategories. The 6 A/B crossover trials represented 4 subcategories and the 14 trials that compared acupuncture with more than 2 control or comparison treatments used more than 7 subcategories of research design. Omitted from Table 1 were trials that used additional subcategories of control or comparison groups, including single treatments of acupressure, laser irradiation or sham electroacupuncture and multiple treatments, such as sham acupuncture plus medication or TENS plus medication. Also omitted from Table 1 were 7 trials that examined the effectiveness of acupressure ($n = 6$) or moxibustion ($n = 1$).

It should be noted that bioethical issues are being increasingly raised as part of the methodological debate. While several of the control groups in Table 1 have been the focus of ethical concerns, the issues are not unique to acupuncture but apply generally to clinical trial design. A major concern, for example, involves the concept, "intent to treat."[1] On the one hand, it is argued that even though informed consent will be obtained for a trial in which patients will be randomly assigned to receive treatment or placebo, it is no longer ethically justifiable to withhold treatment for experimental purposes (Stanley, 1988; Rothman and Michels, 1994). So-called "active controls" are proposed as an alternative research design in which an experimental treatment, such as a new drug (or acupuncture), is compared with an accepted treatment, such as standard medication. The counter argument is that it is unethical to test any experimental treatment if there is no con-

[1]The meaning of the term "intent to treat" in the context of bioethics should not be confused with the different usage of the term in the context of data analysis.

TABLE 1. SURVEY OF RESEARCH DESIGNS OF TRIALS SUMMARIZED IN *ACUPUNCTURE EFFICACY: A COMPENDIUM OF CONTROLLED CLINICAL TRIALS*

Research design	*Subtype*[a]		
	A vs. B	*A/B Crossover*	*>2 groups*[b]
1. *Acupuncture vs. no treatment*			
Delayed treatment (wait-list control)	3[c]	–	3[d]
No treatment	1[e]	–	5[f]
2. *Acupuncture vs. placebo (noninvasive treatment)*			
Inactive TENS at treatment acupoints	4[g]	–	–
Noninvasive "needling" at nonpoints	2[h]	–	–
3. *Acupuncture vs. sham needling (invasive treatment)*			
Treatment depth at nonpoints	5[i]	2[j]	5[k]
Treatment depth at inappropriate acupoints	2[l]	–	–
Superficial needling at nonpoints	3[m]	2[n]	–
Superficial needling at treatment acupoints	2[o]	–	1[p]
4. *Acupuncture vs. biomedical standard care*			
Medication	11[q]	1[r]	8[s]
Medical device at treatment acu-points	1[t]	1[u]	3[v]
Medical device at injury site	–	–	2[w]
Physiotherapy	4[x]	–	–
5. *Acupunture plus standard care vs. standard care alone*			
Medication	1[y]	–	–
Physiotherapy	4[z]	–	–

[a]Studies from Birch and Hammerschlag, 1996, are sorted into five major research designs, each with three subtypes: *A vs. B* (n = 43), in which patients were assigned to one of two groups receiving either acupuncture or a control or comparison treatment; *A/B crossover* (n = 6), in which all patients received acupuncture and a control or comparison treatment; *>2 groups* (n = 14), in which patients were assigned to acupuncture or to one of two (n = 6), three (n = 6), or four (n = 2) control or comparison groups. Of the 70 trials examined, those not included in the table involved the use of only acupressure (n = 6) or moxibustion (n = 1).

[b]Based on the numbers given in footnote *a*, this column should total 38. The lower total reflects the use in the trials of study groups other than those listed in the table.

[c–z]Clinical trials assigned to each category are listed in the Appendix.

current attempt to ascertain whether it is more effective than a placebo (Rothman and Michels, 1994). Applying this "intent to treat" principle, trials in which an acupuncture groups is compared with a delayed-treatment group or to a group receiving standard biomedical care would be considered more ethical than trials using a no-treatment, placebo, or sham-control group. These issues will be discussed in more detail as each of the five categories of research design highlighted in Table 1 are examined.

WAIT-LIST CONTROLS

The use of a delayed-treatment control group is justifiable in trials of stable, chronic conditions. From a bioethical perspective, the research design is acceptable because all patients receive treatment. While a wait-list group is useful for assessing the rate of spontaneous remission, it does not control for either placebo effects or nonspecific physiological responses to needling. This trial design also does not control for possible nocebo effects (patient-engendered negative effects) in the wait-list group. Such effects, which may occur as a result of disappointment at not being assigned for immediate treatment, can contribute to between-group differences in outcomes.

Conditions for which acupuncture has been compared with wait-list controls in clinical trials include chronic low-back pain (Coan et al., 1980), chronic neck pain (Coan et al., 1982), osteoarthritis (Christensen et al., 1992), and craniomandibular disorders (List et al., 1992).

PLACEBO CONTROLS

The use of a placebo is most commonly associated with the double-blind trial design. In theory, the placebo provides a means of assessing that portion of the overall treatment effect resulting from "expectations of benefit" on the part of both the patient and the practitioner. Since, from the perspective of clinical research, positive outcomes resulting from expectations represent experimental bias and confounding data, the placebo usually plays an obligatory role at the final stage of acceptance of any pharmaceutical therapy or medical device for a given condition.

With acupuncture treatment, as briefly discussed previously, outcome is a composite of three factors: placebo effects, nonspecific physiological responses to piercing the skin, and specific responses to stimulation of the particular acupuncture points chosen for treatment. To assess placebo effects alone, a procedure must be devised that is both noninvasive and credible to the patients (Vincent and Lewith, 1995; Lewith and Vincent, 1996). One approach has been to apply a disconnected TENS electrode at or near the acupuncture treatment points. During this procedure the TENS indicator light is set flashing to reinforce the impression that an active treatment is being provided (Macdonald et al., 1983; Petrie and Langley, 1983; Dowson et al., 1985). In a three-arm trial, patients were assigned to electroacupuncture, subthreshold TENS, or dead-battery TENS under conditions where the physical therapist was blinded to whether the TENS was active or inactive (Lehmann et al., 1986). It is of interest that in the only acupuncture trial reporting on patients' assessment of mock TENS as a placebo, the two procedures were considered equally credible by acupuncture-naïve, neck pain patients (Petrie and Hazleman, 1986).

When the placebo treatment involves mock needling it is virtually impossible to blind the acupuncturist. Blinding the patients is possible, however, particularly when the trial is restricted to acupuncture-naïve patients. Furthermore, the use of blinded treatment assessors strengthens the methodological rigor of the single-blind trial. Such noninvasive, mock needling placebos have included touching the skin surface either with acupuncture needles (Jensen et al., 1979), the blunt end of the needle (Hesse et al., 1994), or a pencil-like probe (Molsberger and Hille, 1994). Alternatively, in studies where true acupuncture was administered using needles maintained within plastic guide tubes, the placebo treatment involved light tapping on the skin with an empty guide tube (Lao et al., 1995) or a blunted cocktail stick introduced through the guide tube (White et al., 1996). When possible, patients were kept from viewing the needling procedures by strategies such as selecting acupoint sites on their back or by placing gauze over their eyes. As with the use of mock TENS, it is critical to the validity of the trial to establish that patients cannot differentiate the true from the placebo treatment (Vincent, 1990). Of the five studies cited, credibility of the placebo was assessed in three (Hesse et al., 1994; Lao et al., 1995; White et al., 1996).

SHAM CONTROLS

Sham procedures have been defined in this review as the use of *invasive* but inappropriate needling. Because they closely mimic true acupuncture they readily control for placebo effects. In addition, because they are invasive, they control for a range of nonspecific physiological effects induced by needling (Table 2). Such generalized responses to needle insertion are likely to include local circulatory and immune reactions (Kendall, 1989) and the neurally mediated diffuse noxious inhibitory control that provides rapid modulation of sharp pain (Le Bars et al., 1991). The use of sham needling also enables testing one of the fundamental tenets of acupuncture: needling at specific points matters.

Using the 70 clinical trials surveyed in Table 1 as a representative sampling, it is clear that considerably more trials have used sham needling ($n = 22$) than placebo procedures ($n = 6$) as controls. It is also apparent that no consensus exists as to what the sham treatment should be. Site and depth of needling are the major variables in the choice of sham.

The use of "inappropriate" acupuncture

points (those unlikely to be beneficial for the condition being treated) offers the unique advantage of permitting a true double-blind trial in which an acupuncturist with no knowledge of the patient's condition can be told which of two sets of points to needle (Godfrey and Morgan, 1978). The disadvantage of inappropriate points, however, is the paucity of information regarding all possible effects of needling any given acupuncture point. Most studies, therefore, have opted for needling at sites near but not on traditional acupuncture points. Such nonpoint sites are identifiable by their conductivity readings that are several orders of magnitude lower than those at true points (Helms, 1987; Bullock et al., 1989).

While acupuncture is more closely mimicked when sham needles are inserted to a similar depth as the treatment needles, superficial needling is preferable in that it triggers most of the nonspecific responses to needling while minimizing the specific effects (Birch, 1995; Vincent and Lewith, 1995). Such "minimal needling," defined by Vincent and Lewith (1995) as superficial insertion at nonpoints with little manipulation, is becoming increasingly favored as the most appropriate sham control. Of the 8 studies in Table 1 that used this procedure as their sham control, 6 were performed in 1990 or later, whereas only 3 of the 14 studies using same depth needling were performed since 1990. Examples of trials using minimal needling are those for facial pain (Hansen and Hansen, 1983), migraine (Vincent, 1989), fibromyalgia (Deluze et al., 1992), and xerostomia (Blom et al., 1992). Sham needling was rated as a credible control by patients in the migraine study (Vincent, 1989).

The contribution of nonspecific effects of needling to the overall efficacy of acupuncture treatment is best appreciated by examining results of trials in which patients were randomly assigned to three groups: acupuncture, sham needling, and no treatment. In a study of dysmenorrhea (Helms, 1987), pain score was significantly reduced in the acupuncture group relative to both other groups, but sham needling outperformed no treatment. Similar findings were obtained in preliminary results of a trial of acupuncture as adjunctive treatment to antiemetic medication (Shen et al., 1997). With all women receiving the same regimen of medication, those who received sham needling experienced relief from nausea and vomiting at a level intermediate between those receiving acupuncture and those receiving no adjunctive treatment.

As discussed earlier, the use of either placebo or sham controls has raised bioethical concerns because they violate the "intent to treat" principle. One means of satisfying this concern, applicable to clinical trials of chronic conditions, is to provide genuine acupuncture to control group patients at the end of the trial period (Jobst et al., 1986).

COMPARISON TO BIOMEDICAL STANDARD CARE

Rather than using a placebo or sham-control group, many clinical trials have been designed

TABLE 2. COMPONENTS OF THE ACUPUNCTURE RESPONSE TRIGGERED BY PLACEBO OR SHAM CONTROLS

	Components of healing		
Type of treatment	*Placebo effects*	*Nonspecific effects of needling*[a]	*Specific effects of acupuncture*
Placebo (Noninvasive procedures[b])	X		
Sham (Invasive procedures[b])	X	X	
Acupuncture	X	X	X

[a]Such generalized responses to needle insertion are likely to include local circulatory and immune reactions (Kendall, 1989) and the neurally mediated diffuse noxious inhibitory control (Le Bars et al., 1991).

[b]See Table 1 and text for examples.

to compare an experimental treatment with a standard treatment. This is commonly done with a new pharmaceutical or surgical procedure, but the strategy works equally well for intertreatment comparisons. Of interest here are a variety of trials in which patients were randomly assigned to groups for acupuncture or for treatment with medication, a medical device or physiotherapy. Included in category 4 of Table 1, for example, are trials comparing acupuncture to a β-blocker for migraine prophylaxis (Hesse et al., 1994), anti-emetic medication or TENS for controlling postoperative vomiting (Ho et al., 1990), analgesic medication for renal colic pain management (Lee et al., 1992) and physiotherapy for treatment of cervical spondylosis (Loy, 1993).

In contrast to placebo or sham-controlled trials, in which acupuncture must significantly outperform the control treatment, trials using a biomedical care comparison group require acupuncture to perform only at least as well as the standard care to establish its efficacy. A corollary is that a control group may not be essential in these trials, provided that acupuncture is being compared with a pharmaceutical, medical device, or physiotherapy treatment that has been proven effective against a placebo or sham control in a prior trial. It is important to consider that a control group may, in fact, be needed because of major variations in treatment styles. In the case of trials comparing acupuncture with medication, in which needling usually involves significantly greater time and attention than treatment with medication, an acupuncture control group has been used to enhance a trial's credibility. An example is the previously cited migraine study in which patients were randomly assigned to groups receiving either placebo acupuncture plus medication or acupuncture plus placebo medication (Hesse et al., 1994).

From an ethical perspective, the merit of the intertreatment research design is that, unlike placebo or sham-controlled trials, there is an "intent to treat" all patients in the study. An additional valuable feature of acupuncture versus biomedical care trials is the potential for side-by-side comparisons not only of efficacy, but of onset, duration, side effects, quality of life, and cost effectiveness of the two treatments. Examples include a more rapid analgesic onset of acupuncture than medication for relieving renal colic (Lee et al., 1992), a greater percentage of low-back pain patients in the acupuncture than the physical therapy group able to return to their original or equivalent jobs (Gunn et al., 1980), and fewer adverse side effects from acupuncture than medication in patients treated for renal colic (Lee et al., 1992) or migraine (Hesse et al., 1994). Also, in this last study, acupuncture was as effective as metoprolol for reducing frequency and duration of migraine attacks, but was patient-rated as less effective than the β-blocker in "global effects" on their headaches.

Clinical trials comparing acupuncture with biomedical care were the focus of a recent systematic review (Hammerschlag and Morris, 1997). Of 52 studies that met inclusion criteria (trial outcome was not a selection factor), 29 were excluded for use of historical controls, experimentally induced test conditions, procedures other than acupuncture alone as the test treatment, or biomedical treatment that had not been previously proven effective under placebo-controlled conditions. The qualifying trials were evaluated on the basis of 25 criteria of good study design and reporting.

On a rating scale of "adequate," "partial," or "not attempted/not reported," only 3 of the 23 qualifying trials scored "adequate" on at least 60% of the criteria. Two of the most important criteria for intertreatment trials had widely differing scores. Randomization (to prevent practitioner or patient bias) was used/reported in 20 of the 23 trials (87%), whereas blinding of outcomes assessors (to overcome the impossibility of blinding either practitioners or patients in intertreatment trials) was reported in only 4 trials (17%). Overall, 4 criteria were rated "adequate" on at least 80% of the trials whereas 8 fell below the 20% mark. An important cautionary note implied in these generally low scores is that statistically significant differences in end points are not sufficient to guarantee credibility of results. A positive outcome can readily be questioned, for example, if the treatment assessor was not blinded to group assignment. Conversely, a negative outcome can be questioned if there is insufficient information about the acupuncture protocol because

reduced efficacy can be a result of inadequate or inappropriate treatment (Birch, 1997).

ACUPUNCTURE PLUS STANDARD CARE COMPARED TO STANDARD CARE ALONE

The last category of research design listed in Table 1 involves the evaluation of acupuncture as adjunctive care. From an ethical perspective, this trial design should be given highest marks. Whereas the appeal of A vs. B comparisons of acupuncture and biomedical care is the intent to treat all patients, the greater appeal of the A + B vs. B design is that all patients receive a treatment previously established as effective. An impetus for adjunctive trials is that a given standard care is not fully effective and the question asked is whether acupuncture may improve the outcome.

Clinical trials of this design include studies of acupuncture as adjunctive to physiotherapy for low-back pain (Gunn et al., 1980) or stroke (Naeser et al., 1992; Hu et al., 1993; Johansson et al., 1993; Sallstrom et al., 1996), and to medication for chemotherapy-induced nausea and vomiting (Shen et al., 1997) or stroke-related intracranial pressure (Zhang, 1996). It should be noted, however, that only two of these studies administered sham needling to the group receiving standard care alone (Naeser et al., 1992; Shen et al., 1997). Without such a control, it cannot be formally established that a finding of enhanced efficacy of standard care is a result of the specific acupuncture treatment, as opposed to the added attention that the treatment provides or the nonspecific effects of the needling (as discussed earlier).

A final note regarding the A + B vs. B research protocol is the value of expanding it to a three-arm design. As previously cited, preliminary results from a trial of acupuncture as adjunctive treatment to anti-emetic medication indicate that the group receiving medication plus acupuncture experienced significantly greater benefit than the group receiving medication alone (Shen et al., 1997). However, a third group in this study, receiving medication plus sham acupuncture, benefited to an intermediate extent. Comparison of adjunctive acupuncture to adjunctive sham needling provides evidence that acupuncture *per se* can be an effective complementary medicine. In addition, by comparing adjunctive acupuncture to no adjunctive treatment, the three-arm design provides a measure of the total benefit of supplementary acupuncture treatment, as it would be delivered in clinical practice.

SUMMARY AND CAUTIONARY NOTE

The phrasing of the guideline questions to the NIH Consensus Panel at the November 1997 conference on acupuncture reflected the importance of methodological issues to the outcome of that historic meeting (NIH, 1997). Of the five questions, those relevant to clinical trials asked, in effect, "Is there sufficient evidence to conclude that acupuncture is more effective than placebo?"; "Does acupuncture perform as well as standard care?"; and, "Is acupuncture an effective adjunctive treatment to standard care?" The following outline of research design issues presented at the Consensus Conference can serve as a useful summary of the present review.

- *Wait-list control*: Useful for stable, chronic conditions. Control group assesses the rate of spontaneous remission but does not provide a measure of either placebo effects or nonspecific effects of needling. Design is ethical because all patients receive treatment.
- *Placebo control (noninvasive procedures including inactive TENS and mock needling)*: Best used as a modified double-blind protocol in which patient and treatment evaluator are blinded (the acupuncturist cannot be blinded). Patient blinding should be validated. The design does not control for nonspecific effects of needling (Table 2). Ethical questions have been raised because there is no intent to treat the control group.
- *Sham control (invasive procedures including shallow needling at nonacupoint sites)*: Best used as a modified double-blind protocol (see placebo control above). Patient blinding should be validated. Sham procedures control for placebo effects as well as nonspecific effects of needling (Table 2). Ethical questions are similar to those for placebo controls.
- *Comparison with biomedical standard care (med-*

ication, medical device, or physiotherapy): To be considered effective, acupuncture needs to perform only at least as well as the standard care provided the latter has previously outperformed a placebo. Useful design for comparing onset, duration, side effects and cost effectiveness, in addition to medical effectiveness, of the two medicines. Ethical design because all patients receive treatment.

- *Adjunctive to biomedical standard care (ie, standard care with or without acupuncture)*: Best when acupuncture and sham needling are compared as adjunctive treatments. Highly ethical because all patients receive standard care.

In closing, a cautionary note should be considered when evaluating the efficacy of acupuncture from the results of controlled clinical trials. Based on methodological considerations, a case can be made that acupuncture has been underevaluated in a substantial majority of these trials. When diagnosis is framed primarily in biomedical terms and the acupuncture needling protocol is standardized, as has been the case in most acupuncture trials, the question driving these trials becomes: Is acupuncture effective when delivered as a fixed course of treatment based on biomedical diagnosis? In short, this question becomes: Is acupuncture an effective biomedical treatment? In contrast, it must be remembered that when acupuncture is delivered in clinical practice, a condition-specific subgroup of Oriental medicine diagnoses is found to underlie many biomedically defined conditions. Treatment point selection is then informed by this Oriental medicine diagnosis and is often modified to become patient-specific. Future clinical trials that test acupuncture within its own medical traditions are likely to provide a more appropriate and more clinically meaningful assessment of acupuncture efficacy than the generation of clinical trials published to date.

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REFERENCES

Birch S. Testing the clinical specificity of needle sites in controlled clinical trials of acupuncture. Proc Soc Acupunct Res 1995;2:274–294.

Birch S. Issues to consider in determining an adequate treatment in a clinical trial of acupuncture. Complement Ther Med 1997;5:8–12.

Birch S, Hammerschlag R. Acupuncture Efficacy: A Compendium of Controlled Clinical Studies. Tarrytown, New York: National Academy of Acupuncture and Oriental Medicine, 1996.

Blom M, Dawidson I, Angmar-Mansson B. The effect of acupuncture on salivary flow rates in patients with xerostomia. Oral Surg Oral Med Oral Pathol 1992;73: 293–298.

Bullock ML, Culliton PD, Olander RT. Controlled trial of acupuncture for severe recidivist alcoholism. Lancet 1989;1:1435–1439.

Christensen BV, Iuhl IU, Vilbek H, Bulow HH, Dreijer NC, Rasmussen HF. Acupuncture treatment of severe knee osteoarthrosis: A long-term study. Acta Anaesthesiol Scand 1992;36:519–525.

Coan R, Wong G, Coan PL. The acupuncture treatment of neck pain: A randomized controlled study. Am J Chin Med 1982;9:326–332.

Coan RM, Wong G, Ku SL, Chan YC, Wang L, Ozer FT, Coan PL. The acupuncture treatment of low back pain: A randomized controlled treatment. Am J Chin Med 1980;8:181–189.

Deluze C, Bosia L, Zirbs A, Chantraine A, Vischer TL. Electroacupuncture in fibromyalgia: Results of a controlled trial. Br Med J 1992;305:1249–1252.

Dowson DI, Lewith GT, Machin D. The effects of acupuncture versus placebo in the treatment of headache. Pain 1985;21:35–42.

Ernst E, White AR. A review of problems in clinical acupuncture research. Am J Chin Med 1997;25:3–11.

Eskinazi DP, Jobst K, Wootton J, eds. NIH Technology Asssessment Workshop on Alternative Medicine: Acupuncture. J Altern Complement Med 1996;2:1–256.

Godfrey CM, Morgan P. A controlled trial of the theory of acupuncture in musculoskeletal pain. J Rheumatol 1978;5:121–124.

Gunn CC, Milbrandt WE, Little AS, Mason KE. Dry needling of muscle motor points for chronic low-back pain. Spine 1980;5:279–291.

Hammerschlag R, Morris MM. Clinical trials comparing acupuncture with biomedical standard care: A criteria-based evaluation of research design and reporting. Complement Ther Med 1997;5:133–140.

Hammerschlag R, Parfitt AG. Research proposals on the clinical effectiveness of acupuncture: Guidelines and suggestions for grant writing. Am J Acupunct 1994;22:55–60.

Hansen PE, Hansen JH. Acupuncture treatment of chronic facial pain: A controlled cross-over trial. Headache 1983;23:66–69.

Helms JM. Acupuncture for the management of primary dysmenorrhea. Obstet Gynecol 1987;69:51–56.

Hesse J, Mogelvang B, Simonsen H. Acupuncture versus metoprolol in migraine prophylaxis: A randomized trial of trigger point inactivation. J Intern Med 1994;235:451–456.

Ho RT, Jawan B, Fung ST, Cheung HK, Lee JH. Electroacupuncture and postoperative emesis. Anaesthesia 1990;45:327–329.

Hu HH, Chung C, Liu TJ, Chen RC, Chen CH, Chou P, Huang WS, Lin JCT, Tsuei JJ. A randomized controlled trial on the treatment for acute partial ischemic stroke with acupuncture. Neuroepidemiology 1993;12:106–113.

Jensen LB, Melsen B, Jensen SB. Effect of acupuncture on headache measured by reduction in number of attacks and use of drugs. Scand J Dent Res 1979;87:373–380.

Jobst K, Chen JH, McPherson K, Arrowsmith J, Brown V, Efthimiou J, Fletcher HJ, Maciocia G, Mole P, Shifrin K, Lan DJ. Controlled trial of acupuncture for disabling breathlessness. Lancet 1986;ii:1416–1419.

Jobst KA. Acupuncture in asthma and pulmonary disease: An analysis of efficacy and safety. J Altern Complement Med 1996;2:179–206.

Johansson K, Lindgren I, Widner H, Wiklund I, Johansson BB. Can sensory stimulation improve the functional outcome in stroke patients? Neurology 1993;43:2189–2192.

Kendall DE. A scientific model for acupuncture. Am J Acupunct 1989;7:251–268.

Lao L, Bergman S, Langenberg P, Wong RH, Berman B. Efficacy of Chinese acupuncture on postoperative oral surgery pain. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;79:423–428.

Le Bars D, Villaneuva L, Willer JC, Bouhassira D. Diffuse noxious inhibitory control (DNIC) in man and animals. Acupunct Med 1991;9:47–57.

Lee YH, Lee WC, Chen MT, Huang JK, Chung C, Chang LS. Acupuncture in the treatment of renal colic. J Urol 1992;147:16–18.

Lehmann TR, Russell DW, Spratt KF, Colby H, Liu YK, Fairchild ML, Christensen S. Efficacy of electroacupuncture and TENS in the rehabilitation of chronic low-back pain patients. Pain 1986;26:277–290.

Lewith GT, Vincent C. On the evaluation of the clinical effects of acupuncture: A problem reassessed and a framework for future research. J Altern Complement Med 1996;2:79–90.

List T, Helkimo M, Andersson S and Carlsson GE. Acupuncture and occlusal splint therapy in the treatment of craniomandibular disorders, Part I. A comparative study. Swed Dent J 1992;16:125–141.

Loy TT. Treatment of cervical spondylosis-electroacupuncture versus physiotherapy. Med J Austr 1993;2:32–34.

Macdonald AJR, Macrae KD, Master BR, Rubin AP. Superficial acupuncture in the relief of chronic low back pain. Ann R Coll Surg Engl 1983;65:44–46.

Molsberger A, Hille E. The analgesic effect of acupuncture in chronic tennis elbow pain. Br J Rheumatol 1994;33:1162–1165.

Naeser MA, Alexander MP, Stiassny-Eder D, Galler V, Hobbs J, Bachman D. Real versus sham acupuncture in the treatment of paralysis in acute stroke patients: A CT scan lesion site study. J Neuro Rehab 1992;6:163–173.

National Institutes of Health. Acupuncture: NIH Consensus Statement. 1997 Nov. 3–5; 15(5):in press.

Petrie JP, Hazelman BL. A controlled study of acupuncture in neck pain. Br J Rheumatol 1986;25:271–275.

Petrie JP, Langley GB. Acupuncture in the treatment of chronic cervical pain: A pilot study. Clin Exp Rheumatol 1983;1:333–336.

Rothman KJ, Michels KB. The continuing unethical use of placebo controls. N Engl J Med 1994;331:394–398.

Sallstrom S, Kjendahl A, Osten PE, Stanghelle JH, Borchgrevink CF. Acupuncture in the treatment of stroke patients in the subacute stage: A randomized, controlled study. Complement Ther Med 1996;4:193–197.

Shen J, Wenger N, Glaspy J, Hays R, Elliott M, Choi C, Shekelle P. Adjunct antiemesis electroacupuncture in stem cell transplantation. Proc Am Soc Clin Oncol 1997;16:42a.

Stanley B. An integration of ethical and clinical considerations in the use of placebos. Psychopharmacol Bull 1988;24:18–20.

Vincent CA. A controlled trial of the treatment of migraine by acupuncture. Clin J Pain 1989;5:305–312.

Vincent C. Credibility assessment in trials of acupuncture. Complement Med Res 1990;4:8–11.

Vincent C, Lewith G. Placebo controls for acupuncture studies. J R Soc Med 1995;88:199–202.

White AR, Eddleston C, Hardie R, Resch KL, Ernst E. A pilot study of acupuncture for tension headache, using a novel placebo. Acupunct Med 1996;14:11–15.

Zhang Z. Acupuncture + medication versus medication alone in lowering intracranial pressure in apoplectic patients. Int J Clin Acupunct 1996;7:17–21.

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APPENDIX: REFERENCES TO CLINICAL TRIALS CITED IN TABLE 1

[c]Christensen BV, Iuhl IU, Vilbek H, Bulow HH, Dreijer NC, Rasmussen HF. Acupuncture treatment of severe knee osteoarthrosis: A long-term study. Acta Anaesthesiol Scand 1992;36:519–525.
Coan R, Wong G, Coan PL. The acupuncture treatment of neck pain: A randomized controlled study. Amer J Chin Med 1982;9:326–332.
Coan RM, Wong G, Ku SL, Chan YC, Wang L, Ozer FT, Coan PL. The acupuncture treatment of low back pain: A randomized controlled treatment. Amer J Chin Med 1980;8:181–189.

[d]Johansson A, Wenneberg B, Wagersten C, Haraldson T. Acupuncture in treatment of facial muscular pain. Acta Odontol Scand 1991;49:153–158.
List T, Helkimo M, Andersson S, Carlsson GE. Acupuncture and occlusal splint therapy in the treatment of craniomandibular disorders, Part I. A comparative study. Swed Dent J 1992;16:125–141.
Thomas M, Lundberg T. Importance of modes of acupuncture in the treatment of chronic nociceptive low back pain. Acta Anaesthesiol Scand 1994;38:63–69.

[e]Christensen PA, Noreng M, Andersen PE, Nielsen JW. Electroacupuncture and postoperative pain. Brit J Anaesth 1989;62:258–262.

[f]Dundee JW, Ghaly RG, Bill KM, Chestnutt WN, Fitzpatrick KTJ, Lynas AGA. Effect of stimulation of the P6 antiemetic point on postoperative nausea and vomiting. Brit J Anaesth 1989;63:612–618.
Ghaly RG, Fitzpatrick KTJ, Dundee JW. Antiemetic studies with traditional Chinese acupuncture: A comparison of manual needling with electrical stimulation and commonly used antiemetics. Anaesthesia 1987;42:1108–1110.
Helms JM. Acupuncture for the management of primary dysmenorrhea. Obstet Gynecol 1987;69:51–56.
Ho RT, Jawan B, Fung ST, Cheung HK, Lee JH. Electro-acupuncture and postoperative emesis. Anaesthesia 1990;45:327–329.
Tashkin DP, Bresler DE, Kroening RJ, Kerschner H, Katz RL, Coulson A. Comparison of real and simulated acupuncture and isoproterenol in methacholine-induced asthma. Annals Allergy 1977;39:379–387.

[g]Dickens W, Lewith GT. A single-blind, controlled and randomised clinical trial to evaluate the effect of acupuncture in the treatment of trapezio-metacarpal osteoarthritis. Compl Med Res 1989;3:5–8.
Ellis N, Briggs R, Dowson D. The effect of acupuncture on nocturnal urinary frequency and incontinence in the elderly. Compl Med Res 1990;4:16–17.
Macdonald AJR, Macrae KD, Master BR, Rubin AP. Superficial acupuncture in the relief of chronic low back pain. Ann Roy Coll Surg Eng 1983;65:44–46.
Petrie JP, Langley GB. Acupuncture in the treatment of chronic cervical pain: A pilot study. Clin Exp Rheumatol 1983;1:333–336.

[h]Lao L, Bergman S, Langenberg P, Wong RH, Berman B. Efficacy of Chinese acupuncture on postoperative oral surgery pain. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;79:423–428.
Molsberger A, Hille E. The analgesic effect of acupuncture in chronic tennis elbow pain. Brit J Rheumatol 1994;33:1162–1165.

[i]Bullock ML, Culliton PD, Olander RT. Controlled trial of acupuncture for severe recidivist alcoholism. Lancet 1989;1:1435–1439.
Bullock ML, Umen AJ, Culliton PD, Olander RT. Acupuncture treatment of alcoholic recidivism: A pilot study. Alcohol Clin Exp Res 1987;11:292–295.
Cahn AM, Carayon P, Hill C, Flamant R. Acupuncture in gastroscopy. Lancet 1978;1:182–183.
Jobst K, Chen JH, McPherson K, Arrowsmith J, Brown V, Efthimiou J, Fletcher HJ, Maciocia G, Mole P, Shifrin K, Lane DJ. Controlled trial of acupuncture for disabling breathlessness. Lancet 1986;2:1416–1419.
Naeser MA, Alexander MP, Stiassny-Eder D, Galler V, Hobbs J, Bachman D. Real versus sham acupuncture in the treatment of paralysis in acute stroke patients: A CT scan lesion site study. J Neuro Rehab 1992;6:163–173.

[j]Dundee JW, Ghaly RG, Fitzpatrick KTJ, Abram WP, Lynch GA. Acupuncture prophylaxis of cancer chemotherapy-induced sickness. J Roy Soc Med 1989;82:268–271.
Fung KP, Chow OKW, So SY. Attenuation of exercise-induced asthma by acupuncture. Lancet 1986;2:1419–1422.

[k]Dundee JW, Ghaly RG, Bill KM, Chestnut WN, Fitzpatrick KTJ, Lynas AGA. Effect of stimulation of the P6 antiemetic point on postoperative nausea and vomiting. Brit J Anaesth 1989;63:612–618.
Ehrlich D, Haber P. Influence of acupuncture on physical performance capacity and haemodynamic parameters. Int J Sports Med 1992;13:486–491.
Helms JM. Acupuncture for the management of primary dysmenorrhea. Obstet Gynecol 1987;69:51–56.

Sung YF, Kutner MH, Cerine FC, Frederickson EL. Comparison of the effects of acupuncture and codeine on postoperative dental pain. Anesth Analg 1977;56:473–478.
Tashkin DP, Bresler DE, Kroening RJ, Kerschner H, Katz RL, Coulson A. Comparison of real and simulated acupuncture and isoproterenol in methacholine-induced asthma. Annals Allergy 1977;39:379–387.

[l]Chang PL. Urodynamic studies in acupuncture for women with frequency, urgency and dysuria. J Urol 1988;140:563–566.
Lipton DS, Brewington V, Smith M. Acupuncture for crack-cocaine detoxification: Experimental evaluation of efficacy. J Subst Abuse Treatment 1994;11:205–215.

[m]Blom M, Dawidson I, Angmar-Mansson B. The effect of acupuncture on salivary flow rates in patients with xerostomia. Oral Surg Oral Med Oral Pathol 1992;73:293–298.
Deluze C, Bosia L, Zirbs A, Chantraine A, Vischer TL. Electroacupuncture in fibromyalgia: Results of a controlled trial. Brit Med J 1992;305:1249–1252.
Vincent CA. A controlled trial of the treatment of migraine by acupuncture. Clin J Pain 1989;5:305–312.

[n]Hansen PE, Hansen JH. Acupuncture treatment of chronic facial pain—a controlled crossover trial. Headache 1983;23:66–69.
Vincent CA. The treatment of tension headache by acupuncture: A controlled single case design with time series analysis. J Psychosomatic Res 1990;34:553–561.

[o]Haker E, Lundeberg T. Acupuncture treatment in epicondylalgia: A comparative study of two acupuncture techniques. Clin J Pain 1990;6:221–226.
Wyon Y, Lindgren R, Lundeberg T, Hammar M. Effects of acupuncture on climacteric vasomotor symptoms, quality of life, and urinary excretion of neuropeptides among postmenopausal women. Menopause 1995;2:3–12.

[p]Thomas M, Eriksson SV, Lundeberg T. A comparative study of diazepam and acupuncture in patients with osteoarthritis pain: A placebo controlled study. Amer J Chin Med 1991;19:95–100.

[q]Brattberg G. Acupuncture therapy for tennis elbow. Pain 1983;16:285–288.
Gerhard I, Postneek F. Auricular acupuncture in the treatment of female infertility. Gynecol Endocrinol 1992;6:171–181.
Hao J, Zhao C, Cao S, Yang S. Electric acupuncture treatment of peripheral nerve injury. J Trad Chin Med 1995;15:114–117.
Hesse J, Mogelvang B, Simonsen H. Acupuncture versus metoprolol in migraine prophylaxis: A randomized trial of trigger point inactivation. J Internal Med 1994;235:451–456.
Junnila SYT. Acupuncture superior to Piroxicam™ in the treatment of osteoarthritis. Amer J Acupunct 1982;10:341–346.
Lee YH, Lee WC, Chen MT, Huang JK, Chung C, Chang LS. Acupuncture in the treatment of renal colic. J Urol 1992;147:16–18.
Luo H, Jia Y, Zhan L. Electro-acupuncture vs. amitriptyline in the treatment of depressive states. J Trad Chin Med 1985;5:3–8.
Margolin A, Avants SK, Chang P, Kosten TR. Acupuncture for the treatment of cocaine dependence in methadone-maintained patients. Amer J Addict 1993;2:194–201.
Wang HH, Chang YH, Liu DM. A study in the effectiveness of acupuncture analgesia for colonoscopic examination compared with conventional premedication. Amer J Acupunct 1992;20:217–221.
Yang X, Liu X, Luo H, Jia Y. Clinical observation on needling extrachannel points in treating mental depression. J Trad Chin Med 1994;14:14–18.
Zhang W, Li S, Chen G, Zhang Q, Wang Y. Acupuncture treatment of apoplectic hemiplegia. J Trad Chin Med 1987;7:157–160.

[r]Loh L, Nathan PW, Schott GD, Zilkha KJ. Acupuncture versus medical treatment for migraine and muscle tension headaches. J Neurol Neurosurg Psychiat 1984;47:333–337.

[s]Clavel F, Benhamou S, Company-Huertas A, Flamant R. Helping people to stop smoking: Randomised comparison of groups being treated with acupuncture and nicotine gum with control group. Brit Med J 1985;291:1538–1539.
Dundee JW, Ghaly RG, Bill KM, Chestnut WN, Fitzpatrick KTJ, Lynas AGA. Effect of stimulation of the P6 antiemetic point on postoperative nausea and vomiting. Brit J Anaesth 1989;63:612–618.
Ghaly RG, Fitzpatrick KTJ, Dundee JW. Antiemetic studies with traditional Chinese acupuncture: A comparison of manual needling with electrical stimulation and commonly used antiemetics. Anaesthesia 1987;42:1108–1110.
Ho RT, Jawan B, Fung ST, Cheung HK, Lee JH. Electro-acupuncture and postoperative emesis. Anaesthesia 1990;45:327–329.
Martelete M, Fiori AMC. Comparative study of the analgesic effect of trans-cutaneous nerve stimulation (TNS), electroacupuncture (EA) and meperidine in the treatment of postoperative pain. Acupunct Electrother Res 1985;10:183–193.
Sung YF, Kutner MH, Cerine FC, Frederickson EL. Comparison of the effects of acupuncture and codeine on postoperative dental pain. Anesth Analg 1977;56:473–478.

Tashkin DP, Bresler DE, Kroening RJ, Kerschner H, Katz RL, Coulson A. Comparison of real and simulated acupuncture and isoproterenol in methacholine-induced asthma. Annals Allergy 1977;39:379–387.

Thomas M, Eriksson SV, Lundeberg T. A comparative study of diazepam and acupuncture in patients with osteoarthritis pain: A placebo controlled study. Amer J Chin Med 1991;19:95–100.

[t]Laitinen J. Acupuncture and transcutaneous electric stimulation in the treatment of chronic sacrolumbalgia and ischialgia. Amer J Chin Med 1976;4:169–175.

[u]Fox EJ, Melzack R. Transcutaneous electrical stimulation and acupuncture: Comparison of treatment for low-back pain. Pain 1976;2:141–148.

[v]Ho RT, Jawan B, Fung ST, Cheung HK, Lee JH. Electro-acupuncture and postoperative emesis. Anaesthesia 1990;45:327–329.

Martelete M, Fiori AMC. Comparative study of the analgesic effect of trans-cutaneous nerve stimulation (TNS), electroacupuncture (EA) and meperidine in the treatment of postoperative pain. Acupunct Electrother Res 1985;10:183–193.

Wang L, Wang A, Zhang S. Clinical analysis and experimental observation on acupuncture and moxibustion treatment of patellar tendon terminal disease in athletes. J Trad Chin Med 1985;5:162–166.

[w]Johansson A, Wenneberg B, Wagersten C, Haraldson T. Acupuncture in treatment of facial muscular pain. Acta Odontol Scand 1991;49:153–158.

List T, Helkimo M, Andersson S, Carlsson GE. Acupuncture and occlusal splint therapy in the treatment of craniomandibular disorders. Part I. A comparative study. Swed Dent J 1992;16:125–141.

[x]Ahonen E, Hakumaki M, Mahlamaki S, Partanen J, Riekkinen P, Sivenius J. Acupuncture and physiotherapy in the treatment of myogenic headache patients: Pain relief and EMG activity. Adv Pain Res Ther 1983;5:571–576.

Carlsson J, Fahlcrantz A, Augustinsson LE. Muscle tenderness in tension headache treated with acupuncture or physiotherapy. Cephalalgia 1990;10:131–141.

Loy TT. Treatment of cervical spondylosis—electroacupuncture versus physiotherapy. Med J Australia 1983;2:32–34.

Raustia AM, Pohjola RT, Virtanen KK. Acupuncture compared with stomatognathic treatment for TMJ dysfunction. Part I: A randomized study. J Prosth Dent 1985;54:581–585.

[y]Aglietti, Roila F, Tonato M, Basurto C, Bracarda S, Picciafuoco M, Ballatori E, Del Favero A. A pilot study of metoclopramide, dexamethasone, diphenhydramine and acupuncture in women treated with cisplatin. Cancer Chemother Pharmacol 1990;26:239–240.

[z]Gunn CC, Milbrandt WE, Little AS, Mason KE. Dry needling of muscle motor points for chronic low-back pain. Spine 1980;5:279–291.

Hu HH, Chung C, Liu TJ, Chen RC, Chen CH, Chou P, Huang WS, Lin JCT, Tsuei JJ. A randomized controlled trial on the treatment for acute partial ischemic stroke with acupuncture. Neuroepidemiology 1993;12:106–113.

Johansson K, Lindgren I, Widner H, Wiklund I, Johansson BB. Can sensory stimulation improve the functional outcome in stroke patients? Neurology 1993;43:2189–2192.

Sallstrom S, Kjendahl A, Osten PE, Stanghelle JH, Borchgrevink CF. Acupuncture in the treatment of stroke patients in the subacute stage: A randomized, controlled study: Compl Ther Med 1996;4:193–197.