Considerable intellectual and practical effort has been expended on designing and evaluating placebo controls in acupuncture studies. Somewhat less attention has been paid to the question: Why use a placebo in a randomized trial of acupuncture? This is partly because placebo controls have generally been seen as an inherent part of randomized trial methodology. As a result, most acupuncture trials have included a placebo-control group. A large number of different placebo techniques have been used in these trials. The design and choice of placebo techniques has typically depended on purely theoretical considerations, without empirical validation of physiological inactivity and psychological credibility. Principles can be developed for deciding whether to use placebo or another form of control in a randomized trial. These include issues of ethics, practicality and methodology. Such principles apply regardless of the intervention; they can and should be applied to acupuncture research.
Considerable intellectual and practical effort has been expended on the issue of placebo controls in acupuncture studies. Researchers have designed a variety of acupuncture placebos, developed scales to measure their credibility, and then compared and contrasted different techniques in review papers. Somewhat less attention has been paid to the question: Why use a placebo in a randomized controlled trial (RCT) of acupuncture? Accordingly, the issue of when it is appropriate to use and avoid acupuncture controls has been insufficiently explored.

In this article, I describe the debate on placebo in acupuncture trials and give an overview of different placebo techniques. I then discuss the rationale of choosing placebo as a control group, both in general and with specific reference to acupuncture research. I conclude by giving examples of specific trials in which a decision had to be made whether to use placebo control. On a terminological note, I avoid the semantic minefield of what constitutes a “placebo” or a “placebo effect” by using an operational definition: For the purposes of this article, placebo is an intervention used in a clinical trial that is administered with the intention of mimicking some other intervention so that an unbiased comparison can be made.

THE DEBATE ON PLACEBO IN ACUPUNCTURE TRIALS

For many years, there has been an active debate about the methodology of research in complementary and alternative medicine (CAM) (Vickers, 1996a). Methodological issues in acupuncture research need to be placed in the wider context of this debate. Many of the key writers on acupuncture research methods (Vincent & Lewith, 1995) are best known for their contribution to CAM research in general (Lewith & Aldridge, 1993). Moreover, acupuncture has often been a key issue in papers on CAM research methodology (Vickers et al., 1997).

To understand current perspectives on the role of placebos in randomized trials of acupuncture, it is necessary to understand that both proponents and opponents of RCTs in CAM have generally seen placebo controls as an inherent part of RCT methodology. This is best illustrated when commentators use the terms “RCT” and “double blind trial” interchangeably (double blinding generally implies...
placebo control in CAM research). For example, one prominent critic of conventional research methodology has complained that “there is increasing pressure on alternative therapy to document effects by using the randomized, double-blind controlled clinical trial (in the following, just called the controlled clinical trial)” (Launsø, 1994). Similarly, Dossey (1995) referred to conventional medical research as “double blinding” and described researchers as “double blinders.” Proponents of RCTs in acupuncture similarly conflate placebo control and randomization. In a review article, Vincent and Lewith (1995) stated that “the major problem [of acupuncture research] is the definition of an appropriate placebo control” (p. 199). Moreover, a section entitled “Solutions to the Problem of the Acupuncture Control” only lists placebo acupuncture techniques.

Conducting an acupuncture RCT has thus generally been taken to mean randomizing patients to real or placebo acupuncture. Accordingly, most RCTs of acupuncture have incorporated placebo control. I randomly sampled 100 acupuncture RCTs from the registry of controlled trials of the Complementary Medicine Field of the Cochrane Collaboration (Ezzo, Berman, Vickers, & Linde, 1998). Trials conducted in Europe or North America that were published with an abstract were eligible; trials comparing different acupuncture techniques were excluded. Of the study sample, an overwhelming majority of trials (79%) included a placebo control group.

AN OVERVIEW OF PLACEBO TECHNIQUES USED IN ACUPUNCTURE RCTS

Using figures from the Cochrane Collaboration registry, it can be calculated that there have probably been more than 300 RCTs of acupuncture that incorporated placebo control. There are no standard methods for acupuncture placebo, so a wide range of different techniques has been used. A comprehensive review of acupuncture placebos is beyond the scope of this article. Following is a selection of the most common and important techniques.

Needling of true acupuncture points that are inappropriate for the condition being studied. In a study of asthma, for example, Dias, Subramaniam, and Lionel (1982) randomized patients to receive acupuncture at one of two sets of points. Patients in the acupuncture group
received an active treatment formula; placebo controls received treatment at points thought to be inactive for pulmonary disease. The advantage of this technique is that it is a highly credible placebo: The patient’s experience of needling at appropriate and inappropriate locations will be almost identical, and patients are unlikely to know which are the verum points. The disadvantage of this method is the possibility that the placebo treatment is actually active. As there are disagreements in traditional Chinese medicine about treatment practices, a point described as inactive for a particular condition in one textbook may be part of a treatment formula in another. Indeed, the asthma trial of Dias has been criticized on exactly these grounds (Jobst, 1995). Moreover, even if acupuncturists were currently to agree about the function of different acupuncture points, it is probable that they do not have a complete understanding of the effects of all treatment formulae. Just as in conventional medicine it has been discovered that a pain drug (aspirin) can treat heart disease and that antimalarials can be effective for rheumatoid arthritis, so it may be that particular formulae of acupuncture points have unexpected effects.

Needling of nonacupuncture points. Gaw, Chang, and Shaw (1975), for example, randomized osteoarthritis patients to receive acupuncture at true points or at those away from classical acupuncture points. The advantages and disadvantages of this method are similar to needling inappropriate points: The technique is likely to be a reasonably credible placebo but may have at least some physiologic activity. This is particularly true in pain, as any form of needling is likely to have an analgesic effect through counterirritation and possibly endorphin release. In conditions in which counterirritation and endorphins do not contribute to a treatment effect—nausea would be an example—needling of nonacupuncture points appears to be an effective placebo (Vickers, 1996b).

Noninsertion of needles. Some researchers have rubbed (Borglum-Jensen, Melsen, & Borglum-Jensen, 1979) or touched (Junnila, 1982) needles to the skin or tapped on a guide tube (Lao, Bergman, Langenberg, Wong, & Berman, 1995; White, Eddleston, Hardie, Resch, & Ernst, 1996). These methods are physiologically inactive and, if used carefully, feel similar to actual needle insertion. However, to maintain blinding, either the acupuncture loci have to be out of the
line of sight of the patient or the patient has to be blindfolded, a rather artificial step that may cause compliance problems over the course of a long-term trial.

Sham acupressure. Some RCTs have tested acupressure devices such as “seabands,” an elasticized wristband that puts pressure on an acupuncture point indicated for nausea. These can be deactivated by removing the plastic stud situated at the acupuncture point (Barsoum, Perry, & Fraser, 1990). Although probably credible and of moderate physiologic activity, such devices clearly have only limited application.

Sham electrical stimulation. Transcutaneous electrical nerve stimulation (TENS) is a treatment for pain in which a low-intensity electric current is applied to the skin as a form of counterirritation. Trials of this intervention have often used a control known as “mock TENS”: A TENS machine is set up in the normal way but no current passes through the electrodes; patients are told that they are receiving a “subliminal” level of stimulation. Mock TENS has been used as the control in several acupuncture trials (Axelsson, Andersson, & Gu, 1994; Dowson, Lewith, & Machin, 1985). It undoubtedly has no physiologic activity, but questions must be raised about its credibility. Even if patients think that mock TENS might be an effective form of treatment, it is clearly distinguishable from acupuncture. One corollary is that consent documents may need to be worded in a misleading manner.

Minimal acupuncture. A technique developed by Vincent (1989) for a well-known trial of acupuncture for migraine, minimal acupuncture involves superficial needle insertion at points away from classical acupuncture or trigger points. The technique is designed to provide only a minimal physiologic stimulus, but because it involves actual needle insertion, the technique has good credibility.

Placebo needles. Possibly the most sophisticated acupuncture placebo to date is the placebo needle of Streitberger and Kleinhenz (1998). This is a blunt-tipped needle that moves inside its handle. Accordingly, when it is pressed against the skin, the patient feels a slight prick and sees the handle of the needle moving towards the skin.
as if the needle has been inserted. However, the needle does not penetrate the skin and instead moves upward inside the handle (see Figure 1). The placebo needle has low physiologic activity (especially if placed away from true points) and high patient credibility. It has been successfully implemented in an RCT (Kleinhenz et al., 1999). Park, White, Lee, and Ernst (1999) have developed a similar needle. There are several disadvantages to placebo needles. The primary problem is that the needle requires a device to keep it in place: The Park needle, for example, uses a guide tube that attaches to the skin. This device must also be used in the verum group to maintain blinding. Not only is it very time consuming to attach the devices, but some acupuncturists complain that they interfere significantly with needling technique. It is possible that using placebo needles in a trial may therefore lessen the effect of verum treatment.

**CONTROLS WITHOUT PLACEBO**

There are two general categories of control other than placebo: no treatment and active control. “No treatment” generally means “no additional treatment.” Patients receive clinical care as though they were not in the RCT, but they receive no additional care because they
are in the RCT. Conversely, in an active control trial, patients not random-ized to acupuncture received another treatment that they might not have received if they were not trial participants. For example, compare two trials of acupuncture of chronic headache. In both trials, patients received normal clinical care for headache, including analge-sics and prophylactic medication for some migraine patients. In a no-treatment trial in progress (Vickers, Rees, Zollman, Smith, & Ellis, 1999), patients are randomized to receive acupuncture plus care from their primary care physician or primary care alone. In the active-control trial of Carlsson, Augustinsson, Blomstrand, and Sullivan (1990), patients were randomized to receive either acupuncture or a series of physiotherapy treatments including relaxation, massage, TENS, cryotherapy, and coping techniques.

**EMPIRICAL VALIDATION OF PLACEBO TECHNIQUES**

An ideal acupuncture placebo must be biologically inactive. It would, for example, have no effect on a sleeping or unconscious patient. It must also be psychologically credible, meaning that patients believe that the technique could be effective and will not be able to distinguish it from real acupuncture. In the overview above, I discussed credibility and biological activity by making educated guesses. This is common practice in review articles. However, methodologies can and should be investigated empirically.

The credibility of acupuncture placebos can been assessed used a “credibility of treatment rating scale” (Vincent & Lewith, 1995). Patients are asked to answer four questions (see Table 1) on a 5-point, Likert-type scale that ranges from strongly disagree to strongly agree. As answers to these questions are confounded by treatment effects—for example, if a course of acupuncture relieves pain, a patient is likely answer question 2 more positively—credibility questionnaires are normally given early on in treatment. Patients can also be asked whether they thought they were receiving true acupuncture or not, and why, at the end of the study.

Numerous acupuncture RCTs have formally assessed credibility using a credibility assessment questionnaire (Bayreuther, Lewith, & Pickering, 1994; Kleinhenz et al., 1999; Vincent, 1989). In each of the trials, scores on the credibility scale were compared between groups
and the placebo treatment declared “credible” when no statistically significant difference was found. There are several problems with this approach. First, sample sizes have been small (ranging from 15 to 25 per group), and statistical analyses may therefore have been under-powered. Second, hypothesis testing does not seem an appropriate statistical approach. The question should not be: Is the placebo credible? If so, then we’re fine; if not, throw away the results. Rather, we should ask: How much might differences between groups be attributed to differences in credibility of treatment techniques? As a result, credibility might best be incorporated into a multivariate model to produce an adjusted estimate of treatment effects.

At the time of writing, there has been little research on the biological activity of placebo acupuncture techniques. It is often assumed that if both groups improve in a placebo-controlled acupuncture RCT, then the placebo arm must have been active (Jobst, 1995). This is an unwarranted conclusion: Patient improvements in such trials may be due to a number of factors, including placebo effects, cointerventions, or regression to the mean. Possibly the only original research is a meta-analysis of 127 clinical trials in which the sham technique involved needle insertion (Sanchez Aranjo, 1998). The primary question concerned whether needle placement in the placebo group was in the same dermatome as verum treatment. The authors claim that trials in which placebo involved needling far from the active points were more likely to have positive results. This was explained in terms of counterirritation. Although questions might be raised about the use of a univariate analysis that did not incorporate variables such as sample size, indication, and country of publication (Vickers, Goyal, Harland, & Rees, 1998), this article provides empirical evidence for choice of needle location in sham trials.
WHY USE PLACEBO CONTROLS IN AN RCT?

In an extensive review of the literature, Anton de Craen and myself examined a number of journal articles and textbooks to look for reasons to use placebo controls in clinical trials of any intervention (Vickers & de Craen, 2000). We found two reasons: facilitating blinding and controlling for the placebo effect. We pointed out that although the importance of blinding was well understood, the importance of controlling for the placebo effect was insufficiently argued: Methodologists seem to take it as obvious that the placebo effect should be eliminated in clinical trials and did not explain further. As it happens, there are good reasons to control for the placebo effect in RCTs, even though these have never been made explicit in the literature. First, it is worth asking whether certain therapies have more than placebo action to plan research strategically. For example, research comparing different dosages and formulations of an intervention (be that aspirin or acupuncture) are not appropriate until it has been shown, in a placebo-controlled trial, that dosage and formulation could have anything to do with the intervention’s therapeutic effect. Second, the size of the biological effect of an intervention arguably is more stable than that of its placebo component. The psychological effects of a treatment are likely to vary considerably depending on the outlook of the individual patient and clinician, current therapeutic fashions, media hype, and so on.

De Craen and I also discussed reasons to avoid placebos in clinical trials. The first considerations are feasibility, ethics, and practicability. It is not feasible to design credible placebos for many interventions—plastic surgery would be an obvious example. It is unethical to give a placebo if this would cause undue risk, discomfort, or inconvenience to a patient or if a patient was thereby denied care of proven value. With respect to practicability, it is widely thought by clinicians that patients do not like placebos and that it is more difficult to recruit patients to placebo-controlled trials. Indeed, there is direct empirical evidence that patients are less likely to agree to participate in a hypothetical trial if it involves a placebo arm (Welton, Vickers, Cooper, Meade, & Marteau, 1999).

There are also methodological reasons to avoid placebos in randomized trials. First, placebo-controlled trials may interfere with accurate estimation of effect size. This is because such trials measure
only the specific effect of treatment: In the case of therapies for which the placebo component of the treatment effect is large, and acupuncture might be a good example, placebo-controlled trials may show only a small effect size even when the total effect, including placebo, is of significant clinical value (see Figure 2). Second, placebo-controlled trials may interfere with nonspecific aspects of treatment. There is evidence that both clinician confidence and patient expectation are linked to improved outcome (Gryll & Katahn, 1978; Skovlund, 1991; Thomas, 1987). It seems likely that a placebo-controlled trial will reduce both clinician confidence and patient expectation: It is difficult to give or receive acupuncture with enthusiasm and maintain blinding. Third, placebo-controlled trials do not inform real decisions. Clinical practice does not normally involve a decision between giving a treatment or a placebo. Typically, the decision that needs to be made is which of several treatments should be given or whether a treatment is preferable to no intervention. It is this second set of choices that should therefore determine the control groups in clinical trials. For instance, knowing that antidepressant A is better than placebo and that antidepressant B is also better than placebo may be useful, but it does not help a psychiatrist choose which drug to prescribe: A randomized trial comparing the two drugs is required.
WHY USE PLACEBOS IN ACUPUNCTURE TRIALS?

The principles developed by de Craen and myself are directly applicable to acupuncture research. The issue of feasibility is not applicable: Suitable acupuncture placebo techniques have been developed. With respect to ethics, acupuncture does not involve significant risk or discomfort. It is unlikely that administration of an acupuncture placebo would ever require, or be seen to involve, withdrawal of care already proven effective. The issue of ethics in placebo-controlled trials in acupuncture therefore turns on whether placebo control would cause undue inconvenience to patients. A good example of this, involving cancer patients, is described below. Practicability is as much an issue in acupuncture research as in any other area for RCTs. A primary consideration is the sample size relative to the available eligible population; see the example of shoulder pain below.

The issue of controlling for the placebo effect is more complicated. For the sake of simplicity, I will assume that it is important to investigate whether placebo completely explains acupuncture and, moreover, that a demonstration that acupuncture is not only a placebo is a prerequisite for RCTs without placebo control. What is unclear is the degree to which such a demonstration is specific to a particular condition or disease. If one accepts that acupuncture has been demonstrated to have specific effects in at least some conditions, such as dental surgery pain (Ernst & Pittler, 1998) or postoperative nausea (Lee & Done, 1999; Vickers, 1996b), can one conclude that “acupuncture is not a placebo” and therefore conduct trials without placebo controls in any condition, including, say, fatigue or eczema? Or can one only conclude that “acupuncture is not a placebo in postoperative nausea and dental surgery pain” and that trials in other conditions must have placebo controls? Or might one be slightly more liberal and say that “acupuncture is not a placebo in pain”? These questions require further elucidation.

Dealing with the remaining methodological issues is essentially a matter of balance. RCTs with placebo controls ease blinding and therefore increase internal validity but are less applicable to clinical practice. Trials without placebo controls have better practical applicability but are more prone to bias. Researchers need to decide on a case-by-case basis whether the risks of bias outweigh the advantages of practical application or vice versa.
PRACTICAL EXAMPLES OF DECISIONS ABOUT PLACEBO IN ACUPUNCTURE RCTS

To illustrate the principles discussed above, I provide examples from my personal experience of three acupuncture RCTs in which a decision had to be made whether to administer placebo to a control group.

Acupuncture for chronic headache in primary care. This trial aims to assess the effects of acupuncture on pain, medication, and quality of life in primary care patients with chronic headache, predominantly migraine. The trial also incorporates a cost-effectiveness component. Commissioned by the UK National Health Service, the overall aim of the trial is to determine whether acupuncture services should be expanded or curtailed. Given the practical orientation of the trial, it was clear early on that we would not use placebo controls. This approach seems justified because trials have been published that show differences between acupuncture and placebo for headache (Melchart et al., 1999). We assumed that a patient trying a new and somewhat unusual therapy for a chronic and refractory condition—most of the patients in the trial have had a chronic headache complaint for more than 20 years—would experience some nonspecific benefit, and we wanted to incorporate this in our measure of treatment effect. After all, this benefit would be experienced by patients in everyday clinical practice outside the context of the trial. Moreover, we predicted that, in terms of resource use, acupuncture would have a substitution effect: Acupuncture might meet a patient’s need for care and result in fewer physician consultations; this effect would not be apparent in a placebo-controlled trial in which patients were unsure of whether they were receiving real treatment. Accordingly, this trial randomizes patients to a policy of “use acupuncture” or one of “avoid acupuncture” and no placebo is used.

Acupuncture for shortness of breath in cancer patients. Shortness of breath is a common and distressing problem for patients with advanced cancer. Acupuncture is an appealing modality because of its simplicity and lack of toxicity. There is, moreover, some evidence that acupuncture is of benefit in pulmonary disorders (Jobst, 1995) and an uncontrolled trial showing effectiveness in a palliative care population (Filshie, Penn, Ashley, & Davis, 1996). Because existing research in
this area is very limited, the trial’s overall aim is a “proof of principle”: Can we demonstrate that acupuncture has effects on breathlessness in this population? As such, we plan to evaluate breathlessness before and after a single treatment session. Our outcome measure is a subjective rating scale because the sensation of cancer-related breathlessness correlates poorly with objective measures of lung function. Accordingly, we decided on a placebo-controlled trial using the placebo needle technique. A single acupuncture treatment cannot be seen as an undue inconvenience, especially to a hospitalized population. Placebo control is therefore ethical and is unlikely to impact recruitment rates significantly.

*Acupuncture for shoulder pain after neck dissection.* Shoulder pain and dysfunction is common after surgery for head and neck cancer. It was immediately obvious to us that any methodological advantages of placebo control would be outweighed by considerations of ethics and practicality: the practitioners expect to give about eight sessions of treatment; the trial is set at a large cancer center in the middle of a major city; the patient group is predominantly elderly with a median survival of about 5 years. Asking such a group of patients repeatedly to spend considerable travel time to receive a treatment known to be of minimal benefit is ethically dubious. Moreover, it is probable that many patients would not consent to the trial given the possibility of a placebo, a serious consideration given that the patient population is limited. Moreover, we are confident that a trial without placebo control is scientifically justified. A very rigorous trial using the placebo needles technique has reported acupuncture to be superior to placebo for shoulder pain and dysfunction (Kleinhenz et al., 1999). Moreover, the outcome measure we plan to use incorporates objective measures (e.g., range of motion) that will be assessed by a researcher blinded to treatment allocation.

**CONCLUSION**

Placebo control has long been seen as an inherent part of RCTs on acupuncture. The rationale for using placebo in any particular trial has rarely been made explicit. I have argued that there are a variety of options for a control group in an acupuncture RCT and that the reasons
for choosing between them must be carefully explained. The decision whether to use placebo control can be based on ethical, practical, and methodological criteria that are applicable to RCTs generally, regardless of intervention.

REFERENCES


