Reflections on the German Acupuncture studies

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Abstract

The author discusses the recent German acupuncture trials showing how there remain difficulties in understanding their results. Among these are unresolved questions about the acupuncture/sham acupuncture interventions, and the issue of whether their results can be generalised outside of the practice of acupuncture as an adjunctive treatment by physicians.

Clinical research into acupuncture can be a critical aspect of how acupuncture is accepted by society. A number of large controlled trials of acupuncture have been undertaken in Germany, some of which have been recently published [Diener et al. 2006, Linde et al. 2005, Melchart et al. 2005, Scharf et al. 2006, Witt et al. 2005]. Several of these studies are perhaps the largest controlled trials to date of acupuncture [Haake et al. 2003, Streng 2007]. It is thus important to fully understand the results and their implications. Trials of acupuncture have been plagued by problems in the past, making interpretation of their results often difficult. Below I discuss how problems with these large trials also make such interpretation difficult.

When clinical research studies are undertaken it is important to know why the studies were done and for whom. Sometimes the reasons and target audience for a study become confused as researchers try to answer different questions for different reasons in the same study. Additionally, in acupuncture trials there have been calls for many years to ensure that the tested treatment is valid and that an appropriate control is used, with various recommendations about study design requirements depending upon the type of question and study. It is my contention that these big German acupuncture studies on low back pain, migraine, tension headache and osteoarthritis of the knee raise many questions and give rise to contradictory interpretations of results, lingering controversies and unresolved questions.

Why were the studies done? Acupuncture has historically been paid for by the social insurance system in Germany, provided that it is administered by a physician who meets the minimum training required by the association the doctor is a member of. There have been as many as 20,000-50,000 physicians using acupuncture in their practices in Germany as a result of this [Streng 2007]. The so-called GERAC studies and those done through collaboration between Munich and Berlin based research groups (ART studies) were initiated because of a desire to maintain national insurance coverage for acupuncture in Germany [Ernst 2004, Haake et al. 2003]. The social insurance system had declared acupuncture of questionable effectiveness and stated their intention to stop paying for it. In response to this, negotiations between the physician acupuncture groups and these authorities decided that acupuncture could still be paid for provided the patient was being treated for one of four medical conditions and that the patient was enrolled in a trial of acupuncture for that condition. The four medical conditions that were judged to have a promising evidence base were low back pain, migraine, tension headache and osteoarthritis of the knee [Stux G, personal communication, Molsberger A, personal communication]. But even this is somewhat controversial. For example, one German physician reports participating in an early meeting about the trials where the stated reason for the trials was quite different: the insurance companies wanted to make compensation for acupuncture treatments part of a package, resulting in significantly less payment per treatment for the physician. Many physicians did not want this and, after negotiations, these studies were the result [Prost C, personal communication]. Further, the judgment about which four medical conditions to focus on is also somewhat controversial. When these four medical conditions were chosen because they had sufficient evidence to warrant further investigation for their inclusion in future insurance reimbursement, the clinical trial evidence for acupuncture had drawn different conclusions. At that time only two medical conditions (nausea and vomiting and post operative acute dental pain) had demonstrated treatment effectiveness in trials [Acupuncture 1998, Birch et al. 2004, BMA 2000], neither of which has been included in either trials or the new insurance coverage in

Germany. Several other conditions showed similar levels of positive evidence such as tempero-mandibular disorder, stroke rehabilitation, fibromyalgia [Birch et al. 2004] yet these were not included in the German studies. At the time of these discussions in Germany, systematic reviews had drawn contradictory conclusions regarding osteoarthritis of the knees, low back pain and migraine, with single studies drawing tentative positive conclusions, but other studies not, while the evidence for tension headache has lagged behind those three [Birch et al. 2004]. The decision of what conditions to focus on have been made partly on scientific grounds and partly socio-political grounds.

There are clear study designs for answering questions that arise on socio-political grounds. Typical questions and models are: How effective is acupuncture compared to standard care? [e.g. Carlsson, Rosenhall 1990]. How effective is acupuncture in addition to standard care compared to standard care? [e.g. Hu et al. 1993]. How effective is the offer of acupuncture compared to not offering it? [e.g. Eisenberg et al. 2005, Vickers et al. 2004]. How cost effective is acupuncture? [Ratcliffe et al. 2006, Wonderling et al. 2004]. These questions are of particular socio-political interest and compare acupuncture to no treatment or a standard treatment [Thomas, Fitter 2002].

The German federal committee that decided on these studies required the inclusion of sham arms in the trials [Streng 2007] which answers a different type of question: how effective are the active ingredients of acupuncture treatment? This kind of question is generally thought to be of interest to academics [Haselen 2005] and uses a sham comparison design intended to control for placebo effects [Thomas, Fitter 2002]. This is important because the use of the acupuncture versus no treatment or standard treatment has been widely used outside of Germany in reimbursement related trials in the US and UK [Cherkin et al. 2001, Eisenberg et al. 2005, Thomas et al. 2006, Vickers et al. 2004, Wonderling et al. 2004] and is usually thought to be the preferred design for this kind of question [Thomas, Fitter 2002]. The GERAC and ART studies ended up using a three-arm design where acupuncture was compared to sham acupuncture and a wait-list or standard therapy. They tried to address scientific and socio-political questions at the same time. Unfortunately the requirements of the two study designs, acupuncture versus sham acupuncture and acupuncture versus no or standard treatment are quite different. In normal clinical studies of drugs, these are not such huge issues, but in acupuncture studies, where design issues are far more complex, these designs do not fit well, if at all, together. In the acupuncture versus no or standard therapy design, the acupuncture can be more natural, less constrained and as real-world as possible, with minimal limitations on the techniques that are applied and no concern about interactions between the therapist and his staff with the patient [Thomas, Fitter 2002]. In the acupuncture versus sham comparison, studies tend to a very constrained model with more rigid treatment protocols and complex requirements to maintain the blinding [Thomas, Fitter 2002]. They also have to pay considerable attention to the interactions between patient and therapist and his staff so that they can limit and attempt to control for the non-specific effects that arise in clinical practice [Birch 2004, Lewith, Vincent 1996, Margolin et al. 1998, Vincent, Lewith 1995]. These are contradictory approaches for a study. Naturally, the researchers conducting these studies attempted a compromise, thereby introducing potentially fatal flaws and leaving us with difficulty in interpreting the results. For example, the ART study on tension headache was proclaimed to be a success for acupuncture since both the acupuncture and sham were significantly more effective than standard therapy [Melchart et al. 2005], and similarly for the ART migraine study [Linde et al. 2005]. On the other hand, others outside of Germany have proclaimed these studies very negative for acupuncture since acupuncture was not more effective than the sham [Ernst 2004, Henderson 2005]. On the surface it seems that both interpretations are correct since the first is related to the more socio-political insurance question and the second to the more academic question [Haselen 2005].

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However, appearances are deceptive. The second major problem with these studies lies in the question: what is acupuncture? This is a complex question as its practice varies in different countries and among different traditions and practitioners [Birch Felt 1999, Birch, Kaptchuk 1999, MacPherson, Kaptchuk 1997]. Sometimes it is used as a stand-alone complete medical system, sometimes as part of a complete medical system alongside, for example, herbal medicine, and sometimes it is used simply as a technique, added by medical personnel to their treatment toolbox [Birch, Felt 1999]. The training requirements for acupuncture vary considerably according to who is practising it, in what context and as part of what overall system of

health care. This makes it quite difficult to generalise results of acupuncture practice in one situation to practice in other situations. In some countries, such as China, the US, Japan and parts of Australia, acupuncture education is regulated by government established or approved agencies. There are minimum standards of education required for different kinds of practitioners. In other countries regulation of training is more internally controlled: to join organisation X one must meet its minimal educational requirements after which one can enjoy the benefits of being a member of that organisation, for example insurance reimbursement of treatment. This is the situation for acupuncture when practised by physicians in Germany.

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The World Health Organisation in consultation with numerous international acupuncture organisations (medical and non-medical) developed international educational guidelines for acupuncture [WHO 1999]. For any non-physician to practise acupuncture they recommend a minimum of 2,500 hours of study (including 1000 hours of biomedical studies). For a physician who wants to work primarily as an acupuncturist they recommended a minimum of 1,500 hours of acupuncture study and for physicians who want to use acupuncture techniques in their medical practice, they recommend not less than 200 hours of acupuncture study [Moir 2007a]. Of course these are guidelines only, but they are relevant when we look at how acupuncture was tested in the German studies, the probable training of the practitioners in these clinical trials and how well these results generalise to the practice of acupuncture elsewhere.

Up until a few years ago in Germany there was a general agreement that for physicians to join one of the major acupuncture organisations and get insurance reimbursement, a minimum of 130 hours of acupuncture education was required. Over the last years this number was increased in some groups to 350 hours [Stux G, personal communication], more recently called the a-level and b-level licenses [Streng 2007]. But the issue of the number of hours of basic training in acupuncture required by organisations has been contentious. Understandably many would rather do the minimum necessary since they only use acupuncture occasionally as an auxiliary technique in their medical practice. It is thus rather convenient for those arguing for less hours of training that the acupuncture did not outperform the sham acupuncture as it supports their argument. Did this issue play any role in the trials and how the participating physicians performed their treatments?

The various studies conducted in Germany recruited physicians from among the professional organisations to perform the acupuncture. In the GERAC low back pain study, as many as 50 physicians in private practice were recruited [Haake et al. 2003], a similar number were recruited for the GERAC migraine study [Stux G, personal communication] and 320 for the knee osteoarthritis study [Scharf et al. 2006]. The basic training of many of these will have been similar to or less than that recommended by the WHO for a physician who wants to use acupuncture as an auxiliary technique within their medical practice. Further, some of the studies attempted to provide 'TCM' type acupuncture [e.g. Haake et al. 2003, Stux 2007]. The minimum training programmes to learn TCM acupuncture involve many hundreds of hours of study. Acupuncture programmes in the UK and Canada are a minimum of 1,200 and 1,900 hours of study respectively, while acupuncture and TCM programmes in the US, Australia and New Zealand are a minimum of 2,625, 2,500 and 3,600 hours respectively [Moir 2007b] The numbers in Japan recently were a minimum of 2,235 hours [Birch, Ida 1998:305-307]. If the physicians who performed the acupuncture in these studies had completed the basic training required in Germany to join one of the associations, it is quite probable that they were not trained in TCM sufficiently to be able to make full TCM diagnostic decisions and apply treatment accordingly. Furthermore, in analyses of the treatments that were provided in two of the ART studies, the researchers acknowledged that an important percentage of the participating acupuncturists felt that they would have performed the treatments differently than they were allowed by the study design [Linde et al. 2006, Melchart et al. 2005]. Some of the participating practitioners [24% - Melchart et al. 2005, 20% Linde et al. 2006] thought that the number of treatments may not have been enough. These complex issues lead to two questions.

Were all the participating acupuncturists adequately trained? It is possible that some of the participating physicians were not sufficiently equipped to perform the TCM acupuncture treatments they were asked to perform. Although some see them as having been well trained [Baeker et al. 2007], others have questioned this [Stux 2007]. An important number

of participants wanted to apply more treatment but were constrained by study design. Many in the non-physician community, who use acupuncture as a complete system of therapy rather than as just an adjunctive technique within a medical practice, have questioned how well prepared the participating practitioners really were [Stux 2007]. This leads to the second question.

Can we generalise these results beyond the practice of acupuncture by physicians trained only to use acupuncture as an adjunctive technique within general medical practice? Can we proclaim that acupuncture does or does not work? I think not. It is necessary to state clearly what was done; the nature of the acupuncture given, by whom and how the results relate to that alone and not attempt to make grandiose statements [Ernst 2004] about acupuncture. I believe that all we can say is that when physicians trained to use acupuncture techniques in their medical practice compared such treatments to techniques they were unfamiliar with (the sham - more on this below), they could produce no difference in results between their chosen treatments and sham treatments and that both forms of 'acupuncture' were generally better than or equal to the treatment they usually provide for the same conditions. Although it is difficult to interpret this finding, it certainly does not sound the death knell of acupuncture as some would try to have us believe [Ernst 2004].

The next major issue with the study was the sham acupuncture. Sham interventions are usually used in order to control for placebo effects so that the specific effects of the therapy can be examined. However, as the study authors acknowledge [Linde et al. 2005, Scharf et al. 2006], their sham (minimal acupuncture) is an active sham and is not a placebo treatment. I need to emphasise this because many that see a sham controlled study reflexively interpret it as a placebo controlled study. Thus when, in this case, acupuncture did not outperform the sham, it is seen as meaning it was no better than placebo. This conclusion is not valid and cannot be drawn from sham acupuncture studies unless particularly difficult procedures are also followed [Birch et al. 2002, Birch 2004, 2006-a]. Any sham technique that is not inert needs to have been investigated in pilot studies so that one can determine what it is capable of doing and to ensure that it is not (unbeknownst to the researchers) a highly active treatment [e.g. Wyon et al. 1995, see Birch 1997 and Medici et al. 2003, see Birch 2003a]. There is no evidence of pilot studies having been conducted in these German studies [e.g. Haake et al. 2003, Melchart et al. 2005]. Hence these studies potentially suffer from a double fault with regards to the two types of acupuncture treatment given: i. the acupuncture treatments that were provided may have fallen short on adequacy through the variability and nature of the training of the participating physicians, and ii. these treatments were compared to sham acupuncture treatments of unknown physiological and clinical effectiveness. Perhaps this is why some study authors concluded: "Our observation raises the question of whether there is a single optimal point selection and whether deep needling with stimulation and deqi is superior to shallow needling" [Scharf et al. 2006]. Besides these questions, the issue of whether one can generalise from studies where acupuncture was used primarily as an adjunctive therapy in medical practice to the general practice of acupuncture still remains.

Some people reading these studies have noted that the lack of significant difference between the 'real' and 'sham' arms of the trials implies that it does not matter where one inserts the needles and that thus the theories of acupuncture are unnecessary [Ernst 2004]. This is an invalid conclusion. In order to answer questions about site specificity, or the relative role of the sites at which the needles are inserted, it is necessary to apply the same techniques to both those sites and the control sites [Baecker et al. 2007, Birch 2003]. This was not done in these studies. Both the sites of needle insertion and types of needling varied.

Finally, there are questions concerning recruitment. Patients were generally recruited out of the practice of participating physicians. For a social or economic comparison study this is a proper recruitment strategy, but for a sham study it makes it virtually impossible to guarantee that all the strict requirements needed for sham studies were followed [Margolin et al. 1998]. Because the therapist is not blind to treatment assignment, it is important to keep the therapist out of all communications with the patient except for those necessary for the correct administration of the treatment. It is very difficult to eliminate the possibility of unintended communication when the therapist is involved in patient selection and screening, treatment assignment, setting up the study with the patient and administering the treatments. [Margolin et al. 1998] A second problem concerns how strictly the inclusion-exclusion criteria were applied and monitored. In the original idea of the studies, patient treatments were to be paid for by the insurance companies if the patient was treated for one of the four conditions studied and was enrolled into the relevant study. In fact reimbursement would continue only for patients with one of these problems, provided they participated in the studies. The Munich-Berlin group conducted a number of lesser controlled studies to examine adverse effects [Melchart et al. 2004], epidemiological factors [Linde et al. 2006, Melchart et al. 2006] and cost effectiveness [Witt et al. 2006]. This allowed the research teams to include huge numbers of patients in the various studies. Given how patient recruitment was performed in these studies, can we be sure that physicians wanting to treat a patient with another medical problem (such as menstrual pain or IBS) did not enroll the patient into one of the studies because they also complained of one of the four symptoms, thereby

ensuring that their treatments would be paid for? This is unlikely in the ART studies where participating physicians could refer patients into the larger lesser controlled studies. But it is likely to be more of a problem for the GERAC studies where the studies did not offer this out to the participating physicians. From the study descriptions, it appears that recruiting physicians applied the inclusion-exclusion criteria themselves to patients in their practices, without the presence of an independent observer which is necessary to ensure proper application of inclusion-exclusion criteria [Birch, 2004, Margolin et al. 1998]. Although there was periodic external monitoring, this cannot exclude inadvertent problems.

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In summary, I believe that the design used in these studies makes contradictory interpretations possible. It looks as though some or all of these studies may have suffered from problems with the training of the acupuncturists, adequacy of treatments and importantly, use of an unvalidated and untested sham. These issues make interpretation of the real-sham comparisons difficult. It is difficult to generalise the results of these studies outside the practice of acupuncture as adjunctive therapy in medical practice. Further the strict requirements for a sham acupuncture study were either not followed and/or not well monitored or regulated; there are issues around recruitment methods, treatments settings, blinding of key study personnel and monitoring of these. However there remains the puzzling finding that when physicians used acupuncture in these trials, regardless of what treatment they did, the acupuncture was generally as or much more effective than the standard therapy. This is difficult to explain.

As a result of these studies, acupuncture is now paid for in Germany by the social insurance scheme if administered by a qualified physician for chronic low back pain and osteoarthritis of the knee, but not tension headache or migraine [Bovey 2006, Streng 2007]. This decision was made partly on the results of the studies and partly for socio-political reasons [Streng 2007]. Thus these studies have started to affect delivery of acupuncture in Germany. It remains to be seen how the international community deals with them. What impact will they have on insurance reimbursement outside of Germany? Will the fact that specific German socio-political factors influenced the choice of study, their design and the interpretation of results be taken into account by scientists and health care analysts in other countries? How will they be interpreted in systematic reviews and what effect will they have on the conclusions and potential applications of those systematic reviews [Birch 2007]? Have these studies exposed problems with how acupuncture is understood to work? If so will this trigger demands for more studies investigating specific effects using 'sham controlled' trials or have they finally demonstrated the inherent difficulty of conducting them [Birch 2006-b]? Is it now time to acknowledge that placebo, rather than being a nuisance variable in clinical trials, is a poorly constructed term that captures some of the ways that the body heals itself and thus maybe should not be controlled for? Answers to these questions will only emerge over time. ■

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