

Recent Progress in Clinical Research of Acupuncture

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I. Introduction

This report mainly summarise the results of recent clinical trials and systematic reviews of acupuncture on musculoskeletal disorders. Several issues regarding sham intervention and placebo effects in acupuncture trials are discussed because they affect the way clinical research should be interpreted. Results of cost-effectiveness analysis of acupuncture trials are also briefly introduced. Research on safety of acupuncture could not be referred in detail but its safety is confirmed in numerous clinical trials.

II. Evidence of effectiveness of acupuncture

1. Randomized controlled trial (RCT)

A series of carefully designed, large scale, three-arm RCTs compared acupuncture with sham (off point, shallow) needling and with usual care were conducted in German with financial support by the German insurance companies. The target diseases were musculoskeletal disorders such as knee osteo-

arthritis, low back pain, migraine and tension-type headache. **Figure 1** shows two typical examples of three arm RCTs of knee pain. One is real acupuncture, sham acupuncture and waiting list, and the other is real acupuncture, sham acupuncture and drug therapy. The pain was measure using WOMAC score. Acupuncture induced long-lasting pain suppression. Both RCTs indicate significantly stronger effects of acupuncture than waiting list or drug therapy groups.

In general, recent RCTs demonstrated that acupuncture is significantly better than usual care for patients. The size of the effect was clinically useful. But in the comparisons with sham acupuncture, acupuncture repeatedly showed a non-significant trend towards superiority. It was only significantly superior in one study of acupuncture for osteoarthritis of the knee. (see **Figure 1**, Witt 2005). Safety of acupuncture intervention by trained practionaers has been well established in several different countries.

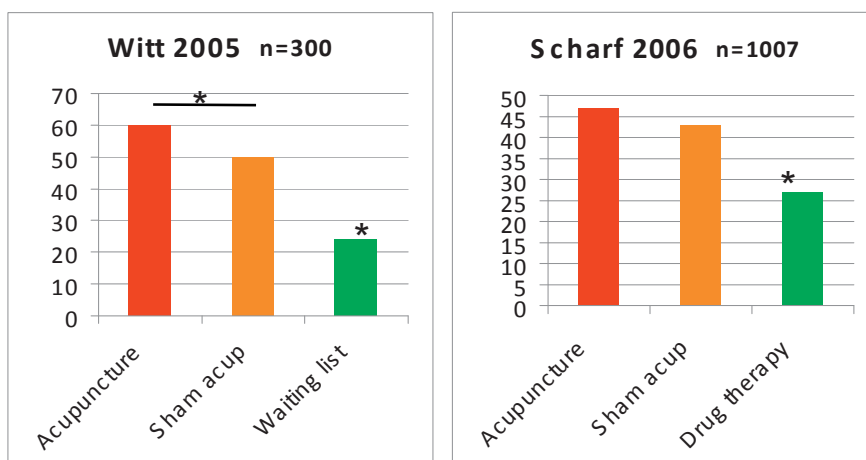


Fig. 1. Two RCTs of acupuncture on knee pain

Real acupuncture vs usual care pain, short term (N=927)

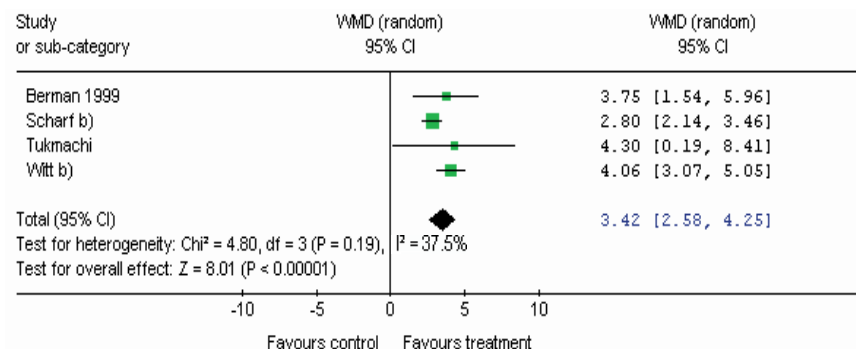


Fig. 2. Meta-analysis of acupuncture on knee OA. White et al. *Rheumatology* 2007; 46(3): 384-90.

Real acupuncture vs sham acupuncture pain, short term (n=1334)

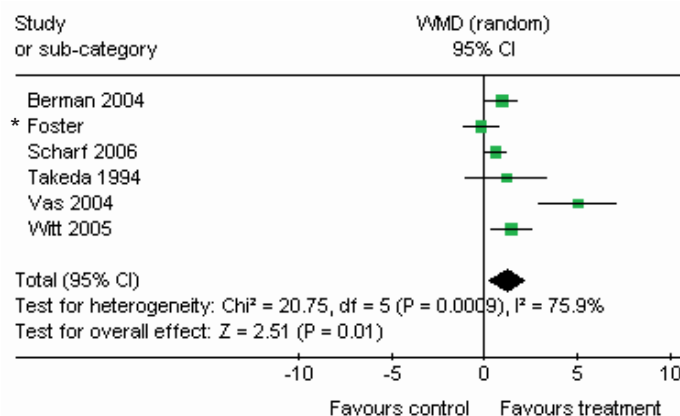


Fig. 3. Meta-analysis of acupuncture on knee OA. Modified from White et al. *Rheumatology* 2007.

2. Systematic review and meta-analysis of clinical trials

Systematic reviews of RCTs represent the highest level of evidence, and the increasing number of high quality trials has allowed recent reviews to provide a more reliable summary of the evidence on acupuncture.

Figure 2 and 3 demonstrate the results of meta-analysis using pooled data of several RCTs of acupuncture for knee pain. In comparison of real acupuncture with usual care, a highly significant difference, favour to acupuncture, was obtained (Fig. 2, $p < 0.00001$). Slight but still significant difference was observed in comparison of real acupuncture with sham acupuncture. (Fig. 3, $p < 0.01$).

In two cases, earlier reviews which were unable to reach conclusions have now been updated, with positive results. For low back pain (Manheimer et al. 651–63) and for osteoarthritis of the knee, (White et al. 384–90) acupuncture is superior both to sham acupuncture and to usual care. Although the size of the effect of acupuncture when compared with sham is not large, the size of acupuncture's effect on knee pain is large enough to be similar or even superior to the effect of non-steroidal anti-inflammatory drugs (NSAIDs). Figure 4 illustrates the comparison of effect sized between them.

It is interesting to note that two recent, high quality studies showed no effect of acupuncture for knee pain compared with sham acupuncture; in

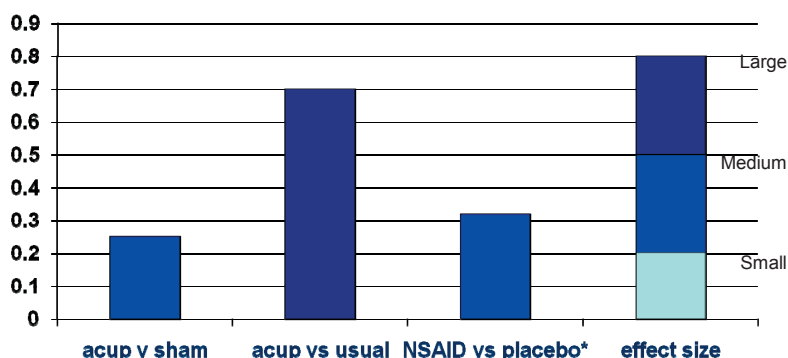


Fig. 4. Comparison of effect size of acupuncture and NSAIDs on knee pain. White and Kawakita *Acupunct Med* 2006; 24(supp): 71-6.

both studies, acupuncture was given in addition to exercise therapy. It seems probable that exercise allowed patients to achieve the maximum improvement possible and acupuncture could have no additional benefit (called a 'ceiling effect').

In comparison with sham acupuncture, acupuncture has a significant effect on post-operative pain, a significant but somewhat limited effect on tension headache, and (at least for electroacupuncture) an effect on fibromyalgia. The current evidence is moderately in favour of an effect on neck pain, and there is insufficient evidence on elbow pain. In contrast, there is no effect on migraine compared to sham.

Systematic reviews have for some years consistently demonstrated that acupuncture is effective for nausea and vomiting. More recently, acupuncture was shown to be effective as an adjunct to infertility treatment and in generalised anxiety disorder, but in both cases the amount of evidence is somewhat limited. Systematic reviews have found insufficient good quality evidence for estimating its effect on asthma, bowel diseases, hay fever or insomnia. Current evidence suggests acupuncture is not effective in smoking cessation or for recovery from stroke.

III. Components of acupuncture treatment

An important step forward in understanding acupuncture was the recent study confirming what had long been suspected, but never proved – that a large part of the effect of acupuncture is due to the patient's expectation, loosely called the 'placebo' effect. In patients with irritable bowel syndrome,

the effect of needling is much greater when it is accompanied by the full, elaborate procedures involved in the acupuncture consultation. Expectation plays a part in all medical interventions, but it now seems very likely that the expectation of acupuncture is much greater than that of conventional medical treatment, at least when the patient considers acupuncture to be 'unconventional'.

The question arises: is it very important that a large part of acupuncture's effect is due to expectation? The answer will depend on your viewpoint, and is the distinction between clinical relevant effect and biological effect. Patients and their health care staff will be more concerned with whether acupuncture will improve the patient's symptoms than what is its mode of action. They will accept acupuncture if trials show that it offers additional benefits compared with usual treatment. But scientists, and health care regulators, are more likely to reject acupuncture, on principle, if it cannot be shown to be even slightly superior to placebo, in other words to have a 'specific' effect. The placebo question has dominated the approach to acupuncture research for the last decade, which may not have been in the best interests of patients.

In addressing the placebo question, two problems arise: 1) it seems that this 'specific' effect of acupuncture is small in relation to its expectation effects, and therefore clinical trials need to be very large to demonstrate it. 2) these studies require an inactive 'placebo' control for acupuncture.

IV. 'Placebo' (sham) controls

Finding an inactive 'placebo' control for acupuncture

Table 1. Cost-effectiveness of acupuncture

Condition	Author	N	Cost/QALY	yen
Migraine	Vincent, Wonderling	283	£ 9,951	¥ 2,044,703
Headache	Witt	3182	£ 9,326	¥ 1,916,279
Low back pain	Thomas, Ratcliffe	182	£ 4,241	¥ 871,428
Low back pain	Witt	3093	£ 8,420	¥ 1,730,117
Neck pain	Willich	3451	£ 9,975	¥ 2,049,634
Knee pain	Reinhold	489	£ 14,276	¥ 2,933,391

Maximum acceptable in UK is £20,000 per QALY (about ¥4,100,000) QALY: Quality Adjusted Living Years

is difficult. In the most common version, used in many trials, the control group have received acupuncture needles, but inserted in the wrong site and only superficially, and not stimulated. The patients often believe that they have been given real acupuncture, but this treatment may not be inactive – superficial needling is used as a form of treatment in some settings. An additional, more theoretical, limitation of the ‘placebo’ control is that it only applies in traditional approach to acupuncture, in which it is believed that the correct point has to be treated. Increasing numbers of acupuncturists are coming to use a medical approach to acupuncture, in which reduces the importance of specific acupuncture points, and emphasises the need to stimulate the nervous system in an appropriate way. Needles do not have to be inserted in specific points, and needles inserted into the same spinal segment as the pain, as done in these control groups, may be an active treatment.

The search for a suitable placebo for acupuncture appeared to be over when a blunt, telescopic needle was developed. However, it now seems that this device, even though it amounts to no more than light touch, has significant effects on the pain matrix of the brain, and is far from inactive. (Pariente et al. 1161–67) Although these effects are significant, they are nevertheless different from the effects of needling. It has been suggested that the blunt needle stimulates a subgroup of the C fibres in the skin, the so-called C-tactile fibres.

Since these controls are active, they should be called ‘sham’ rather than ‘placebo’.

V. Evidence of cost-effectiveness

Clinical trials with full economic analysis have now been conducted on acupuncture for migraine, back pain, and osteoarthritis of knee and hip. The results are summarized in **Table 1**. In all cases, the results indicated that the additional cost of acupuncture was less than £20,000 per Quality Adjusted Life Year (QALY). This is the limit usually applied for accepting treatments for the health care of an industrialised nation, and may mean that acupuncture should be adopted more widely. Making decisions on health care on the basis of best value for money.

VI. Conclusion

1. Acupuncture is more effective than placebo (sham) for some conditions (knee OA, low back pain and neck pain).
2. Acupuncture is clearly more effective than usual care for several conditions (migraine, tension headache).
3. Cost- effectiveness of acupuncture is relatively high comparing with usual drug therapies.

Implications for future research

1. Three-arm studies must be approached with great caution.
2. For effectiveness question, acupuncture should be compared with standard care using multi-centre, pragmatic trial design.
3. For specific effect question, acupuncture should be compared with non-penetrating placebo, in a single centre, fastidious experimental design.

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