

# International Reflections on the Conduct of Acupuncture Research

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An article by Assefi and colleagues<sup>1</sup> recently published in the *Annals of Internal Medicine* speaks to the need for new research methods in the study of traditional Chinese medicine (TCM). The article entitled “A Randomized Clinical Trial of Acupuncture Compared with Sham Acupuncture in Fibromyalgia” evaluated acupuncture as a treatment. The authors concluded that verum acupuncture was no better than sham. The findings were picked up by the *Associated Press* and appeared in newspapers and other media channels throughout the United States.

That article was significant for a number of reasons. First, people in the US primarily find out about acupuncture from friends and the media.<sup>2</sup> News of this sort gives consumers the impression that acupuncture is not an effective therapy, which may be sufficient to persuade those who have never tried acupuncture to not consider its use. Second, chronic pain is one of the major reasons for using acupuncture in the US.<sup>3,4</sup> Given that fibromyalgia syndrome (FMS) is one of the most prevalent and costly chronic pain conditions currently being treated in the US,<sup>5</sup> claims about acupuncture's lack of efficacy in treating FMS is significant. Third, this is an example of the type of research designs commonly employed in major research centers. A recent review of the CRISP database on federally funded acupuncture research reveals approximately 70 studies.<sup>6</sup> Although these studies are increasingly including an ‘individualized treatment’ arm in the design, many are not. Arguably, the majority of studies do not reflect actual TCM clinical practice, which may include the use of herbs and other therapies in a given treatment. Also, it is not obvious in the study descriptions that well-qualified traditional Chinese medicine practitioners

are consulted adequately in the study design, and TCM colleges are generally not represented in these grants.

The Assefi study was designed and conducted by thoughtful, well-trained, even-minded researchers and clinicians. The larger issue is not with this group, or this study, but with the limitations in the current dominant strategy for conducting randomized controlled acupuncture trials, and the implications of that approach to clinical TCM practice. In the Assefi study a group of 100 adults with fibromyalgia were randomly assigned to verum acupuncture treatment, which was described as being specifically designed to treat fibromyalgia, or one of 3 acupuncture treatments described as being sham treatments. Two of the sham treatments included acupuncture needle penetration of the skin, and the other simulated penetration. The only outcome measure used was the visual analogue scale (VAS), commonly used in pain studies, but arguably insufficient to determine the impact of treatment. Although this was an interesting study there were problems in terms of its matching the clinical practice of acupuncture. Indeed, the authors themselves stated in the ‘Limitations’ section of their article that the use of fixed points (verum acupuncture treatment) may differ from actual clinical practice in which herbs and other measures could be included.

In response to this article a number of researchers from the international community contributed their thoughts. Those responses were published by *Annals of Internal Medicine* in their *Rapid Responses* online forum.<sup>7</sup> The responses are printed below to show how some researchers are thinking about these research design challenges. More advocacy work in this area is required in order to design studies which more truly reflect actual TCM

clinical practice, studying TCM as it was intended to be practiced. This will require better integration of well-qualified TCM practitioners (MD and non-MD) in the design, conduct and evaluation of studies in this area. Also, doctoral level professional education programs need to train non-MD acupuncturists more effectively in the process and application of scientific research. Greater collaboration between major research institutions, colleges of TCM, and acupuncture/TCM professional organizations would be helpful.

## International Responses to the Assefi Article

### Effectiveness of Acupuncture and Placebo Effect

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Another randomized controlled trial (RCT) done by Affesi and colleagues drew the conclusion that acupuncture was no more effective than sham control (1) or in other words, that acupuncture is not superior to placebo. But does it make any difference whether an RCT draws a positive or negative conclusion, given so many serious methodological flaws concerning RCTs evaluating the effectiveness of acupuncture (2). More and more people question the validity of RCTs in testing acupuncture, and doubt the necessity for further RCTs to be conducted with the same methodological defects as previous ones had, because they do not help make a decisive conclusion. All are expecting high-quality trials concerning acupuncture, but what is high quality in approach to evaluating acupuncture? What we have obtained

from RCTs does not accord with that we get from daily clinical experience, as shown in another recent, pragmatic, non-placebo controlled, randomized trial evaluating the effectiveness of acupuncture on headache in practice (3). It is due to the reason that acupuncture treatment applied in RCTs is reduced to a mere needling deprived of its Traditional Chinese Medicine (TCM) theory basis. TCM identifies symptoms in a different approach to form a characteristic diagnosis, and a particular acupuncture treatment is TCM diagnosis specific. When patients are recruited and classified by biomedical diagnosis as selection criteria to achieve homogeneity in study samples in an RCT, which results in actual heterogeneity according to TCM diagnosis, is it possible to evaluate the effectiveness of acupuncture appropriately? RCTs seem not fit for complex non-pharmacological treatment such as acupuncture (2).

Acupuncture is widely accepted and used, especially in chronic conditions, without sufficient evidence supporting its efficacy. But what is evidence? Is it the sole valid evidence supporting the effectiveness of acupuncture that acupuncture has more than placebo effect? Placebo effect has long been ignored and discounted as unreliable untruthfulness, until recently more and more people view placebo effect with a new eye. A conference held at the National Institutes of Health in the United States in 2002 called for in-depth research on brain and body pathways that mediate placebo effects (4). It seems that effect of acupuncture is neither a specific effect nor a placebo effect if they can be divided; but an interaction mechanism existing between them functioning as the whole effect of acupuncture. Still we do not know how it works, and how it affects overall effectiveness. Acupuncture, entangled with placebo effect, may provide a new way to study and understand placebo effect at least, make research of placebo effect less intangible.

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## What Shall We Conclude From This Randomized Clinical Trial Of Acupuncture?

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Assefi et al have performed an extensive study and attempted to address an important issue about the role of acupuncture in fibromyalgia patients. They have enrolled 25 patients into “true active acupuncture treatment” and 75 patients into assumed control groups. They have concluded that “acupuncture was no better than sham acupuncture at relieving pain in fibromyalgia” (1). A more appropriate conclusion might be “A fixed-points acupuncture protocol based on an interpretation of the Traditional Chinese Medicine (TCM) was no better than pseudo sham acupuncture interventions in a small sample study.”

Acupuncture is a procedure oriented intervention and its effectiveness is felt by TCM practitioners to be largely dependent on the performers with their selected points. In this study, the acupuncture points were chosen by an acupuncturist with 15 years of experience and were approved by 3 other senior acupuncturists. No information was given by the authors about how these acupuncturists decided to choose these points. What was the TCM diagnosis they have reached for these FM patients? Was any such traditional approach used to select the points? It is sad that this randomized Clinical Trial has not supported the acupuncturist's 15 years experience. Its conclusion cannot be generalized to any other acupuncture for fibromyalgia patients. Other regimens need to be tested.

One of the control groups received acupuncture sessions using points based on an unrelated condition, “early menses due to Blood Heat”. The acupuncture points for this so-called unrelated condition are mainly regulating Liver and Spleen meridians, which are two meridians, that could have been affected in fibromyalgia patients based on TCM theory (2). TCM proposes that these points are not inert; they could be beneficial or even deleterious. It is a pseudo sham control at best, which has been a problem in acupuncture research as Dr. Liu has pointed out in his response to this study.

As for fibromyalgia, this is a patient population that has varying constellations of symptoms or even a variety of etiologies as Dr. Burke said in his Letter to the Editor. Pain in one of the manifestation of their underlying disorders, but it is not the only one. The primary outcome measurement in this study is a simple 10 cm visual analogue scale, a measurement for subjective pain. Wouldn't it have been more appreciate to use the validated Fibromyalgia Impact Questionnaires (FIQ)?

Even though approximately 100 patients enrolled into this study, only 25 were chosen into presumably “true TCM based acupuncture group”. Is this really a large enough group to detect any significant effectiveness for acupuncture treatment, an ancient therapy with marginal or moderate effectiveness at best (3)? Furthermore, the study reported here is single blind study, which will probably always be the case for all acupuncture study, because it is impossible to blind acupuncturists who need to relay on many aspects of the treatment melodious sensation (Deqi) to deliver its supposed efficacy.

Acupuncture is an experience driven, ancient technique developed in the pre-scientific era. Its role in our modern evidenced based, scientific proven patient care certainly needs further studies. Great attention was placed by Assefi et al to many details of their study. However, we should evaluate this non-pharmacologic approach by the same

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standards as we do for another other interventions. This requires adequate understanding and knowledge about the details of administering this ancient technique. It is frustrating to see that the *Annals* has published this limited acupuncture study with a broadly implied conclusion about acupuncture for our fibromyalgia patients without more consideration of its limitations.

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### What Shall We Conclude From This Randomized Clinical Trial Of Acupuncture?

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If this study would have been a pharmaceutical study, including only 100 patients, distributed in 4 different arms of 25 patients only, and single blind, no journal would have accepted it. Apart from being insufficient in its study methodology, the authors selected acupuncture points not widely used to treat fibromyalgia, and they omitted specific analgesic points such as Gallbladder 21, Colon 4, Stomach 36. Furthermore, in the control group they needed a point which is even diagnostic for fibromyalgia, spleen 10. To test whether acupuncture works in fibromyalgia one needs no fixed acupuncture formula, one needs to include triggerpoints and much more patients need to be included in less arms! [Submitted to AIM on 18 July 2005]

### Adopting Novel Research Designs in the Evaluation of Complex Health Conditions

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Dr. Assefi and colleagues must be commended on the high quality RCT they conducted comparing acupuncture with sham in the treatment of fibromyalgia. There are, however, limitations in the study that result in non-generalizable findings in terms of the actual clinical practice of acupuncture and traditional Chinese medicine (TCM). First, it is important to remember that fibromyalgia syndrome (FMS) is a recently recognized western medical diagnosis (1). You will not typically find references to the disease in TCM texts, and correspondingly you will not find standard TCM treatments. The authors acknowledge this lack of a "gold standard" in their article. Even within the medical community there is no consensus regarding etiology, with hypothesized causes including neuroendocrine dysregulation, genetics, and sleep abnormalities; and there is no truly effective conventional medical treatment. Western medicine and alternative medicine are equally challenged by such syndromic diagnoses. To date some of the best results have actually been with moderate exercise (2). Given the poor prognosis for these patients they naturally begin to seek alternatives, acupuncture being one of them. One high quality acupuncture study (3), which the authors cite, showed the efficacy of electroacupuncture with FMS symptoms. Electroacupuncture is a useful therapeutic adjunct in pain treatment, and its addition as another arm in the Assefi study could have been informative. Considering how acupuncture has shown evidence of utility with other musculoskeletal disorders in high quality RCTs, such as research by Berman on osteoarthritis of the knee (4), the lack of efficacy in the current study may have more to do with the study design than with acupuncture mechanisms. Unfortunately we cannot say either with confidence given this study alone. Ultimately this very sound RCT study may point to limitations in

our current CAM research strategies. The recent Institute of Medicine report on complementary and alternative medicine (5) recommends more novel study designs in the evaluation of traditional medicines, such as bundled studies focusing on standard practice. A bundled study of TCM for fibromyalgia might potentially include acupuncture, herbs, massage, lifestyle counseling, and provide treatment for a significantly longer period of time. At this point minimizing the value of acupuncture for the treatment of FMS would be premature. What this study suggests is that it is time for the next stage of research to emerge. Given the significant personal, social, clinical and economic costs of FMS, this is undoubtedly what our patients would hope for.

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