

## Acupuncture Storms JAMA

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### INTRODUCTION

Acupuncture has had a dynamic—even controversial—history over the last fifty years since scientific research methodology started to scrutinize its underlying mechanism and clinical effectiveness. This article starts an early example of disputed claims in China and Korea; mentions modern applications of acupuncture therapy which have generated debate, and examines in detail the recent high-profile academia and media storm triggered by the publication of the Hinman paper in the *Journal of the American Medical Association (JAMA)* [1].

Strictly modern applications of acupuncture may be said to have begun in 1958, when Chinese surgeons discovered that acupuncture anesthesia could be either substituted or administered in conjunction with anesthetic pharmaceuticals during surgical procedures [2]. This news was widely disseminated in the Chinese media, as well as through scientific research journals, fueling a surge of both professional and popular interest. In fact, it was acupuncture analgesia/anesthesia which brought the ancient therapeutic technique of acupuncture to the attention of the American public in 1971, when *New York Times* journalist James Reston published an article about his personal experience in a Chinese hospital following an appendicitis attack [3].

From the 1960's many Asian scientists were engaged in efforts to find a physiological basis for the acupuncture meridian system. Bong-Han Kim, a surgeon educated at Seoul National University identified what he called the Kyungrak system. As a professor at the Pyung Yang Medical School in North Korea, Dr. Kim mapped out an intricate network of anatomical structures within the skin, vascular and organ systems that he associated with the energetic acupuncture meridian system. He suggested these previously unidentified structures represented an anatomical basis for the acupuncture meridians [4].

Dr. Kim's research was ground-breaking, as much of the resistance to the acceptance of acupuncture theory and practice stem from the invisible nature of the body's energy system expressed as meridian and qi.

The energy flow through acupuncture meridians has never been successfully attributed to physiological structures, leading to doubt as to the validity of meridians and qi flow. The publication of Bong-Han Kim's findings created a sensation in China. Doctors of traditional Chinese medicine and Western medicine quickly organized a visit to Dr. Kim in North Korea to verify his astounding results. Unfortunately, Dr. Kim's claims and findings couldn't be reproduced, and he committed suicide in the aftermath of this debacle, which became the most dramatic event in acupuncture research history [5].

Throughout the 1970's, leading physicians, health advocates and published research increased awareness of the various medical applications of acupuncture and traditional Chinese medicine. Dr. H. L. Wen, a Hong Kong neurosurgeon, is credited with the application of acupuncture to addiction issues due to a serendipitous observation he made in 1972. Dr. Wen's groundbreaking work [6] on acupuncture for addiction was introduced to America for chemical dependency and substance abuse problems. Ultimately, over 2000 chemical dependency programs were established across the United States: thousands of Americans have been treated for alcoholism, smoking cessation, drug addictions and other substance abuse with acupuncture [7].

In 2002, German clinicians and researchers<sup>8</sup> found compelling evidence that acupuncture could increase the pregnancy rate of women who received *in vitro* fertilization (IVF). This discovery opened another new frontier for integrative acupuncture medicine. Due to the indisputable increased success ratio for IVF implants which incorporate acupuncture, fertility clinics around the world have adopted the use of pre- and post-IVF acupuncture treatments.

Since 1958, the application of acupuncture to anesthesia, fertility and chemical dependency has sparked controversy, as well as inspiring further research studies. The validity, effectiveness and scope of use of acupuncture have drawn both supportive and oppositional debate from scientists, medical doctors, acupuncture practitioners, patients, and the general

public. A recent example of the sort of passionate debate which acupuncture research can generate is centered around the Hinman Paper, which is examined in detail, below. (The clinical trial by Hinman, et al. [1] will be referred to as the “Hinman Paper,” or “Hinman Study” throughout this article).

### THE HINMAN PAPER

In October 2014, Hinman, et al. [1] published the results of a clinical trial in the *Journal of the American Medical Association (JAMA)*, claiming that their findings do not support the use of acupuncture therapy for patients older than 50 years who have moderate or severe chronic knee pain. These findings were immediately disputed by clinical acupuncturists, whose experience supports the effectiveness of acupuncture in knee-pain patients of all ages. The attention generated by this article has opened a dialogue between acupuncture supporters and detractors, and has raised meaningful questions about how to effectively assess the benefits of acupuncture.

The clinical trial by Hinman, et al. [1] originated in 2009, when the authors registered their proposal with the Australia/New Zealand Clinical Trials Registry. The trial started in 2010, data collection was completed in 2012, and the results were published in October, 2014.

In 2012, Hinman, et al. [9] published their pragmatic Zelen-design randomized controlled trial protocol in *BMC Complementary and Alternative Medicine*, the official journal of the International Society for Complementary Medicine Research. Zelen-design allows for randomization to take place before informed consent. The purpose of the study was to investigate both the efficacy and cost-effectiveness of both needle and laser acupuncture for chronic knee pain in patients over 50 years of age. The study was administered by medical practitioners.

The study recruited 282 community volunteers aged over 50 years with chronic knee pain from metropolitan Melbourne and regional Victoria, Australia. Participants originally consented to participate in a longitudinal natural history study but were then covertly randomized into one of four groups. Participants were divided thusly: control (71 patients), acupuncture (70 patients), laser acupuncture (71 patients), and sham acupuncture (70 patients). Acupuncture treatments were performed with a combined Western and Traditional Chinese Medicine style were delivered by general practitioners. Participants received 8–12 visits over a consecutive 12-week period. The study was conducted from February, 2010 to December, 2012.

Participants were assessed at the completion of treatment at 12 weeks. The primary outcomes included pain measured by an 11-point numeric rating scale (NRS) along with self-reported physical function measured according to the Western Ontario and

McMaster (WOMAC) Universities Osteoarthritis Index subscale. Secondary outcomes included quality of life, global rating of change scores and additional measures of pain (other NRS and WOMAC subscale) and physical function measures (NRS). Follow-up assessments were conducted after one year. Relative cost-effectiveness was determined by health service usage and outcome data. The statistics gathered were to be used to determine the efficaciousness and cost-effectiveness of laser and/or needle acupuncture in the management of chronic knee pain, specifically in people over 50 years old.

In 2014, Hinman, et al. [1] completed their clinical trial and published their study. Study participants and family-physician acupuncturists were blinded to laser and sham laser acupuncture. Patients in the control group were unaware of the trial. Analysis was by intention-to-treat using multiple imputation for missing outcome data. Drop-out rates were assessed: 26 participants had discontinued by week 12 (9%), and 50 participants had discontinued by the end of the first year, (18%). Results showed that neither needle nor laser acupuncture significantly improved pain (mean difference;  $-0.4$  units; 95% CI,  $-1.2$  to  $0.4$ , and  $-0.1$ ; 95% CI,  $-0.9$  to  $0.7$ , respectively) or function ( $-1.7$ ; 95% CI,  $-6.1$  to  $2.6$ , and  $0.5$ ; 95% CI,  $-3.4$  to  $4.4$ , respectively) compared with sham at 12 weeks. The study showed that needle and laser acupuncture resulted in modest improvements in pain ( $-1.1$ ; 95% CI,  $-1.8$  to  $-0.4$ , and  $-0.8$ ; 95% CI,  $-1.5$  to  $-0.1$ , respectively) at 12 weeks, but not at 1 year, compared with control. The study also showed needle acupuncture resulted in modest improvement in function compared with control at 12 weeks ( $-3.9$ ; 95% CI,  $-7.7$  to  $-0.2$ ), however, was not significantly different from sham ( $-1.7$ ; 95% CI,  $-6.1$  to  $2.6$ ) and was not maintained at 1 year. No differences for most secondary outcomes and no serious adverse events occurred in the study. The study concluded that neither laser nor needle acupuncture conferred benefit over sham for pain or function in patients older than 50 years who have moderate or severe chronic knee pain.

The Hinman Study [1] was conducted in the Centre for Health, Exercise and Sports Medicine, Department of Physiotherapy, School of Health Sciences, Faculty of Medicine Dentistry & Health Sciences, the University of Melbourne, VIC, Australia and published in *JAMA*. Funding was provided by the National Health and Medical Research Council in Australia.

### PUBLIC REACTIONS AND MEDICAL COMMUNITY COMMENTARIES

The Hinman Paper created a splash in the already dynamic waters of integrative medicine. In a society striving to improve the safety and effectiveness of medical intervention, where far-reaching healthcare decisions are made according to evidence-based research, this study evoked significant dialog. As the negative

findings in the Hinman study have rippled outwards, this study has received a reciprocal wave of responses from interested parties.

#### RESPONSE TO THE HINMAN ARTICLE FROM VARIOUS MEDIA SOURCES:

In *HealthDay*, reporter Tara Haelle [10] wrote that acupuncture may not help chronic knee pain. Ms Haeller interviewed and quoted Dr. Steven Novella, an assistant professor of neurology at Yale University School of Medicine. Dr. Novella, a known skeptic, was a little surprised that the difference between the treatment and control groups was not larger due to placebo effects. “There are individual studies with weakly positive effects, but systematic reviews generally either show no effect at all or a slight effect that is not clinically significant. There is also indirect harm of wasted resources and perhaps delaying more effective treatment. If a patient is convinced by placebo effects that acupuncture works, they may seek it out for a non-self-limiting illness, and there are ‘medical acupuncturists’ who will use acupuncture to treat anything, even cancer.”

Fox News [11] titled its report on the subject as: “Acupuncture may not be effective for knee pain, study says.” Andrew Vickers, an attending research methodologist at Memorial Sloan Kettering Cancer Center in New York City, was interviewed. Although he stated that “the new results were very similar to those of a review of individual patient data in 2012,” he also stated that “the new review may have found a benefit from real acupuncture compared to sham acupuncture if the study included more people.” He also showed support for the use of acupuncture by saying, “About three million Americans try acupuncture per year, and chronic pain is the most common indication. People with chronic pain should see a pain specialist, as there are many options for treatment, including acupuncture.” The Fox News report also quoted Dr. A. Abhishek, an arthritis researcher and associate professor at the University of Nottingham in the UK: “As the authors suggest, the findings of this study are applicable to patients with moderate to severe persistent knee pain, and acupuncture may be effective in some people with neuropathic pain.”

Daniel Pendick, Executive Editor of **Harvard Men’s Health Watch** wrote “Acupuncture is a popular form of complementary and alternative therapy, but it has yet to win universal endorsement in the medical community—and usually isn’t covered by health insurance. Many satisfied customers continue to pay for treatment out of pocket in spite of mixed findings on the effectiveness of this ancient healing art.” The Hinman study is “just one moderately-sized study in a long and continuing series, and there’s still credible evidence to suggest that acupuncture helps some people with common pain conditions.” Daniel Pendick cited Peter Wayne, PhD, research director of the

Osher Center for Integrative Medicine at Harvard-affiliated Brigham and Women’s Hospital, and said “I would be careful saying acupuncture doesn’t work for all pain conditions and no one should do it; we simply do not know enough yet. . . This is a small study that replicates what we already know. When you compare acupuncture to no treatment, there seems to be clinically meaningful differences for many pain conditions, including back pain and knee pain. Based on this pragmatic comparison, if I were deciding whether to send a family member or friend for a pain-related acupuncture treatment, I would say ‘yes’” [12].

David Wild from *Pain Medicine News* wrote an article entitled “Acupuncture Provides Minimal Benefits After Study Design Bias Is Removed.” [13] He said, “People with osteoarthritis receiving needle and laser acupuncture have negligible and short-lived effects compared with sham acupuncture or usual care, when they don’t know what treatment they will be receiving, according to a study published in *JAMA*.” David Wild quoted Nortin Hadler, MD, attending rheumatologist at the University of North Carolina Hospitals, in Chapel Hill, and professor of medicine and microbiology/immunology, as saying that “these results—like in some prior studies—show that on average, acupuncture is associated with slight and short-lived benefits. Individuals who were administered acupuncture and other alternative and complementary modalities, or even treatments for pain described as placebos have also reported improvement. These ‘responders’ should not be dismissed as gullible. There are certain individuals who, because of their worldview and beliefs, will find comfort in alternative and complementary treatments that have been proven to be no more effective than placebo. Whether it is ethical for clinicians to offer patients these ‘comforting’ treatments remains a topic of debate.”

The repercussions of a research paper published in a leading medical journal can be felt strongly from these four reports. A careful scrutiny of the established evidence is necessary.

#### ESTABLISHED EVIDENCE: TRIALS, SYSTEMATIC REVIEWS AND META-ANALYSIS

Chronic knee pain is one of the most applicable conditions treated by acupuncture. Acupuncture has been performed on knee pain since its inception several millennia ago in China. Expert opinions, case histories, anecdotal stories and observational studies are abundant on the success of acupuncture treatment for chronic knee pain. Although many previous trials of acupuncture for osteoarthritis have produced conflicting results due to small samples, a limited number of treatment sessions, or other limitations, acupuncturists’ observation, patients’ feedback, previous clinical trials, as well as basic researches, all suggest that acupuncture can effectively treat knee pain. Large well-

designed rigorous studies also emerged in the new millennium.

The study by Berman, et al. [14] published in *Annals of Internal Medicine* (Dec 2004) might be considered to contain the most influential and convincing evidence in favor of the application of acupuncture to pain caused by osteoarthritis of the knee. This randomized, controlled trial was designed to determine whether acupuncture provides greater pain relief and improved function compared with sham acupuncture or education in patients with osteoarthritis of the knee.

The study was conducted at the following venues: two outpatient clinics (an integrative medicine facility and a rheumatology facility) located in academic teaching hospitals; the clinical trials facility of the Integrative Medicine Clinic of the University of Maryland School of Medicine, Baltimore, Maryland; the Innovative Medical Research Center (a private research firm), Towson, Maryland; and the Hospital for Special Surgery, New York City, New York. The study recruited 570 patients with osteoarthritis of the knee and divided them into an acupuncture group and a control group. The patients in the acupuncture group received 23 true acupuncture sessions over 26 weeks. The patients in the control group received 6 two-hour sessions over 12 weeks or 23 sham acupuncture sessions over 26 weeks. Changes in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores at 8 and 26 weeks were the primary outcome assessment tool. Patient global assessment, 6-minute walk distance, and physical health scores of the 36-Item Short-Form Health Survey (SF-36) were secondary outcomes.

The patients in the true acupuncture group received 26 weeks of gradually tapering treatment according to the following schedule: 8 weeks of 2 treatments per week followed by 2 weeks of 1 treatment per week, 4 weeks of 1 treatment every other week, and 12 weeks of 1 treatment per month. Acupuncture points selected included five local points: Yanglingquan (GB 34), Yinlingquan (SP 9), Zhusanli (ST 36), Dubi (ST 35), and Xiyan (extra point); and four distal points: Kunlun (BL 60), Xuanzhong (GB 39), Sanyinjiao (SP 6), and Taixi (KI 3). These points were applied to the affected leg. If both knees were affected, nine points were stimulated in each leg. The sham acupuncture treatment was conducted in the following procedures: Acupuncturists inserted two needles into the sham points in the abdominal area, approximately 3 cm lateral to and slightly above the umbilicus bilaterally, and then immediately applied two pieces of adhesive tape next to the needles. In addition, they tapped a mock plastic needle guiding tube on the surface of each of the nine true points in the leg to produce some discernible sensation and then immediately applied a needle with a piece of adhesive tape to the dermal surface, without needle insertion. The sham acupuncture procedure was given on the same schedule as the true

acupuncture group and used the same active needle placements, except actual insertion did not occur at these nine points.

The results showed that patients in the true acupuncture group experienced greater improvement in WOMAC function scores than the sham acupuncture group at 8 weeks (mean difference,  $-2.9$  [95% CI,  $-5.0$  to  $-0.8$ ];  $P = 0.01$ ) but not in WOMAC pain score (mean difference,  $-0.5$  [CI,  $-1.2$  to  $0.2$ ];  $P = 0.18$ ) or the patient global assessment (mean difference,  $0.16$  [CI,  $-0.02$  to  $0.34$ ];  $P > 0.2$ ). At 26 weeks, the true acupuncture group experienced significantly greater improvement than the sham group in the WOMAC function score (mean difference,  $-2.5$  [CI,  $-4.7$  to  $-0.4$ ];  $P = 0.01$ ), WOMAC pain score (mean difference,  $-0.87$  [CI,  $-1.58$  to  $-0.16$ ];  $P = 0.003$ ), and patient global assessment (mean difference,  $0.26$  [CI,  $0.07$  to  $0.45$ ];  $P = 0.02$ ). The study concluded that acupuncture seems to provide improvement in function and pain relief as an adjunctive therapy for osteoarthritis of the knee when compared with credible sham acupuncture and education control groups.

A systematic review and updated meta-analysis was conducted by Cao, et al. [15] who reviewed 490 potentially relevant articles on the efficacy of treatment with acupuncture for knee osteoarthritis from PUBMED, EMBASE, and the Cochrane Central Register of Controlled Trials databases up to October 2011. Only randomized controlled trials that compared needle acupuncture with sham acupuncture, standard care, or waiting list control groups in patients with knee osteoarthritis were selected. Fourteen RCTs involving 3,835 patients were included in the meta-analysis. As a standard procedure, two authors independently extracted outcome data on short-term and long-term pain and functional measures. The meta-analysis found that compared with sham acupuncture control group, acupuncture was significantly better at relieving pain ( $p = 0.002$ ) and restoring function ( $p = 0.01$ ) in the short-term period, and relieving pain ( $p = 0.06$ ) and restoring function ( $p = 0.06$ ) in the long-term. And compared with the standard care and waiting list control treatments, acupuncture was significantly better at relieving pain and restoring function. They concluded that acupuncture provided significantly better relief from knee osteoarthritis pain and stronger improvement in function than sham acupuncture, standard care treatment, or waiting for further treatment.

A more comprehensive systematic study with meta-analysis was conducted by Vickers, et al. [16]. The databases MEDLINE and the Cochrane Collaboration Central Register of Controlled Trials were searched, as well as the citation lists of other systematic reviews through 2008 for studies pertaining to the use of acupuncture for four chronic pain conditions: back and neck pain, osteoarthritis, chronic headache, and shoulder pain. They conducted a systematic review and meta-analysis, which became an often-

cited source. In their review, they identified 955 clinical studies from which individual patient data meta-analyses were conducted using data from 29 of 31 eligible RCTs, with a total of 17,922 patients analyzed. In their primary analysis, including all eligible RCTs, acupuncture was superior to both sham and no-acupuncture control for each pain condition ( $P < .001$  for all comparisons). After exclusion of an outlying set of RCTs that strongly favored acupuncture, the effect sizes were similar across pain conditions. Patients receiving acupuncture had less back and neck pain, with scores that were 0.23 (95% CI, 0.13–0.33) standard deviations (SDs) lower than sham controls. Effect sizes were 0.55 (95% CI, 0.51–0.58) SDs in comparison to no-acupuncture controls. They found these results to be very robust. They concluded that acupuncture is effective for the treatment of chronic pain. The meta-analysis demonstrated that the significant differences between true and sham acupuncture revealed that acupuncture was more than a placebo, although the relatively modest differences suggested that factors in addition to the specific effects of needling were important contributors to the therapeutic effects of acupuncture.

Why are these rigorous studies challenged by Hinman Paper? Or has the Hinman Study shaken the foundation that these studies have established? Are there any standards for scientific research or clinical trials? Responses from the acupuncture research community and acupuncture profession are anxiously awaited.

#### ACUPUNCTURE-COMMUNITY CRITIQUES OF THE HINMAN STUDY

The involvement of the acupuncture community and their response to the Hinman study was unprecedented. The Traditional Chinese Medicine American Alumni Association (TCMAAA) immediately took action in responding to the Hinman study, sending a number of letters-to-the-editor to be published in *JAMA*. A series of deep analyses were conducted by Dr. A.Y. Fan [17]. *Acupuncture Today* organized interviews in response to the Hinman study. These responses to the Hinman paper can be organized into the following four categories:

##### *Flawed Research Design*

Dr. A.Y. Fan [17] pointed out that the research design of the Hinman Paper was flawed in terms of choices of primary testing factor and control.

Fan [17] stated that there is a major mistake in the primary testing factor in this study: the laser acupuncture should be the primary testing factor, not the needle acupuncture. Fan stated that in a vigorous randomized controlled trial, there is a primary testing factor or objective which should be a new therapy with unknown efficacy. The major testing factor should be

compared with a non-intervention (control) group, negative control (sham intervention group) group, or a positive control (effective therapy) group. There are four groups (control group, needle acupuncture group, laser acupuncture group and sham laser acupuncture group) in the Hinman study. In this study, the major testing factor is laser acupuncture; needle acupuncture served as a positive control which is supported by the Berman et al study that acupuncture is an effective therapy for chronic knee pain. The authors registered this trial as testing laser acupuncture, instead of needle acupuncture. If acupuncture was the major testing factor as the study title indicated, it should have had the proper control group. But in this trial with a Zelen design, the patients in the control group did not have informed consent, and the patients in the acupuncture group did have informed consent. Differences arisen in informed consent among the groups, therefore there was no comparability between these groups as the patients were not blinded. It is improper to test two different testing factors in one randomized control trial such as both laser acupuncture and needle acupuncture in this study design.

##### *Misinterpretations of Results*

Several responders criticized the Hinman paper for missing (or intentionally avoiding) reporting the clinical effectiveness of acupuncture in comparison with the control.

White, et al. [18] reviewed the Hinman Study and found that Hinman, et al. misinterpreted their own results and even “missed opportunities.” White, et al. summarized the existing evidence that already indicates a large and useful difference between acupuncture and no-acupuncture, and claimed that the effect of acupuncture in this study is consistent with previous evidence. The Hinman Study showed that after 12 weeks, knee pain was significantly reduced by acupuncture compared with the no-acupuncture control group. Even the secondary outcomes showed significant differences in favor of acupuncture for six out of eight secondary outcomes. And the response rate, which is the most patient-orientated measure of success, was 76% in the acupuncture group compared with 32% in the no-acupuncture control group. White, et al. pointed out that the study by Hinman, et al. with sub-optimal acupuncture protocol still gives clinically relevant benefits for patients with knee osteoarthritis who have few options other than surgery. White, et al. interpreted the Hinman study as giving a powerful and positive result that is consistent with the best data from other studies. “Instead of concluding that their findings do not support acupuncture for these patients, they should have concluded that patients with knee osteoarthritis should consider acupuncture as an option. Indeed, acupuncture is more likely to give relief than any other option: a network analysis comparing physical interventions for knee

pain shows acupuncture to be best. The global evidence clearly shows that acupuncture offers real and meaningful benefits for these patients with real pain and disability,” White, et al. wrote. White’s rebuttal was initially sent to *JAMA*, but was rejected.

In a careful investigation, A. Y. Fan [19] re-sorted the Hinman data, including moving the 21 participants who did not receive any treatment from the intervention group to the control group. He re-analyzed the statistics after re-adjusting the data and came to the conclusion that both laser acupuncture and needle acupuncture would be effective in Hinman’s clinical trial. Therefore, Fan strengthened White’s previously-stated conclusion.

Lao, et al. [20] found that according to the previously published protocol<sup>7</sup>, there were three primary hypotheses, mainly testing the effect of laser acupuncture against needle acupuncture, sham laser acupuncture, and no treatment at 12 weeks, as well as needle acupuncture vs. no treatment at 12 weeks. The authors’ original primary end point of the trial was at 12 weeks instead of a 1-year follow-up. Hinman’s results supported the hypothesis that needle acupuncture was superior to no treatment in improving pain and function scores at 12 weeks.

#### *Questionable Acupuncture Protocols*

The acupuncture protocols used in Hinman Paper were criticized as sub-optimal, non-standardized, and even inferior, as several responders pointed out.

Zhang, et al. [21] noted multiple deficiencies of acupuncture protocols in the Hinman study. The dosage of acupuncture with a twenty minute treatment once or twice a week for 12 weeks, with 8 to 12 sessions in total and a total 160 to 240 minutes in 12 weeks delivered is far from adequate from the professional standard in which 12 sessions of 30 min duration, administered over 8 weeks were used. “Deqi,” regarded as a prerequisite of an effective acupuncture treatment, was missing. Details of needling, such as needle manipulation, depth of needle insertion, and points selected unilateral, bilateral or both, was questionable. The dose of laser acupuncture, 0.2 J per acupuncture point, is considered too low from evidence suggested 0.5 J per point minimum to achieve a clinical effect. Zhang, et al. believed that the trial used an inferior treatment regimen.

In the letter to the *JAMA* editors, He [22] questioned the non-standard acupuncture points used in the study and the details necessary to ascertain whether the provided interventions were representative of acupuncture sessions appropriate for chronic knee pain. The inconsistency of the acupuncture protocols stood out: some patients receiving less than one treatment per week, some patients receiving one treatment per week, and others receiving two treatments per week for 12 weeks. The study failed to report how many patients received one or two treatments per

week. This is far from the commonly used frequency of acupuncture treatments for chronic knee pain due to osteoarthritis. The study also did not provide acupuncture with electrical stimulation, which not only has a dose-dependent effect on the degree of analgesia, but also induces differential neurotransmitter responses depending on the electrical frequency used. Zhang concluded that the unsystematic acupuncture regimens in the study by Hinman, et al. did not result in significant clinical benefit to patients with chronic knee pain.

#### *Violation of Research Ethics*

The Hinman Paper was evaluated from an ethical viewpoint. Its selective reporting of the results was regarded as unethical, as pointed out by Fan [23], Li [24] and others.

As Fan [23] stated in regard to the research design of the study, there is a fatal flaw in the primary testing factor in this clinical trial: the laser acupuncture should be the primary testing factor, instead of the needle acupuncture. The study was a failed clinical trial for laser acupuncture. “It is unethical to publish a ‘professional’ paper, with a group of almost-scraped data and confusing logic that misleads the readers, including the general public, physicians and policy makers, as well as fellow researchers. Hinman appears to have the intention to mislead the editors and readers.”

In a letter to the *JAMA* editors, Li [24] pointed out that “the comparison of needle acupuncture with sham laser acupuncture was not in the aims or hypotheses of this trial. In the original trial registration in 2009 and baseline publication of the protocol in 2012, all the specific aims of the trial focused on testing laser acupuncture. None of the original nine hypotheses referred to the comparison of needle acupuncture with sham laser acupuncture. Needle acupuncture appeared to be a positive control for laser treatment because it has been proven effective in a previous trial. Therefore, the conclusion that needle acupuncture was not better than sham treatment was based on a *post hoc* hypothesis. Sham laser acupuncture is not a valid control for needle acupuncture.” This was demonstrated by Hinman’s paper, Hinman’s previous paper, and the Australia/New Zealand Clinical Trials Registry: “Acupuncture for chronic knee pain trial” [registry identifier: ACTRN12609001001280. 2015-02-22.] Based on the above evidence, Fan<sup>20</sup> believed that “Dr. Hinman and her colleagues deliberately adjusted the study objectives, published for conflicting interests, and intentionally made errors to create a negative result regarding acupuncture for knee pain; and may have the intention to harm the acupuncture profession.”

#### CONCLUSION

We expect that debate around the Hinman Paper will continue. This is a healthy phenomenon for acu-

puncture research specifically, and for the acupuncture profession generally. The Hinman Paper has been intensely scrutinized by those both inside and outside of the acupuncture profession, and the resulting commentary will provide rich nourishment for further studies by acupuncture researchers and the scientific community. This is the first acupuncture study incorporating Zelen-design (randomization occurred before informed consent) and the patient-centered concept of minimal clinically-important difference (MCID), which is defined as the smallest amount an outcome must change to be meaningful to patients. MCID is a concept that captures both the magnitude of the improvement and also the value patients place on any change in their condition, though the application of both concepts in the Hinman Paper was challenged by various authors in their rebuttals. If the Hinman study aspired to be the last word in the debate about acupuncture's efficacy with knee pain, it has failed. Instead, the Hinman Paper has generated a plethora of vigorous responses which will result in more rigorous acupuncture studies.

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