Evidence-Based Medicine Skills for Acupuncturists Part I: The Hinman Trial on Chronic Knee Pain and the Importance of Critical Appraisal Skills

By **Jacob Godwin,** DAOM, Dipl OM, LAc, and **Arthur Fan**, CMD, PhD, LAc

The authors' biographies and an addendum can be found at the end of this article.

Abstract

Evidence-based medicine (EBM) skills are critical to clinical effectiveness and to developing and maintaining an effective intellectual ecosystem of clinicians, researchers, policy-makers, and academics. One important competency within the evidence-based medicine paradigm is the ability to appraise research papers critically. The authors first discuss the value of research literacy among acupuncturists and then demonstrate the importance of this skill by critically appraising a randomized controlled trial (RCT) on chronic knee pain published by Hinman et al. in *The Journal of the American Medical Association* (JAMA) in 2014.

Keywords: evidence-based medicine, Hinman trial, acupuncture, research literacy, acupuncture competencies

Introduction

Four universally accepted core competencies in EBM are required of clinicians: the ability to 1) turn clinical practice problems into focused questions, 2) systematically retrieve published literature to address their questions, 3) appraise the literature they find for applicability and scientific validity, and 4) apply their appraisal to the clinical case before them (1).

This paper focuses on the third competency, the ability to appraise clinical research critically for scientific validity and applicability to a clinical question. The example described below, a small (n=282) RCT of chronic knee pain published by Hinman et al. in 2014 (2), is particularly applicable to the issue of validity.

It received a considerable amount of media exposure considering its small size and numerous methodological flaws. This trial provides an example of how important EBM skills are to licensed acupuncturists.

The ability of the acupuncture profession to make clinical decisions based on scientific research and to respond to emergent research data depends on the level of research literacy of professional acupuncturists. Research literacy is one of the most important issues facing the acupuncture profession in the United States and is a critical competency for all healthcare providers operating under a scientific evidence-based paradigm.

How to best teach EBM competencies is a question that mainstream medicine has been grappling with for years (3,4). Research literacy is especially critical to acupuncturists as the profession integrates with mainstream medicine and assimilates with the EBM paradigm. Efforts to develop acupuncture under the evidence-based paradigm have been underway for at least a decade. The process of retooling a practice as old, complex, and diverse as acupuncture is not without significant problems to be solved (5,6). Fortunately, acupuncturists do not have to grapple with this subject alone, and they do not have to develop a new paradigm.

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Ensuring the Best Available Care for Patients

Woolf et al. (7) describe two main strategies for improving clinical outcomes and patient care. The first is what they call *fidelity,* which describes how precisely the healthcare system delivers appropriate care to patients. The second is *efficacy* and *effectiveness,* which refer to a successful intervention and the degree to which it is successful, respectively. Fidelity includes the ability of the patient to make his or her need for care clear, the ability of the clinician to recognize the indications for the interventions at his or her disposal, and the often complex mechanisms of infrastructure, information, protocol, regulation, and technology that exist between the clinician and the patient. Fidelity depends on the ability of a clinician to apply the best evidence in his or her patient's case—to know what is indicated, what is available, and how best to apply it. Collectively, these factors usually determine whether a patient receives the best care available or something inferior.

Fidelity describes how precisely and efficiently the best care available is delivered to those who need it, rather than how effective the intervention is or how to make it better. One estimate puts the percentage of American adults receiving recommended care at 55% (8). This percentage is obviously less than optimal. Discovering and perfecting the best care, and making sure that care is delivered to the patients who need it, is an ongoing improvement project across all healthcare disciplines. As difficult as this project is for other healthcare providers, it is much more difficult for licensed acupuncturists for several reasons.

Acupuncture, as an intervention, suffers from weaknesses related to both fidelity and efficacy/effectiveness. First, though efficacy has been demonstrated, research methodologies are not yet sufficiently developed to study acupuncture efficacy with much precision (9,10). The double-blind randomized controlled trial, the gold standard of medical research, depends on appropriate inert controls. Finding an inert acupuncture control has been difficult (10)—a fact that confounds nearly all clinical acupuncture research. Despite such overwhelming obstacles, acupuncture efficacy and effectiveness have been demonstrated at every level of the traditional evidence hierarchy, including large, high-quality meta-analyses (11). The barriers to improved efficacy and effectiveness data are eroding now as talented researchers wash them away gradually. However, the issue of fidelity is much more problematic.

Improving EBM Skills for Acupuncturists

The acupuncture profession is under tremendous pressure to reorganize as an evidence-based discipline capable of integrating with mainstream medicine (12,13). This pressure comes from clinicians within the profession who want to improve acupuncture through scientific models, from professional acupuncturists who are frustrated with the difficulties of making a living practicing acupuncture, and from patients who are frustrated by the lack of access and general discontinuity between acupuncture care and other therapies they may be using.

This same pressure has also been mounting from regulatory agencies outside of the acupuncture profession, but inconsistencies in educational standards, training, and practice acts, which vary widely among the states, are barriers to developing normative standards (14).

From 2000 to 2006, the National Center for Complementary and Alternative Medicine (now the National Center for Complementary and Integrative Health, or NCCIH), of the National Institutes of Health (NIH), provided R25 funding to nine Complementary and Alternative Medicine (CAM) colleges to develop EBM programs. That the NIH is funding programs to improve EBM skills demonstrates how important these skills are in modern healthcare. Zwickey et al. reviewed the competencies and teaching strategies developed and implemented to enhance research literacy at all nine R25-funded institutions (5). They found that the implementation of evidence-based competencies faces many challenges.

Zwickey et al. reported that faculty members at three of the nine colleges were "unclear about how to integrate clinical relevance into teaching about research" (5). While nine schools constitute a small sample, this finding is still disturbing. The study reported that at five institutions many courses used poor-quality research materials and articles that were not peer-reviewed. This is a common problem at all levels of acupuncture education and training in which students are taught from anecdotal evidence with little regard for scientific rigor. Further findings only deepen concern: "Other faculty members, especially those in Chinese medicine programs, tended to use historical clinical texts as substitutes for research literature. Many faculty reported that they 'used EBM' if they listed references on course materials. In fact, many of those references had been superseded by more current research or were never specifically incorporated into the curricular content" (5). Acceptance of historical texts as evidence has become a common deleterious habit among acupuncturists. Historical texts are anecdotal and can never supplant scientific research. That faculty believed they were "using EBM" by citing references is indicative of how far acupuncturists must go to reshape the profession.

Zwickey et al. found that although introducing EBM competencies to college curricula posed certain challenges, it also had "unintended benefits," including positive changes in institutional culture. The paper rightly concluded, "Practitioners in the 21st century will need to understand how research and evidence-based practice are related, and support one another in order to truly bring about optimal patient care" (5).

This paper focuses on an example of how research literacy and EBM skills protect clinicians and our profession from bad science rather than subject them to it. Critics of EBM often incorrectly characterize its standards as some sort of tyranny. Sackett addressed this misconception from the earliest days of EBM: "Evidence based medicine is not 'cookbook' medicine. Because it requires a bottom-up approach that integrates the best external evidence with individual clinical expertise and patients' choice, it cannot result in slavish, cookbook approaches to individual patient care. External clinical evidence can inform, but can never replace, individual clinical expertise, and it is this expertise that decides whether the external evidence applies to the individual patient at all, and if so, how it should be integrated into a clinical decision" (1). In addition, "evidence based medicine is not restricted to randomized trials and meta-analyses. It involves tracking down the best external evidence with which to answer our clinical questions" (1).

It is clear from the literature that from its inception, EBM has been about the responsibility of the clinician to treat individual patients based on available evidence of the highest quality. EBM is also about the clinician's ability to appraise this evidence and make clinical decisions accordingly. Among the four universally accepted EBM competencies listed above, number three calls for the clinician to appraise the evidence. Number four calls for that evidence to be applied, again by the clinician, to an individual patient. These two requirements clearly prioritize the clinician's decision-making ability.

Having established the importance of EBM skills for acupuncturists, we now turn our attention to the specific skill of critical appraisal, and how to apply it, by reviewing the example paper on chronic knee pain by Hinman et al.

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Reading a Research Paper

The first questions a clinician should ask about a research paper he or she is reading are: 1) What is the research question this paper tries to answer? 2) Does the paper answer it? 3) Can the results of the research be applied to clinical practice? These initial questions will weed out papers that cannot be relied upon either due to methodological flaws or to a lack of applicability to clinical practice. These questions are where we begin with the Hinman trial.

Many researchers published letters—in *JAMA, Acupuncture in Medicine*, and the *British Medical Journal*, among others—elaborating the many problems with the Hinman chronic knee pain trial following its publication in *JAMA*. The flaws in this trial were significant enough to prompt the Traditional Chinese Medicine American Alumni Association (TCMAAA) to file an official complaint (published in the present volume as an addendum to this paper) with the National Health and Medical Research Council (NHMRC) which funded the study. These problems include flaws in study design, problems with choices regarding the acupuncture protocol and dosing, and the statistical methods used in the study. One design flaw was that sham acupuncture should not be used as a control in acupuncture trials as small as the Hinman study (15,16). The Hinman study also used a suboptimal acupuncture protocol

with a dose that was lower than the threshold established in the literature (15,17). Finally, the Zelen design used by Hinman et al. led to a high drop-out rate and a dilution of effectiveness in the acupuncture group, along with mistakes in sample-size calculation (16-19).

What Was the Question?

The first question asked by a competent practitioner is: What is the aim of this study? There is confusion regarding the question Hinman et al. were asking in their trial. From the trial proposal, it appears that the original intent was to study "laser acupuncture," which was defined in the trial registration as "the aiming of laser light with a small pen-like device, which is applied to the skin" (17). The Hinman trial was designed to first compare the effectiveness of laser acupuncture in treating chronic knee pain to that of sham laser acupuncture. Secondly, the trial was intended to compare laser acupuncture to needle acupuncture. Finally, the trial was reportedly designed to compare laser acupuncture, sham laser acupuncture, and needle acupuncture to no treatment at all. The trial included patients aged 50 years and above with chronic knee pain. Acupuncturists certainly see this population for this condition, but did this trial ask and answer a valid clinical question?

In their conclusion (2), Hinman et al. state that "In patients older than 50 years with moderate or severe chronic knee pain, neither laser nor needle acupuncture conferred benefit over sham for pain or function. Our findings do not support acupuncture for these patients." However, this conclusion may not be supported by the findings reported in the paper. The only sham intervention was sham laser acupuncture, which is a strange choice of control for acupuncture considering the significant differences between the two interventions and the fact that laser acupuncture is not a common therapy (17). Even if it were a valid control, comparison to sham treatment provides data only on the efficacy of needles themselves. Data demonstrating clinically relevant efficacy already have been provided by much larger studies (11,20,21). We already know from these larger studies that acupuncture is superior to sham. A clinician must ask whether the Hinman trial is asking a question that already has been answered.

No trial can conclude "acupuncture is ineffective" for any condition. A trial can only demonstrate the efficacy of a particular acupuncture procedure. A trial tests a tightly controlled procedure, not an entire therapeutic intervention. An RCT finding that a particular analgesic is not effective for migraine headaches would not be used to conclude that all drugs are ineffective for migraine headaches. Likewise, an RCT testing a particular acupuncture protocol should not be used to draw conclusions about all acupuncture protocols.

It is critical that clinicians examine the procedures used in a trial before incorporating trial data into their own clinical decision-making. The selection of treatment sites, needling methods, stimulation, and other details of the protocol used in the trial must be considered. Hinman et al. did not follow the Revised Standards of Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) (22). Therefore, a clinician would have a difficult time applying the results of this trial to clinical practice. STRICTA requires that details such as the rationale, depth of insertion, intended response to a needle (e.g., *deqi*, muscle twitch), and other details that help clinicians evaluate the clinical relevance of trial results, be reported.

Another consideration is the frequency of treatment in the Hinman trial. Determining the proper dosing of acupuncture is an ongoing research topic (23). This aspect of clinical acupuncture research is a common problem area. A clinician has to know how frequently acupuncture was performed before he or she can appraise the outcome of the trial. Hinman et al., for example, delivered eight to twelve 20-minute procedures over a 12-week period. Patient compliance was not reported, but even if we assume full compliance, 0.67–1.00 treatment per week over the 12-week period was the average. According to the literature (21), performing acupuncture once a week for 20 minutes with only manual stimulation of the needles is likely to be inadequate for patients over 50-years-old with chronic knee pain. Zhang et al. are correct in pointing out that Hinman et al. chose a treatment frequency well below what is established in the literature (15). Witt et al. demonstrated the

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efficacy of acupuncture for osteoarthritis (OA) of the knee using an average of 1.5 procedures per week over an eight-week period (20). The question then is, why did Hinman et al. decide to use a small number of treatment sessions?

Was the Question Answered?

Even if we consider the research question and study design to be clinically relevant, it remains unclear whether Hinman et al. answered the question. One of the biggest problems in acupuncture research is that of small sample sizes. Recent evidence suggests that acupuncture trials require a sample size of at least 800 patients to be considered reliable (24). Hinman et al. had 0.0875 of that number, with only 70 patients receiving acupuncture. Thus, the Hinman trial is grossly underpowered.

Underpowered studies with cohorts that are too small are common in the literature (25). Typically, such studies lead to a type II error—the incorrect conclusion that an intervention has no effect. This is a likely error made by Hinman et al. Assessing the power of a study can be difficult for non-statisticians, but Trisha Greenhalgh enlightens readers on this and many other aspects of developing EBM skills for clinicians in her book *How to Read a Paper: The Basics of Evidence-Based Medicine* (25).

A clinician is not likely to find the outcomes of a suboptimal protocol reported in an underpowered trial to be of much use in clinical decision-making. Can anything be learned from the Hinman et al. data?

Salvaging Useful Data from Bad Papers

Digging into the data of a paper is the quintessence of EBM. The job of a clinician is to strip a paper down to its pure data—the actual results, not the interpretation of those results. So what does the Hinman et al. trial tell us?

Drs. White and Cummings, in a letter to *Acupuncture in Medicine* (17), provide a detailed analysis of the Hinman et al. trial on chronic knee pain, including the problems with the statistical evaluations performed in the trial. By using better-supported statistical analyses and considering the Hinman et al. results in light of the current literature, they concluded, "The correct message from the study by Hinman et al. is that even suboptimal acupuncture gives clinically relevant benefits for patients with knee OA who have few options other than surgery. Their results give a powerful and positive outcome that is clearly 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 OA should consider acupuncture as an option" (18). White and Cummings pointed out that a recent meta-analysis has demonstrated that acupuncture is more likely to give relief than any other option for patients with OA of the knee (26).

Negative results can be meaningful. Remember that Hinman et al. reported minimal improvement at an average frequency of ≤1 procedure per week over a 12-week period, while Witt et al. reported better results at an average of 1.5 procedures per week over an 8-week period. This can give us an idea of just how often this population needs to be treated—about 2 procedures per week for at least 8 weeks.

Digging into a paper and analyzing the data in different ways can salvage important lessons from papers that might otherwise be ignored.

Conclusion

The ability to critically appraise acupuncture research is crucial to the concept of fidelity described earlier. Patients, payers, regulatory agencies, and the public assume that clinicians are delivering the best available care based on the latest and highest-quality evidence. The contemporary acupuncturist must have the skills to retrieve, critically appraise, and apply to his or her patients' conditions the very best evidence available. Developing the skills demonstrated in this paper and by the many experts active in acupuncture research should be a priority for any clinician practicing acupuncture.

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Jacob Godwin, DAOM, Dipl OM, LAc, received his doctoral degree from Oregon College of Oriental Medicine and is in private practice in the State of Washington, specializing in pain management for neurological and musculoskeletal conditions. Dr. Godwin practices acupuncture based on a modern scientific model. He is also the Vice President of the AAAOM Board of Directors.

Arthur Yin Fan (Fan Ying), CMD, PhD, LAc, is an independent researcher and a leading specialist in Acupuncture and Chinese Medicine with three decades of clinical experience in both Traditional Chinese Medicine (TCM) and Western medicine. He was awarded an MD in Chinese Medicine (1986) and a PhD in Chinese Internal Medicine (1998). He also had an additional year of training in neurology as well as a four-year residency combining Chinese and Western internal medicine in integrative medicine. He was the first NIH fellow in Chinese medicine in 2002-2005. Dr. Fan has been a reviewer of medical research grants and academic papers for several peer-reviewed journals for more than fifteen years. He has published over eighty academic papers. He has been a consultant for the Center for Integrative Medicine at the University of Maryland School of Medicine. As a researcher in acupuncture, he has investigated its effect and mechanism on reducing pain and inflammation. He has also done research in herbal medicine and on the efficacy and safety of nutritional supplements. Practicing in the Washington, DC, area since 2002, Dr. Fan employs acupuncture and Chinese herbal medicine as alternative or complementary treatment for patients with various conditions. From 1998 to 2001, Dr. Fan was one of the major designers and founders of the Nanjing Chinese Medicine Center for Strokes, which combines the medical resources of ICU, neurology, acupuncture, Chinese herbal medicine, physical therapy, hyperbaric oxygen chambers, and other therapies to maximize patients' survival and recovery in a limited time. Currently, this center is listed as one of the key stroke centers in China.

P.O. Box 2255, Largo, FL 33779, USA; www.tcmaaa.org
Tel: 727-392-7782; Email:tcmaaahelp@gmail.com
TCM American Alumni Association

May 1, 2015

BY EMAIL

Prof. Kathryn North AM
Chair, Research Committee, National Health and Medical Research Council (NHMRC)
GPO Box 1421
Canberra ACT 2601 Australia

RE: Complaint Concerning Clinical Research and Reporting by Dr. Rana S. Hinman & Co-Investigators in NHMRC-Funded Research (Project 566783; FT130100175; FT0991413)

Dear Professor North and Research Committee Members:

This complaint letter was written on behalf of the Traditional Chinese Medicine American Alumni Association (TCMAAA)* and 22 other professional organizations in the United States, Australia, Canada, and the Netherlands, representing more than 40,000 professionals in traditional Chinese medicine (TCM) and acupuncture (listed below). We appreciate the continuous efforts of NHMRC, one of Australia's national organizations, in developing public health standards, advising research communities, and funding clinical research, especially in the field of complementary and integrative medicine (including acupuncture) in the recent years. We appreciate the endeavor and the striving for ensuring rigorous supervision of research integrity by NHMRC during the grant application, funding, and monitoring research implementation progresses. However, we are deeply concerned about research integrity and the credibility of Dr. Rana S. Hinman regarding one of the NHMRC-funded research projects. We believe that the report by Dr. Hinman and her colleagues regarding acupuncture for knee pain is highly biased and possibly manipulated. We thus purport a prompt and thorough investigation of the project related to acupuncture for knee pain led by Dr. Rana S. Hinman.

On October 1, 2014, Dr. Hinman and her colleagues published the results of an NHMRC-funded trial in the Journal of the American Medical Association (JAMA) (1). In the paper, the authors concluded that "in patients older than 50 years with moderate or severe chronic knee pain, neither laser nor needle acupuncture conferred benefit over sham for pain or function. Our findings do not support acupuncture for these patients" (2). Immediately after its publication, global experts questioned the design, execution, and conclusion of this trial (3).

On top of these research concerns/flaws, we believe that Dr. Hinman and her colleagues have violated research integrity. The clinical trial seems to have been originally designed and funded to test laser acupuncture while using needle acupuncture for a positive control, which was clearly stated in the authors' own submission to the Trials Registry (4) and publications (5) before the initiation of the trial. Therefore, the power of the test and other resources were only optimized to evaluate one testing treatment (laser) in the trial. This differs from the final JAMA report that the intent was to evaluate two testing treatments in one trial, namely, "laser acupuncture" (not real acupuncture) and needle acupuncture. As the original design (282 patients divided into 4 groups) was for one testing treatment of "laser acupuncture," the later amended intent of testing two unknown treatments is inappropriate and the results were thus falsified.

The major conclusion of this trial, that "needle acupuncture did not work for knee pain," is solely based on post hoc hypotheses and analyses as the specific aim of comparison between "needle acupuncture vs. sham laser" was not among the 19 pre-specified comparisons stipulated in 3 independent protocols published by the authors before the initiation of the trial (3 aims in Trial Registry, 9 aims in baseline publication, 4 and 7 aims in the protocols submitted to JAMA). As per clinical research guidelines set by the International Conference on Harmonisation, the Declaration of Helsinki, the U.S. Food and Drug Administration (FDA), and other regulatory agencies and professional organizations, conclusions from post hoc hypotheses and analyses must be stated clearly in a final clinical report (6). Further, post hoc analyses do not constitute a prospective study, but rather retrospective data comparisons. Any results obtained from post hoc analyses must, accordingly, be interpreted with caution. The authors failed to report the nature of post hoc analyses in their publication in JAMA, which may be explained as a glaring omission that violates clinical research trial guidelines and well-established reporting protocols. Therefore, conclusions drawn from such analyses in the JAMA report are questionable.

In a letter to the editor, Dr. Li raised this issue to JAMA; however, in the reply, Dr. Hinman and her colleagues stated: "He (Dr. Li) is correct that we did not explicitly state that we would compare needles with sham laser. We believed it was inherent within the planned analysis that all 3 acupuncture groups would be compared with each other…." Unfortunately, Dr. Hinman and her colleagues refused to answer the question as to why the trial hypotheses were amended after collecting the data. The authors' "[apologies] for any confusion" are insufficient and not acceptable.

Even with the flawed and underpowered study design, Dr. Hinman and her colleagues failed to draw a fair conclusion based on their research findings. In the results section of the published report, Dr. Hinman and her colleagues stated that needle acupuncture showed modest decrease in pain at 12 weeks as compared to control. The results indicate that needle acupuncture is both statistically and clinically effective for pain control at 12 weeks. However, Dr. Hinman inexplicably states the opposite as "their findings do not support acupuncture for patients with moderate or severe chronic knee pain."

We cannot know the motivation of Dr. Hinman and her colleagues in this issue. With all these flaws and mistakes related to the report by Dr. Hinman and her colleagues (see appendix 8 and 9, five papers), we are highly concerned that the intention of the report is to purposefully and maliciously undermine the profession of acupuncture and its practice. Hence, we urge the NHMRC Research Committee to investigate this matter to ensure the integrity of clinical research and true and accurate reporting of study results (7,8).

For the interests of patients, insurance companies, health care policy makers, and all relevant parties, we respectfully request transparency in any such investigation, and that the NHMRC provide results to the medical community, other relevant parties, and the public in a timely fashion. Without justifiable reasons for the flaws and mistakes, especially the failure to report the use of post hoc analyses, we believe that Dr. Hinman and her colleagues should promptly retract their publication from JAMA.

Your rapid response is appreciated. Should you have any questions, please contact the undersigned.

Sincerely,

Arthur Yin Fan, CMD, PhD, LAc
Chair, Scientific Study & Academic Affairs Committee, TCMAAA
8214A Old Courthouse Road, Vienna, VA 22182 USA
Phone: (703) 499-4428; Fax: (703) 547-8197
E-mail: ArthurFan@ChineseMedicineDoctor.US

* TCMAAA is a non-profit organization of licensed acupuncture practitioners and scholars of Complementary and Integrative Medicine in the United States. TCMAAA, similar to other TCM/Oriental Medicine and acupuncture organizations, is dedicated to the advancement of TCM/Oriental Medicine and acupuncture in research and clinical practices. We aim to facilitate the development of high-quality healthcare systems with great cost-efficiency throughout the world.

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