Journal of Traditional and Complementary Medicine Vo1. 2, No. 3, pp. 158-163

Journal of Traditional and Complementary Medicine
Journal homepage http://www.jtcm.org

Building an Evidence-Base for TCM and Integrative East-West Medicine: A Review of Recent Developments in Innovative Research Design

Sonya Pritzker* **and Ka Kit Hui**

UCLA Center for East West Medicine
David Geffen School of Medicine at UCLA

Abstract

There are many challenges to developing an evidence base for Traditional Chinese Medicine and Integrative East-West Medicine. This article offers a review of these challenges alongside an introduction and review of several innovations in healthcare research that have successfully been applied to the study of Traditional Chinese Medicine and Integrative Medicine. Such innovations include developments in Whole Systems Research, Comparative Effectiveness Research, Health Services Research, and qualitative Social Sciences Research. Each of these approaches expands upon conventional approaches to clinical research and can also be combined with clinical trial data to yield a mixed-methods approach. We conclude with a commentary on the necessity for such mixed methods studies in the continued establishment of an evidence base for TCM and IM.

Key words: Chinese Medicine (TCM), Research, Evidence-Based Medicine, Integrative Medicine (IM)

Introduction& Background

The importance of evidence-based medicine (EBM) in recent medical discourse cannot be disputed. Physicians are increasingly required to demonstrate that their clinical choices are based solidly in research evidence. For both traditional Chinese medicine (TCM) and Integrative East-West Medicine (IM), this demand has created a vibrant research community where both laboratory scientists and clinical trial specialists work to develop the evidence-base for these modalities. The findings have been mixed, and while they are sometimes quite robust, they are generally limited by the constraints imposed by existing biomedical research models. Such models, by and large, utilize disease-oriented methods aiming to understand the efficacy of a single, well-defined and self-limited treatment on one distinct outcome measure—blood serum cholesterol levels, for example, or body mass index (BMI). For both TCM and IM, this approach to research often falls short of describing the complexity of real treatment, where multiple modalities such as acupuncture, herbal medicine, patient education, and massage work together to treat a complex set of patterns and conditions within the individual.

Some innovative research that challenges existing models of clinical evaluation has recently emerged, however, and an increasing number of researchers have applied this expansion to TCM and IM. Their work has focused not only demonstrating the effectiveness of TCM and IM, but also on highlighting the cultural and personal value of these modalities in the U.S., China,

**Correspondence to:*
Dr. Sonya Pritzker, Tel: (310) 794-0712, Fax: (310) 794-3310, E-mail: SPritzker@mednet.ucla.edu,

and Europe. Several of these studies have found success through the development of mixed-methods approaches, including a combination of both quantitative and qualitative methodologies. Furthermore, many of these studies have moved beyond a strictly disease-focused model of inquiry and instead have incorporated a systems perspective on the individuals experiencing disease. With this expansion of conventional clinical research methods, these studies have successfully shown the value of a more holistic or comprehensive research approach to TCM and IM, and have further played a role in the reevaluation of research methodology for the study of medicine more broadly in the West. This article first offers an overview of the importance of EBM and the challenges of developing evidence in TCM and IM. We then describe some of the advances in innovative research methodologies, including Whole Systems research, Comparative Effectiveness Research, and social science approaches to the research of TCM and IM. We conclude with a discussion of the critical need for such innovations in the establishment of an evidence base for TCM and IM. In light of the very real crises in health care worldwide, where multiple, chronic diseases that are complicated, expensive, and difficult to manage are rapidly becoming the norm, it is imperative that researchers in China as well as the West develop research methodologies that address multiple conditions as multiple aspects of illness experience and healing process simultaneously (Briggs, 2009; Hui and Zhang, 2010; Zhao et al., 2011).

Evidence-Based Medicine

Evidence-based Medicine (EBM), briefly, relies on "the conscientious, explicit, and judicious use of current best evidence from clinical care research in the management of individual patients" (Sackett et al., 2007). An expert clinician is urged to merge this evidence, which largely derives from randomized control trials (RCTs) evaluating the efficacy of certain treatments, with "individual clinical expertise" in order to generate an individually tailored approach to treatment (Sackett et al., 2007).Practice that is evidence-based, and "evidence-informed" (Evans et al., 2012; Glasziou, 2005) at the same time as taking into account the patient's priorities and the practitioners' wisdom is thought to encourage the development of a genuine partnership between the physician and a well-informed patient. Ideally, a process of shared decision making emerges out of such an interaction. Here, EBM overlaps with the emerging discourse on "patient-centered medicine" in contemporary healthcare (Barry and Edgman-Levitan, 2012; Clancy and Collins, 2010;Reuben and Tinetti, 2012).

Although EBM offers a seemingly ideal solution for the complex decision-making process in contemporary medicine,conclusions regarding it's practical use continue to be debated. Critics have highlighted, for example, the tendency to devalue evidence based on clinical experience in most EBM discourse, which favors knowledge based solely in research evidence, primarily the randomized clinical trial (RCT).Several scholars have indeed shown the broad gap between clinical evidence and research evidences in the everyday practice of medicine (Duggal and Menkes, 2011; Hay et al., 2008). Other critics point out the limitations of most RCT evidence, underscoring the facts that most randomized clinical trials are flawed in terms of sample size, generalizability, and researcher bias (Duggal and Menkes, 2011; Feinstein and Horwitz, 1997). Finally, critics argue that the application of the "average effects" of clinical trials to individual patients offers no guarantee of success, and they express frustration with the extensive skills required to communicate evidence to patients in a meaningful way (Duggal and Menkes, 2011; Liu, 2011). Regardless of these limitations, EBM is here to stay, and researchers in both TCM and IM must take the call to establish an evidence base for clinical decision making quite seriously.

Creating Research Evidence in TCM & Integrative East-West Medicine—The Hurdles

As many readers will recognize, research in both TCM and IM comes with unique set of challenges. The first, most obvious challenges have to do with the core differences between biomedicine and TCM. Such disparities range from fundamental differences in understanding about how the body works to differences in diagnostic practice and treatment approach. For example, in TCM the body is ideally understood as an interconnected network of mental, physical, and spiritual processes, each of which is constantly affected by the other. Health is understood as an intricate and ongoing balance of these multiple processes, and disease is understood to be a manifestation of imbalance at many levels of the self (Hui et al., 2006).

Differences like these can make it difficult to research either TCM or IM with current medical research

models, including especially the gold standard clinical trial or RCT. The RCT, in general, attempts to research one variable, such as a specific drug or procedure, on another variable, such as a score on an objective scale measuring distress, or a biological marker such as cortisol levels, in relation to one disease or condition. For TCM and East- West IM researchers who are committed to looking beyond single biomedical diagnoses, the RCT can be problematic due to the need for TCM practitioners to diagnose sometimes multiple TCM patterns in conjunction with subjects' biomedical assessments (Lao et al., 2001; Ruggie, 2004). Treatment variations based on pattern differentiation further complicate the research process. There are also issues with outcomes measurement, where in comparison to the single or sometimes double outcomes of the conventional RCT, TCM looks to many outcomes at once to understand effectiveness (Lao et al., 2001; Ritenbaugh et al., 2010).

The second major set of challenges in both CAM and IM research has to do with getting financial support from government and private funding organizations (Ritenbaugh et al., 2010). In the U.S., the National Institutes of Health (NIH) funds many CAM and IM studies through the National Center for Complementary and Alternative Medicine (NCCAM) as well as through other institutes within the NIH. The overall budget for CAM and IM research is small, however. There also remains a significant amount of resistance to CAM and IM research within the professional medical community (Offit, 2012; Srivastava, 2012). CAM and IM studies are thus particularly challenged by the need to create studies that fit in with the existing demands of medical researchers and grant review committees, where CAM and IM techniques are often approached as if they were new drugs or procedures rather than centuries-old approaches to holistic healthcare (Ruggie, 2004).

A third major challenge facing IM researchers consists of finding publishing opportunities within mainstream medical research journals once they have completed their studies (Ritenbaugh et al., 2010). In the English language, there are several internationally, respected, peer-reviewed journals dedicated to the publication of CAM and IM research, including *BMC Complementary and Alternative Medicine, The Journal of Complementary and Alternative Medicine, The Journal of Traditional and Complementary Medicine, Evidence-Based Complementary and Alternative Medicine (eCAM), Complementary Therapies in Medicine, and Alternative Therapies in Health and Medicine*. There are also several more journals dedicated solely to acupuncture and herbal medicine research in Chinese and IM, such as *The Journal of Chinese Medicine and Acupuncture in Medicine*. When IM researchers want to speak to a broader audience of more mainstream biomedical physicians and researchers, however, they are consistently challenged to adjust their research reports to conform to the underlying assumptions and expectations, including especially the supremacy of the RCT, of more mainstream journals.

Overcoming the Challenges

Despite these many challenges, there have been many research teams at major universities who have made significant inroads into creating an evidence-base for TCM and IM by expanding upon biomedical RCT designs. For example, many TCM researchers, in China especially, utilize research designs ensuring that subjects are treated according to their genuine Chinese medical diagnoses in addition to their standardized biomedical diagnoses. Such work expands on the conventional RCT model where all patients are treated with a standard protocol.

Other innovative strategies for RCT design in TCM and IM draw upon the notion of "Whole Systems Research" or WSR. WSR studies attempt to measure the *effectiveness* of whole medical systems such as Ayurveda or Chinese medicine as they are practiced in real life (MacPherson, 2004; Verhoef et al., 2005). Here, the term "effectiveness" points to a comprehensive, more person-centered notion that the traditional notion of "efficacy." Whereas efficacy usually emphasizes the effect of one treatment agent on a single outcome measure, effectiveness looks at the effects of a treatment or set of treatments on a whole range of outcome measures. Whole Systems studies can thus be classified as a type of "pragmatic" clinical trial, which focus on measuring a whole "package of care" (MacPherson, 2004) and ultimately investigates the effectiveness of care as it is practiced in the "real world" (Briggs, 2009; Witt et al., 2012). In many ways, effectiveness research thus captures the synergistic effects of TCM and IM, and further falls into alignment with the emerging systems biology approach of evaluating traditional medicine (van der Greef, 2011).

Comparative Effectiveness Research, or CER, also often aims to evaluate health care modalities along these lines (Coulter and Khorsan, 2008).The treatment group in such studies thus receives the whole package of care

associated with whole systems of healing in addition to standard biomedical treatment. The control group, on the other hand, receives only biomedical treatment. Examples of such studies include research that looks at acupuncture as a complex package of care for real patients suffering from real conditions such as back pain or headaches, as well as research on combined acupuncture and education for the treatment of cancer-related fatigue (Johnston et al., 2011; Thomas et al., 1999; Vickers et al., 1999). Importantly for both Whole Systems Research and Comparative Effectiveness studies, the U.S. government is increasingly beginning to value these approaches to clinical trial design (Mullins et al., 2010). Along with this increased acceptance will hopefully come more opportunities for publishing this type of research in mainstream medical journals.

Finally, yet other studies of TCM and IM have gone around the RCT altogether, incorporating research models derived from the social sciences as well as from Health Services Research (HSR) to demonstrate the validity of alternative forms of research for these modalities. HSR spans many methodological disciplines beyond clinical medicine, including epidemiology, economics, sociology, anthropology, psychology, and biostatistics (Vargas et al., 2004), and examines how people get access to health care, how much care costs, and what happens to patients as a result of this care. The main goals are to identify the most effective ways to organize, manage, finance, and deliver high-quality healthcare. HSR methodologies include both quantitative approaches, including cost effectiveness measurement, cost benefit analyses, and outcomes research, among others, and qualitative approaches, including surveys, interviews, and document review (Coulter and Khorsan, 2008).

Social science researchers, including sociologists, medical anthropologists, and some psychologists,on the other hand, use in-depth qualitative methodologies such as participant observation, focus group interviews, video-recording, and ongoing semi-structured interviewing. Such techniques, as Claire Cassidy points out, are “time and cost effective for finding out generally what people think is going on.” (Cassidy, 2001). These methods are ideal for the outset of a detailed research study when researchers need to first assess the major social, cultural, economic, and personal themes influencing the process under observation (Creswell et al., 2011; Potrata, 2005). As such, social science methods demonstrate what actually happens in an IM setting--including the way healing spaces are organized, the kinds of explanations offered to patients, the way evidence is interpreted in TCM and IM, and the way students learn the language of TCM and IM. As opposed to simply showing efficacy narrowly defined, such studies offer insight into social and cultural determinants of health behavior, patient-practitioner relationships, and self-care (Deng et al., 2010). In TCM and integrative East-West medicine in particular, these types of studies include examinations of Chinese medicine users in the U.S. (Cassidy, 1998a, 1998b), studies of the ways physicians in integrative hospitals in China negotiate diagnosis and treatment (Karchmer, 2010), the process by which TCM undergoes globalization (Zhan, 2009), or the ways in which contemporary students of Chinese medicine participate in the Chinese-English translation of concepts (Pritzker, 2011, 2012).Many of these social science studies have come a long way towards showing the effectivenessof TCM and IM techniques in treating a range of conditions, especially chronic illnesses and pain. Although these types of qualitative studies are less commonly supported by major medical research grants, and are often relegated to qualitative journals, there has recently been renewed interest at the U.S. Institute of Medicine and the U.S. National Institutes of Health in incorporating more mixed-methods into clinical study design (Creswell et al., 2011; Deng et al., 2010).

The Best of Both Worlds

There is clearly value to the conventional RCT approach. It is highly specific, and especially for single conditions where there is a clear etiology, provides a rigorous methodology for testing the efficacy, and side effects profiles, of particular treatments. The limitations of this approach are quite clear, however, even for strictly biomedical practitioners.RCTs attempting to measure the treatments effects on the average patient often overlook significant differences in individuals, and make it difficult to parse and apply findings in evidence-based practice that, by its very nature, is focused on specific cases (Liu, 2011). RCTs and the compilation of RCTs collected in systematic reviews are complicated by the difficulty in creating unbiased trials that have a large enough sample size, and utilize adequate control mechanisms to ensure reliability. For TCM and IM, moreover, RCTs using discrete biomedical disease categories as a starting point for their inquiries are challenging due to differences in approach to evaluation

and treatment of patients.

From our perspective at the UCLA Center for East-West Medicine, the successful development of both TCM and East-West IM in the contemporary world hinges on the development of evidence that does not sacrifice the integrity of either approach to care. This article has offered several examples of approaches to research that better serve the goal of evaluating TCM and IM as they are practiced in actual clinical settings. Whole Systems Research (WSR), Comparative Effectiveness Research (CER), and qualitative research based in the social sciences all offer promising techniques for building an even stronger and more comprehensive evidence base for TCM and IM. Most importantly, such research techniques, especially when used in combination with conventional RCT approaches in mixed-methods studies, offer more holistic approach to researching TCM and IM by showing real outcomes based on the way they are actually practiced.

Research that emphasizes the emerging health models as they are developed in integrative settings is becoming increasingly important given the prediction that "the current health systems of nations around the world will be unsustainable if unchanged over the next 15 years" (PricewaterhouseCoopers, 2005). In the U.S., the ensuing moves to reform health care to make it more preventative and person-centered at the same time as evidence-based—observable especially in major changes in health care research funding at the government level (Clancy and Collins, 2010)—demand that we establish research methodologies that investigate TCM and IM as they function to treat and manage multiple interconnected, complex and ongoing conditions. From our perspective, it is imperative that researchers in China, Hong Kong, and Taiwan. where there is extensive IM infrastructure already available for research, play a role in the development of such innovative approaches to the evaluation of TCM and IM (Hui and Zhang, 2011).

Authors' Contributions

S. Pritzker drafted the initial article, and K. Hui worked on editing and rewriting the final submission.

Acknowledgements

Organizations providing financial support for this review include the Oppenheimer Family Foundation, the Annenberg Foundation, and the Panda Foundation. This paper is based on K. Hui's presentation at the Taiwan International Symposium on Traditional Chinese Medicine 2011.

References

Barry, M.J., Edgman-Levitan, S., 2012. Shared decision making--pinnacle of patient-centered care. N Engl J Med 366, 780-781.

Briggs, J., 2009. Comments to the IOM. Paper presented at the Summit on Integrative Medicine and the Health of the Public, Washington, D.C.

Cassidy, C.M., 1998a. Chinese medicine users in the United States. Part i: Utilization, satisfaction, medical plurality. J Altern Complement Med 4, 17-27.

Cassidy, C.M., 1998b. Chinese medicine users in the United States. Part ii: Preferred aspects of care. J Altern Complement Me, 4, 189-202.

Cassidy, C.M., 2001. Beyond numbers: Qualitative research methods for Oriental medicine. In G. Stux & R. Hammerschlag (Eds.), Clinical acupuncture: Scientific basis. Berlin: Springer.

Clancy, C., Collins, F.S., 2010. Patient-centered outcomes research institute: The intersection of science and health care. Sci Transl Med, 2, 37cm18

Coulter, I., Khorsan, R., 2008. Is health services research the holy grail of complementary and alternative medicine research? Altern Ther Health Med 14, 5.

Creswell, J.W., Klassen, A.C., Plano, V.L., Clegg Smith, K., 2011. Best practices for mixed methods research in the health sciences. National Institutes of Health Retrieved from http://obssr.od.nih.gov/scientific_areas/methodology/mixed_methods_research/index.aspx.

Deng, G., Weber, W., Sood, A., Kemper, K.J., 2010. Research on integrative healthcare: Context and priorities. Explore (NY) 6, 143-158.

Duggal, R., Menkes, D.B., 2011. Evidence-based medicine in practice. Int J Clin Pract 65, 639-644.

Evans, R., Maiers, M., Delagran, L., Kreitzer, M. J., Sierpina, V., 2012. Evidence informed practice as the catalyst for culture change in CAM. Explore (NY) 8, 68-72.

Feinstein, A.R., Horwitz, R.I., 1997. Problems in the "evidence" of "evidence-based medicine". Am J Med 103, 529-535.

Glasziou, P., 2005. Evidence based medicine: Does it make a difference? Make it evidence informed practice with a little wisdom. BMJ 330, 92; discussion 94.

Hay, M.C., Weisner, T.S., Subramanian, S., Duan, N., Niedzinski, E.J., Kravitz, R.L., 2008. Harnessing experience: Exploring the gap between evidence-based medicine and clinical practice. J Eval Clin Pract 14, 707-713.

Hui, K.K., Hui, E.K., Johnston, M.F., 2006. The potential of a person-centered approach in caring for patients with cancer: A perspective from the UCLA center for east-west medicine. Integr Cancer Ther 5, 56-62.

Hui, K.K., Zhang, W.J., 2010. Innovative clinical scientific research promotes chinese medicine development. Zhongguo Zhong Xi Yi Jie He Za Zhi 30, 789-792.

Hui, K.K., Zhang, W.J., 2011. China is poised to build a better healthcare delivery system. Zhongguo Zhong Xi Yi Jie He Za Zhi 31, 107-110.

Johnston, M.F., Hays, R.D., Subramanian, S.K., Elashoff, R.M., Axe, E K., Li, J.J., Kim, I., Vargas, R.B., Lee, J., Yang, L., Hui, K.K., 2011. Patient education integrated with acupuncture for relief of cancer-related fatigue randomized controlled feasibility study. BMC Complement Altern Med 11, 49.

Karchmer, E., 2010. Chinese medicine in action: On the postcoloniality of medical practice in China. Medical Anthropology 29, 226-252.

Lao, L., Ezzo, J., Berman, B., Hammerschlag, R.,2001. Assesing clinical efficacy of acupuncture: Considerations for designing future trials. In G. Stux & R. Hammerschlag (Eds.), Clinical acupuncture: Scientific basis (pp. 187-209). Berlin: Springer.

Liu, L., 2011. The clinical trail barriers. Nature Outlook 480, S100.
MacPherson, H., 2004. Pragmatic clinical trials. Complement Ther Med 12, 136-140.
Mullins, C.D., Whicher, D., Reese, E.S., Tunis, S., 2010. Generating evidence for comparative effectiveness research using more pragmatic randomized controlled trials. Pharmacoeconomics 28, 969-976.
Offit, P.A., 2012. Studying complementary and alternative therapies. JAMA 307, 1803-1804.
Potrata, B.,2005. 'She did, he said': The use of ethnography in cam research. Complement Ther Med 13, 131-138.
PricewaterhouseCoopers, 2005. Healthcast 2020: Creating a sustainable future (pp. 56). Retrieved from http://www.providersedge.com/ehdocs/ehr_articles/HealthCast2020-Creating_a_Sustainable_Future.pdf
Pritzker, S.E., 2011. The part of me that wants to grab: Embodied experience and living translation in U.S. Chinese medical education. Ethos 39, 395-413.
Pritzker, S.E., 2012. Living translation in U.S. Chinese medicine. Language in Society 41, 343-364.
Reuben, D.B., Tinetti, M.E., 2012. Goal-oriented patient care--an alternative health outcomes paradigm. N Engl J Med 366, 777-779.
Ritenbaugh, C., Aickin, M., Bradley, R., Caspi, O., Grimsgaard, S., Musial, F., 2010. Whole systems research becomes real: New results and next steps. J Altern Complement Med16, 131-137.
Ruggie, M., 2004. Marginal to mainstream : Alternative medicine in america. Cambridge, UK ; New York, NY: Cambridge University Press.
Sackett, D.L., Rosenberg, W.M., Gray, J.A., Haynes, R.B.,Richardson, W.S., 2007. Evidence based medicine: What it is and what it isn't. 1996. Clin Orthop Relat Res 455, 3-5.
Srivastava, R., 2012. What's the alternative? The worldwide web of integrative medicine. N Engl J Med 366, 783-785.
Thomas, K.J., Fitter, M., Brazier, J., MacPherson, H., Campbell, M., Nicholl, J.P., Roman, M., 1999. Longer term clinical and economic benefits of offering acupuncture to patients with chronic low back pain assessed as suitable for primary care management. Complement Ther Med 7, 91-100.
van der Greef, J., 2011. Perspective: All systems go. Nature 480, S87.
Vargas, R.B., 3rd, Landon, B.E., Shapiro, M.F., 2004. The future of health services research in academic medicine. Am J Med 116, 503-507.
Verhoef, M.J., Lewith, G., Ritenbaugh, C., Boon, H., Fleishman, S., Leis, A., 2005. Complementary and alternative medicine whole systems research: Beyond identification of inadequacies of the RCT. Complement Ther Med 13, 206-212.
Vickers, A., Rees, R., Zollman, C., Smith, C., Ellis, N., 1999. Acupuncture for migraine and headache in primary care: A protocol for a pragmatic, randomized trial. Complement Ther Med 7, 3-18.
Witt, C.M., MacPherson, H., Kaptchuk, T.J., Wahlberg, A., 2012. Efficacy, effectiveness, and efficiency. In V. Scheid & H. MacPherson (Eds.), Integrating East Asian Medicine into Contemporary Healthcare. Elsevier, London, pp. 123-138.
Zhan, M., 2009. Other-worldly: Making Chinese medicine through transnational frames. Durham: Duke University Press.
Zhao, J., Hui, K.K.,Cao, H.X.,2011. Whole systems research and comparative effectiveness research in Chinese medicine. Zhongguo Zhong Xi Yi Jie He Za Zhi 31, 1157-1160.