Interview with Professor Jianping Liu, on Evidence-Based Medicine and its Relevance to Chinese Medicine

Xun Li*
Zhaolan Liu

Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, China

Introduction

Prof. Jianping Liu is the Director of Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine. He was awarded in 2006 as 'Chang Jiang Scholar' Professorship under the Ministry of Education in China. He has been working on the clinical effectiveness evaluation of traditional Chinese medicine (TCM) since 1997. He currently leads more than 10 national level projects and has international academic cooperation with researchers and institutes from Australia, the United States, Denmark, the United Kingdom, and Norway. Prof. Liu has more than 370 publications in peer review journals including 69 SCI journal papers. He also has 18 systematic reviews in the Cochrane Database of Systematic Review related to Chinese medicine for various conditions.

Prof. Liu is a member of the Advisory Board of the Cochrane Complementary Medicine Field and editor of the Cochrane Hepato-Biliary Group. He is also on the Editorial Board of another 11 Journals.

Prof. Liu has a broad and in-depth understanding of evidence-based medicine (EBM) and evidence-based practice (EBP).

EBM is not warmly welcomed by many practitioners because most practitioners do not understand what EBM is about and what systematic reviews and clinical trial are for. We invited Prof. Liu to share his views on the current situation, challenges and outlook of EBM in the field of TCM.

The Questions

Li: Hello Prof. Liu. To start our interview, could you please describe your work in China?

Liu: I established the Centre for Evidence-Based Chinese Medicine in Beijing University of Chinese Medicine in 2005. We have six full time staff, six PhD and six master's students. The Centre provides courses in the areas of clinical epidemiology, EBM, health economics, medical literature reading, and medical statistics for undergraduate and postgraduate students at the university. We have more than 30 international and domestic research projects about TCM clinical evaluation. The Centre has become a pioneer in EBM for TCM in China.

Li: Thank you very much! There is a question asked by many practitioners: How should we understand the difference between systematic reviews (SRs) and large trials?

Liu: SRs and well designed multi-centre randomised controlled trials (RCTs) are both regarded as the gold standard of clinical evidence. However trials are the first-level evidence, which collect data directly from patients, whereas SRs are the second-level evidence based on literature. To be more exact, SRs are nowadays mostly based on published clinical trials. Clinical trials give direct data about one intervention while SRs synthesise the data from multiple clinical trials with similar interventions and patient population.

Li: So SRs are based on clinical trials. Then why is it important to conduct SRs of Chinese medicine?

Liu: In spite of the long history of application, there is lack of reliable clinical evidence for the consumers to determine the

* Correspondent author; e-mail: tina000341@163.com

usage of Chinese medicine, which undermines its acceptance. In the past, TCM practitioners have kept their understanding of TCM and experiences in practice mostly in case reports and records of observation. Nowadays, there are more and more clinical studies in TCM area, such as clinical trials, observational studies, and case series. However, it is very difficult and time consuming for the practitioners and patients to read all of them and make judgment.

SR is a very important approach to get a complete view of existing high-level evidence of clinical studies based on literature review and it is used for the development of best practice. Firstly, SRs generate clinical recommendations by presenting a full picture of current clinical evidences, which helps guide the clinical practice and helps health authorities to develop regulations and guidelines. For example, the logo of the Cochrane Collaboration is actually a representation of the results of a SR of RCTs where corticosteroids were given to women at risk of giving birth too early. The first included RCT was reported in 1972, indicating that the treatment was effective in reducing the infant death from complications and immaturity by 30 to 50 per cent. Twenty years later, seven more trials had been reported. However, because no systematic review of these trials had been published until 1989, most obstetricians had not realised that the treatment was so effective. Instead, they applied more expensive and less effective treatments and tens of thousands of premature babies have probably suffered and died unnecessarily. This is just one of many examples of the human costs resulting from failure to perform systematic, up-to-date reviews of RCTs of health care.

Secondly, SRs can help researchers identify knowledge gaps. Based on the comprehensive search and analysis of high level clinical studies, SRs identify adequate clinical evidence for recommendations and also the research gap where reliable evidence is absent.

Thirdly it supports new drug development because once the kind of evidence needed is identified, it becomes easier to proceed with the new drug development. What's more, SRs summarise all existing high-level clinical evidences both qualitatively and quantitatively, which is very helpful for the consumers to get comprehensive, objective and profound knowledge in a short time. Last but not the least, SRs could improve the quality of clinical study design by evaluating the methodological quality of existing studies, so that the researchers can learn from the 'lessons' from the finished studies and improve in the future.

Nowadays, Lancet, one of the world's best known, oldest and most respected general medical journals, requires authors to submit a clinical trial together with a SR, because it is essential for the researcher to get a full picture of the current clinical evidence within the area before initiating and conducting a clinical trial.

Li: It seems that SRs are indeed very important and meaningful nowadays. Actually many practitioners and researchers are interested in conducting a SR, but don't know where to start. What are the priorities in SRs of TCM?

Before determining the topic for a SR, you might consider the following two questions:

First, how many trials have been published in this area? It would be more meaningful to focus on the area with sufficient existing trials because a SR functions as a comprehensive summary, and there is usually more urgent need in the area with greater research interest. For example, it would be better to do a SR of *taiji* for migraine rather than *taiji* for cold. Although it could be also meaningful to explore the effectiveness of *taiji* for cold, it might be difficult to carry out a SR review as there may be limited clinical studies available.

Second, what about the popularity of this TCM therapy by consumers? The ultimate goal of EBM practice is patient-centered care. The interest of the patients, practitioners and policy makers to some degree guides the interest of the researchers. SRs should focus on the TCM widely used by the consumers first, thus being able to bring about reliable recommendations for clinical decision. For example, we should pay more attention to the outcomes which patients care more, such as survival time and quality of life, instead of too many biomarkers and laboratory indices.

Li: Thank you, I think it would be very helpful for those who are thinking about carrying out a SR. Also I remember you mentioned that 50% of the existing SRs concluded that there was still insufficient evidence about acupuncture and Chinese herbal medicine. How should we interpret the findings? How does it compare with other interventions?

Liu: Among the 145 Cochrane reviews in complementary and alternative medicine (CAM) field, there are 82 reviews, 56.6% of the total, that find insufficient evidence for conclusive recommendations.[1] This means that there is still a big research gap in acupuncture and Chinese herbal medicine, and we cannot bring about conclusive recommendations for clinical decisions based on the current findings from the limited number and low quality of clinical trials. There should be more clinical studies with rigorous design and adequate implementation in the future. However, this is not a problem in TCM only, rather it's universal. A review based on the newly published and updated Cochrane review found that only 14% of the 155 papers concluded with adequate evidence.[2] We cannot recommend any treatment method with confidence if

there is insufficient reliable evidence. Instead, we see the gap and need for future research.

Li: There seems to be both difficulties and outlooks in SRs! What are the problems and challenges of current SRs in TCM? Are there other ways if SR does not fit TCM best?

Liu: Currently, SRs usually include only RCTs, thus missing information from other types of studies, for example, non-randomised controlled studies, observational studies and non-controlled studies. On the other hand, SR and RCT were introduced into TCM field in the 1980s. These new concepts have been taken up by Western medicine for a much longer time and are gradually being taken up by TCM.

Although RCTs are believed to be the gold standard of interventional studies, in some areas, they are not the most appropriate type of study design due to ethical issues and size of sample, etc. For example, if patients wish to receive a herbal decoction instead of Western medicine, it would be difficult to randomise the patients into TCM group and Western medicine group. And, actually, most types of clinical information of TCM are within the categories of clinical studies mentioned above.

Secondly, SRs concentrate on the evaluation of internal validity, which undermines the strength of external validity, thus bringing the problem in generalising the study results in a larger population. What's more, due to the general poor study quality of existing TCM studies, there is still insufficient information and inconclusive results for clinical decision.

There are many challenges in conducting SR in TCM area but also solutions.

Firstly, the topic of TCM SR is narrowed down because many of the TCM interventions lack definition and clear classification. When we conduct clinical trials, it's important to identify the intervention in the design stage.

Secondly, there is lack of diversity and capacity of the review team. It is very important for a research team to have expertise in all the relevant areas. I think when doing a SR, the team should consist of researchers with professional skills in clinical, methodological, statistical areas and also language.

Also one of the challenges of SR in TCM lies in the heterogeneity of TCM interventions. There are usually a lot interventions and outcome measurements involved in the clinical literature which is difficult to synthesise. For example, if one trial is about herbal decoction, which is the most traditional format, such as *Xiao Chai Hu Tang,* and another trial is about herbal proprietary medicine such as *Xiao Yao Pill*, even if the control groups receive the same Western medicine and the two trials report the same outcomes, we cannot combine them in one meta-analysis, because different forms of herbal medicine are regarded as different interventions. Even herbal decoctions with different formulae are heterogeneous thus should not be synthesised. In a word, we could not mix apples with oranges when we regard them as different fruits. However, we can still provide qualitative data and analysis in the SR. In the future, the standardisation of interventions, controls and outcome measurements is very important in clinical trial reporting.

Many of the clinical studies of TCM are published in Chinese, which makes it difficult for the English speakers to obtain from outside China. I suggest international cooperation especially at the literature searching stage.

Lastly, the quality of clinical studies is still generally poor. The SRs based on these trials with low methodological quality and reporting are by some people thought as 'garbage in, garbage out', and this is also the main reason for why we always fail to publish SRs of TCM in the top journals. For clinical trials and SRs, we should always conduct research according to relevant international guidelines, produce the protocol before the study, and stick to it along with the whole study process.

When we get away from the challenges and shortcomings, we should also consider the question that, is there any other way for TCM apart from SR? The clinical practice of TCM is individualised and dynamic, and sometimes it's difficult and inappropriate to conduct blinding and randomisation. On one hand, we should work out high quality study designs and figure out the methodology which is more suitable to TCM. On the other hand, apart from SRs, we should also pay attention to the information more relevant to the clinicians, including observational studies, case series and case reports.

Li: That's inspiring. However, many TCM practitioners have the question that would EBM become cookbook therapy and reduce Chinese medicine, for instance acupuncture, a complex intervention, to standard therapy. Some people have the fear that future acupuncture practice will become not real TCM acupuncture; for example, if acupuncture is not better than sham, then acupuncture will not be funded.

Liu: First of all, I don't think there should be any fear or concern that EBM would reduce the use of real TCM. EBM is a method, or idea of presenting the best evidence. It is based on the actual practice, and finally aimed at providing recommendation for the practice. By conducting research and collecting evidence, EBM only reduces the use of practice without actual effectiveness by providing recommendation of 'not doing'. We need to explore better approaches to study TCM as a system of complex intervention.

The clinical research of TCM including acupuncture emerged since the 1980s, which is not long ago. There are still many issues to be discussed and improved in clinical research. There has been a lot of exploration in the types of sham to apply in the acupuncture trials, and we have to say that the answer has not completely been addressed yet. Clinical study develops together with medical practice; and I believe that if something really works and we can use the appropriate study to present it, it can not weaken the popularity, rather, exactly the reverse.

Li: That's very encouraging. But if acupuncture points are used in a few trials, then only these points are to be used in future practice. Do you think this will happen?

Liu: No, I don't think so. We are conducting trials of acupuncture because this whole treatment theory and system needs evidence to be accepted by professionals. In order to meet the design of clinical trials, we have to select some certain points for acupuncture. However, once this individualised system is accepted based on reliable evidence, and if the acupoints do work, they will be applied clinically.

Li: How is EBM developed in China? How will it impact on Chinese medicine practice?

Liu: The medical care in China will be evidence-based in the future, and China's policy makers are promoting the establishment of clinical guidelines and standard pathways in the health system including TCM. Thus I think in the future, EBM practice is more and more important, and could be essential for clinical decision making.

Li: Where will Chinese medicine be in 10 years? EBM only?

Liu: *(Laugh)* Well, I am not sure whether EBM will be the only way. But definitely, it will be prevalent in the next 10 years, and even 100 years. EBM is one way to develop best clinical practice based on not only unbiased evidence, but also respect of the patients' preference and the expertise of the practitioners. So when we hold the data from the evidence-based studies, let's say, SRs in our hands, we still have to listen to patients' attitudes and expectations, also make judgments and decisions together with our experiences. For example, there has been evidence saying that acupuncture is effective for migraine, but your patient really doesn't feel like receiving acupuncture, you have to communicate properly with him/her, or consider other treatment methods such as pain killer, herbal medicine or massage. We should pay attention to the evidence of the effectiveness of Chinese medicine and simultaneously explore the ways to assess the capacity of Chinese practitioners.

Li: That's wonderful. Thank you very much Prof. Liu!

Note: To further understand the definition of various terms mentioned in this interview, please visit http://www.cochrane.org/glossary/5.

References

1. Manheimer E, Berman B, Dubnick H, Beckner W.Cochrane reviews of complementary and alternative therapies: evaluating the strength of the evidence. The 12th International Cochrane Colloquium; 2–6 Oct. 2004; Ottawa.
2. Okwundu CI, Rohwer A, Zani B. Quality of Evidence: Are Cochrane systematic review authors speaking the same language? The 20th Cochrane Colloquium; 30 Sep.–3 Oct. 2012; Auckland.