

REPLY

Evidence for traditional Chinese medication to treat cardiovascular disease

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We thank Dr Xingjiang Xiong for his Correspondence (Integrating traditional Chinese medicine into Western cardiovascular medicine: an evidence-based approach. *Nat. Rev. Cardiol.* doi:10.1038/nrcardio.2014.177-c1)¹ on our Review article (Traditional Chinese medication for cardiovascular disease. *Nat. Rev. Cardiol.* 12, 115–122; 2015).² We would like to take the opportunity to clarify a few issues raised by Dr Xiong.

First, we defined ‘TCM’ as ‘traditional Chinese medication’ rather than ‘traditional Chinese medicine’ in our Review, which was clearly stated in the abstract and introduction.² This distinction is important because most therapeutic effects of traditional Chinese medicine on cardiovascular diseases have stemmed from Chinese herbal medication, although a number of non-pharmacological therapies (such as dietary supplements, acupuncture, moxibustion, massage, and exercise) exist, with scarce evidence from randomized clinical trials (RCTs). Dr Xiong suggests that “numerous appropriate studies on Chinese herbal medicine for the treatment of hypertension”¹ had been omitted from our Review. However, owing to the poor quality of most RCTs of TCM for the treatment of cardiovascular diseases, we had to set strict selection criteria for these RCTs. Consequently, only 68 RCTs out of 1,541 eligible reports identified satisfied our criteria. The two studies given as examples by Dr Xiong were excluded from our Review for the following reasons. In the first study, Tong *et al.* reported blood pressures before and after treatment only in graphs (Figure 3 in their study), but not in numbers and, therefore, we were unable to extract quantitative data from this paper.³ The second study by Xu *et al.* had a Jadad score of 1,⁴ which did not meet our inclusion criteria. A major problem with this study was that some individuals were excluded owing to serious

adverse reactions and poor treatment compliance before randomization.⁴

Second, patients with coronary heart disease are a heterogeneous group, and TCM has been used to treat those with stable angina pectoris, acute coronary syndrome, coronary restenosis, or myocardial ischaemia after CABG surgery or myocardial infarction. To make our Review more concise, we focused on the effects of TCM on angina pectoris (Supplementary Table 1 in our Review), because investigators in most trials of TCM enrolled patients with this condition. We included only one clinical trial on the secondary prevention of myocardial infarction (the Chinese Coronary Secondary Prevention Study⁵) because this study is the only RCT to date in which the therapeutic effects of TCM and placebo on hard clinical end points have been compared. Although Shang *et al.* compared the effects of Qi-Shen-Yi-Qi dripping pills and aspirin on second prevention of myocardial infarction, the number of composite end points in each group was too small to draw definite conclusions.⁶ The 5C Trial⁷ was not included in our Review because it did not meet our selection criteria. The reason that we focused on studies published after 1998 was that the results of most RCTs using TCM have been published in the past 15 years. Our conclusions would not have changed if we had searched for studies published before 1998, because most of these early studies were of poor quality. For example, in the trial from 1982 highlighted by Dr Xiong, the criteria for the diagnosis of coronary heart disease and evaluation of therapeutic effects were not described.⁸ In addition, we searched the three largest Chinese electronic databases—the China National Knowledge Internet, the China Biology Medicine Database, and the VIP database—which we believe covered almost all the Chinese literature. We did not search more Chinese databases,

such as Wanfang, because we found that the majority of the Chinese literature included in the Wanfang database was covered by the three major Chinese databases. Therefore, our exclusion of the Wanfang database is unlikely to have weakened our conclusions.

Third, we agree with Dr Xiong that the quality of most RCTs included in our Review was poor, and no well-designed, placebo-controlled trials exist to evaluate the efficacy and safety of TCM in the treatment of hypertension. However, in either an ‘A + B versus B’ or an ‘A versus B’ study design, both A and B have placebo effects, and the ‘A versus B’ study design has been widely used in many clinical trials of Western medication. The between-study heterogeneity pointed out by Dr Xiong was explained in part by the variability in study design, ingredients of Chinese medication, follow-up duration, and concomitant use of other drugs. To clarify this problem, we have performed a meta-analysis of 10 studies included in our Review^{9–18} using Revman 5.3 software and found that, compared with no intervention, TCM significantly lowered both systolic and diastolic blood pressures, without increasing adverse drug events. Compared with the Western medication group, systolic blood pressure was higher in the TCM group before treatment, but the difference was not significant after treatment. No significant differences in diastolic blood pressure existed between the TCM and Western medication groups before or after treatment. Additionally, the incidence of adverse events was lower with TCM treatment than with Western medication. A similar conclusion was drawn by Xiong *et al.* in their systematic review.¹⁹ Therefore, we believe that our conclusion that “TCM might have moderate antihypertensive effects and seem to be well tolerated”² is evidence-based and reasonable.

Finally, we disagree with Dr Xiong’s conclusion that “no critically appraised evidence

on the efficacy and safety of traditional Chinese medicine exists to justify its clinical use and recommendations¹. TCM has been in clinical use for >2,000 years—pre-dating the advent of modern Western medicine—and more and more data from RCTs are indicating the efficacy of TCM in improving both surrogate and hard clinical end points in patients with cardiovascular diseases. The lack of sufficient evidence from RCTs does not necessarily indicate a lack of efficacy of TCM. Currently, most therapies using TCM in China are based on clinical experience only, and further large-scale RCTs are warranted to test the efficacy of TCM in reducing cardiovascular or all-cause mortality in patients with cardiovascular diseases.

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Competing interests

The authors declare no competing interests.

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