Author's response to reviews

Title: Effect of garlic on blood pressure: A systematic review and meta-analysis

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Version: 2 Date: 23 May 2008

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Response to reviewer-2’s comments:

1) “The included trials are all tiny, include a total of just 500 patients, with short duration follow-up, several have substantial loss to follow-up, and none are adequately powered to detect effects of BP reduction in major vascular events. The authors should acknowledge this in the results and discussion sections.”

Our study is investigating the effect of garlic on blood pressure. As blood pressure is a continuous outcome measure, the sample sizes of the majority of trials included in the meta-analysis are considered adequately powered to detect a difference in blood pressure change between intervention and control groups. Similarly, the total of 500 patients in the meta-analysis on the continuous outcome measure blood pressure is considered sufficient.

We agree with the reviewer that our study does not provide evidence on BP change in relation to cardiovascular morbidity and mortality. To clarify this distinction, we have amended the relevant section in the discussion:

“Our findings may have implications at a population level, where a reduction of 4 to 5 mm Hg in SBP and 2 to 3 mm Hg in DBP has been estimated to reduce the risk of cardiovascular morbidity and mortality by 8-20% [56]. While our study focuses on the short-term effects of garlic on blood pressure, larger scale long-term trials are needed to test the effectiveness of garlic on cardiovascular outcomes.”

We also agree with the reviewer that higher loss of follow up in some trials may have introduced some bias. We have added the following to the discussion:

“Quality of studies included in the meta-analysis was generally high, however, 20% loss to follow up in two trials and non-reporting of drop out rates in three trials might have biased the results in those studies.”

2) “The authors still overstate the strength of evidence provided. In other words,
their conclusion suggests that garlic could be used for the long-term treatment of hypertension (by implication in preference to interventions which have been tested in several thousands or tens of thousands of patients, and for which there is robust evidence of protection against serious vascular events).

At best - in my view - these data might be summarised as 'these preliminary data, which are subject to a number of potential biases suggest that larger scale long-term trials of garlic preparations may be justified.'

We have amended the conclusion to:

“This systematic review and meta-analysis suggests that garlic preparations are superior to placebo in reducing blood pressure in individuals with hypertension. Future large scale long-term trials are needed to investigate whether standardised garlic preparations could provide a safe alternative or complementary treatment option for hypertension in clinical practice.”

3)” A weakness of this review that now cannot be dealt with is that the search strategy is very limited.”

We disagree with the reviewer in this point, as outlined below:

a) While our systematic review included only published trials, we did not find any evidence for publication bias (funnel plot, Egger’s test).

b) An expanded list of search terms did not retrieve additional relevant studies. Search terms used in the expanded list included: (“2-propene sulfenic acid” OR aglio OR ajo OR ajoene OR alisat OR allicin OR alliinase OR "Allium sativum" OR "allyl mercaptan" OR "diallyl disulphide" OR "diallyl sulfide" OR "diallyl sulphide" OR "dipropyl disulphide" OR "dipropyl sulphide" OR garlic OR "garlic extract" OR "garlic oil" OR knoblauch OR Kwai OR Kyolic OR "S-allyl cysteine" OR "thioallyl derivative" OR thiosulfinate* OR "vinyl dithiin OR Glutamylcystein* OR "Glutamyl cystein"* OR ajoene OR alisat OR allicin OR alliinase OR Allium OR "allyl mercaptan" OR "diallyl disulphide" OR "diallyl sulfide" OR "diallyl sulphide" OR "dipropyl disulphide" OR "dipropyl sulphide" OR garlic OR "garlic extract" OR "garlic oil" OR Kwai OR Kyolic OR "S-allyl cysteine" OR thioallyl* OR thiosulfinate* OR "vinyl dithiin") AND (“blood pressure” OR hypertens*)

c) For further clarification, we added the following information under ‘methods/study selection: “We contacted authors of studies with suitable study design but incomplete published data (mean SBP/DBP or SD) to retrieve complete data sets for meta-analysis.” However, only one study group was able to provide us with the data.