Author's response to reviews

Title: Complementary and Alternative Medical Therapies for Chronic Low Back Pain: What Treatments are Surveyed Patients Willing to Try?

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Author's response to reviews: see over
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Dear Matt Hodgkinson:

Thank you for extending the timeline for revisions to our manuscript. We have now completed the revisions requested for our manuscript, originally titled “Complementary and Alternative Medical Therapies for Chronic Low Back Pain: What Treatments are Patients Willing to Try?” (MS Number 1298154837313771). Below we have responded to each of the points raised by the two reviewers.

Reviewer: Kate Thomas

Minor Essential Revisions:

1. We have revised the Methods section of the Abstract to indicate that we used automated visit data to select the sample, that we were able to screen 70% of the sample and all those screened who were eligible actually completed the survey and that respondents were English speaking.

2. As requested, we have now stated in the Conclusion of the Abstract that “Most patients with chronic back pain in our sample …”.

3. In the third paragraph of the Discussion section, we have clarified that we were unable to assess the eligibility status of 30% of the people we attempted to contact, leading to the possibility of a high non-response rate. Because we were interested in interviewing people with chronic low back pain, but could not determine from automated records whether an individual’s back pain was chronic or “low”, we believe that many of the individuals who received an invitation to the study and could not be assessed for eligibility would not have had low back pain at the time they were contacted. Given that we have little information on these non-assessed individuals, we do not know the type of bias that would have been introduced by excluding them. We can speculate that our study may include a greater fraction of people with interests in trying CAM (or greater knowledge or expectations about it), which might cause some of our findings to be more positive than would have occurred with a 100% response rate. However, we have no data suggesting that this is true.

We do know that the fractions of individuals who were unable to be assessed for eligibility were similar among those less than 65 years of age and those 65 and older in each metropolitan area. We present this information in the third
4. We deleted the confusing sentence.

Discretionary revisions
1. Ms. Thomas wondered if we have any information about the known characteristics of the sample compared with those who are ineligible or non-respondents. We have discussed the limited information available to us in Point 3 in the preceding section.

2. Ms. Thomas wondered if we wanted to run a regression analysis for a variable related to “use of any therapy”. As described under our responses to the review by Dr. Refshauge, we have changed the criteria for including variables in our final logistic regression models to 0.01 (instead of 0.05). With the use of more stringent criteria, we found no specific demographic characteristic was related to prior use of more than one specific therapy (Table 4). In view of these findings, we do not believe that creation of a more general analysis would be helpful.

3. While we appreciate that many respondents seemed willing to try acupuncture, even though they had low knowledge of it, we do not have any information about why this might be so. Nonetheless, we have suggested in the 6th paragraph of the Discussion section that further work on this issue is needed.

4. In the first paragraph of the Discussion section entitled “Implications for Clinical Trials”, Ms. Thomas wonders if the relatively small proportion of people who opt for chiropractic as their most preferred treatment in a hypothetical trial of acupuncture, chiropractic, and massage is due to the fact that this is most likely to be available via their health plan. While we cannot know if this notion is correct, we have added a sentence at the end of this paragraph suggesting it as a possible explanation.

5. We have addressed the issue of multiple testing in our response to Dr. Refshauge (Major Compulsory Revisions – Point 3).

Reviewer Kathryn Refshauge:

Major compulsory revisions:

1. The low response rate needs to be addressed. “The response rate does not become acceptable by considering whether non-responders would have been eligible or ineligible”.

   In the context of a survey study, we believe that the response rate is most accurately defined as the proportion of eligible respondents who are actually interviewed. If a substantial proportion of respondents are not screened for eligibility, this can make accurate estimates of the response rate difficult. In this situation, it may be more
reasonable to focus on the proportion of individuals who could be assessed for eligibility. In our study, we were able to assess eligibility status for 70% of the people who received an invitation to the study (80% of the Group Health members and 58% of the Harvard Vanguard members who received an invitation to the study). None of the eligible individuals later refused to be interviewed. We believe that these rates are not exceptionally low and have reworded the third paragraph of the sample subsection of the methods section to make our reasoning clearer.

The fact that a substantial proportion of screened individuals were not eligible for the study reflects the fact that this was a survey of individuals with chronic low back pain, but we were unable to reliably identify individuals with chronic low back pain from automated visit data. Because most persons who visit health care providers for back pain do not go on to develop chronic back pain (which we defined as back pain persisting at least three months), we believe that many of the individuals who received an invitation to the study would not have been eligible. In fact, among the individuals who were actually screened for eligibility, over half were ineligible with the majority lacking chronic low back pain.

2. The “randomization process needs to be elaborated”.

This was not a randomized trial, but rather a study conducted before finalizing the design of a randomized pilot study. We have now clarified this and have described our process in selecting study participants in more detail in the sample subsection (especially the first two paragraphs) of the Methods and also in the Methods section of the Abstract. Our goal was to sample 150 patients with chronic low back pain from the Seattle area and 100 from the Boston area, with 50% of the patients in each location of age 65 or older. In particular, patients in each age category (<65, 65+) with visits to conventional healthcare providers for lumbar or back “region not specified” pain three to 12 months before our survey began were identified using automated visit data from each of the health care systems. Beginning with the most recently diagnosed patients, we mailed letters “in waves” to identified patients until we achieved our sample goals.

3. Statistical analyses: 30 logistic regressions are far too many for this data set. This study looks very much like a “fishing expedition”.

In the Third Edition of *A Dictionary of Epidemiology*, Last defines “fishing expedition” as an “exploratory study to find clues and lead to further study”. He also notes that such studies can be done for “worthwhile causes”. We regard the results of our survey as a basic, descriptive study (we describe it as a descriptive and exploratory study in the second paragraph of the introduction on page 5) to explore patients’ knowledge of, experience with (in general and for back pain), perceptions about and willingness to try five different CAM therapies under two different payment options and in the context of two hypothetical clinical trials. Our study was structured as a series of six questions about five different therapies and then about two hypothetical clinical trials.
In the context of such a study, we believe it is appropriate to carry out a variety of analyses, which we regard as hypothesis generating, rather than definitive, to explore the relationships among these potentially-related variables. This approach is a standard one used by epidemiologists when investigating new research topics and Drs. Sherman and Cherkin (both epidemiologists) discussed this issue explicitly with Dr. Davis (a biostatistician) before finalizing the analytic plan.

Because many of the demographic variables, back pain variables, and CAM variables could plausibly be related to each other, we believe that logistic regression is an efficient method to use when looking for potential associations between our dependent CAM variables (knowledge of each of five CAM therapies, experience with each of five CAM therapies in general and for back pain, expectations of each of five CAM therapies, etc.) and demographic, back pain history, and other CAM variables. In this situation, odds ratios would describe the magnitude of the associations. Even though this was an exploratory study, we developed the analysis plan for the logistic regression models before actually conducting any analyses. That plan is outlined in Table 1 and in the statistical analyses section of the methods.

We believe that issues of multiple comparisons are most critical in hypothesis testing studies. Nonetheless, we have decided to be more parsimonious and our final models have only variables with a p-value of less than 0.01. This has resulted in a simplified Table 4, with only 24 odds ratios instead of 39.

4. It is particularly concerning that a further 22 variables were considered for the second question.

In the context of an exploratory study, we believe that it is appropriate to consider variables that might plausibly be associated with willingness to participate in a clinical trial as such information could be useful for other researchers. As it turns out, using our new criterion of significance of $p <0.01$, none of the 22 variables predicted willingness to participate in a trial of acupuncture, massage, and chiropractic and only one variable (high expectations of meditation) predicted willingness to participate in a trial of massage, t’ai chi and meditation.

5. It is unclear what question the odds ratio is expected to answer.

Odds ratios are useful for describing associations between two variables, with larger odds ratios reflecting larger positive associations and odds ratios much smaller than one reflecting larger negative associations. In this study, the odds ratios indicate which, if any, of the specific characteristics we evaluated are associated with high knowledge of each of five CAM therapies, prior use of each of five CAM therapies, prior use of each of five CAM therapies for back pain, high expectations of success of each of five CAM therapies, likelihood of trying each of five CAM therapies for free, likelihood of trying each of three CAM therapies for a $10 co-pay, and likelihood of participating in each of two trials. We believe that such analyses are appropriate in exploratory studies such as this.
6. The questions were forced choice, not allowing for a preference for none of the therapies.

We suspect this comment refers to the possible answers regarding preferred therapies allowed in the “willingness to participate in a randomized trial” questions. The purpose of these questions was to see whether there was a clear preference for or against one of the three therapies included in each of the two hypothetical trials, which could influence recruitment for the trials or highlight the potential for differential dropouts. In fact, individuals were allowed to express a preference for the control group (who received a book) or for none of those therapies. In Table 5, a small proportion of people indicated they had no preference among any of these therapies.

Minor essential revisions:

1. We have now included the screening rate, our best proxy for response rate, in the Methods section of the Abstract.

2. We have now clarified how we recruited people with back pain into the study in the “Sample” section of the Methods.

3. We have now indicated that an “X” in Table 1 denotes that a particular potential predictor variable was examined to see if it had a relationship with a particular dependent variable. This information is contained in the second paragraph of the Statistical Analyses subsection of the Methods and in a footnote to Table 1.

4. We do not consider the odds ratios reported in the Results section to be “all low”. In Table 4, of the 24 odds ratios that were part of the final models, 11 of them that are over 5 in magnitude and 5 of them that are \( \leq 0.5 \).

Dr. Refshauge may have been referring to the logistic regression data presented in the subsection of the Results related to “Willingness to Participate in a Clinical Trial”. Originally, we found modest associations in each of the two models with three variables. With the more stringent criteria of 0.01 for an association, we found only one characteristic (high expectations of meditation) to be related to willingness to participate in a trial of massage, t’ai chi and meditation and no characteristics related to willingness to participate in a trial of acupuncture, massage and chiropractic. We have shortened this section accordingly.

5. We believe that many previous studies have paid too little attention to the subtleties involved in evaluating extant CAM therapies and that the “Implications for Clinical Trials” section of the Discussion allows us the opportunity to make some important methodological points that have implications beyond our own work. In this section, we are able to tie together findings from all parts of the survey (not just the two questions about willingness to participate in a clinical trial) to touch on broader issues of use for investigators who are planning to test
several CAM therapies in the same clinical trial as well as those who are planning to test CAM therapies that are already in practice.

Discretionary Revisions:

1. We have removed the acronyms from the manuscript.
2. We have revised the Sample section of the methods so that it is more clearly written.
3. In the final paragraph of the Discussion section, we have now clarified that we suggest that patients’ expectations and prior experiences with each treatment should be measured and, if appropriate, controlled for in the analyses. However, if one treatment is vastly more popular than another, it could be difficult to disentangle the effects of expectations and efficacy because of strong colinearity. We believe this caveat is worth noting.

We hope that we have been responsive to the reviewer’s concerns, but welcome the opportunity to provide additional clarification if needed. In addition, while we attempted to format the manuscript according to the BMC guidelines we received, please let us know if changes need to be made. Specifically, we have changed the title slightly to reflect that our study is a survey of chronic back pain patients, we have reformatted the references and have changed some formatting in the tables.

Sincerely,

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On behalf of all the authors of this manuscript.