Author's response to reviews

Title: A pragmatic randomised controlled trial of hydrotherapy and land exercises on overall well being and quality of life in rheumatoid arthritis

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Author's response to reviews: see over
Dear Mrs Puebla, dear Editors

Thank you for your kind consideration of our manuscript. I also want to thank the reviewers for their critical comments, which helped us to clarify the objectives of our manuscript. We apologize for the technical problem with figure 1. The content of the flow diagram disappeared during the upload.

Here is our detailed response to the concerns raised by the reviewers. We have highlighted all changes made to the manuscript.

Please don't hesitate to contact me if you have any problems or questions regarding our manuscript.

With best wishes,

Jean-François Chenot for the authors
Reviewer 1 (Claudia Witt)

Major Compulsory Revisions

Background
1. The part about the model projects is too brief. The different model projects should be quoted clearly to prevent confusion (each has published at least one design paper).

We have cited 3 references [8, 9, 10] referring to the model projects selected by Prof. Basler who acted as a consultant for the model projects. As noted, the results of the LBP arm are not published yet. We have added the following publication, which was not yet published when we reviewed literature relevant to our subject and incorporated it in the background (page 4).


2. The co-payment was not a decision of the physicians. Due to some law regulation in model projects patients have to pay 10% of the acupuncture treatment costs out of pocket. This should be clarified.

We did not want to suggest that co-payment is at the discretion of the treating physician. We have clarified that patients qualifying to receive acupuncture in the model project had to pay only 10% of the treatment (page 3). For further comments regarding the impact of the model project on our study see below.

3. It should also be clarified whether the study was performed at the same time as the model projects or not.

The study was done while the model projects were going on in 2002-2004. We mentioned the date of the recruitment period in the “methods” subsection “patients” on page 5. We do not know if any of the 179 patients who got acupuncture in our study were offered acupuncture within the frame of the project for a reduced fee. We believe that the impact the model project might have had on our study is negligible (see for more details below). We have added information on possible bias with regard to income in the discussion (page 12).

4. The first research question should be clarified.

We have refined and clarified the research question (page 3-4).
Methods
1. The study design should be presented more clearly. Please clarify in which arm of the study the presented cohort is embedded and whether this cohort was predefined.

All patients enrolled in our trial were included in the cohort. We have now clarified this issue (page 4 methods subsection study design).

2. In addition please state that the present analysis was done post hoc.

The statement was added in subsection “strengths and limitations” in the summary (page 2) and in the discussion (page 12) and.

3. The information given about missing data is confusing. Was an imputation of missing data performed or not? Please clarify.

To allow the reader to see how much data was available for analysis, we have always provided the number of analysed patients in tables 1 and 2. For the regression models to predict receiving a specific treatment, we had 1320 patients in the models. We have corrected the numbers in Table 3 and clarified how many patients the data is based on (page 7). For the regression models to predict receiving acupuncture we have indicated how many patients were retained in the model after list wise deletion in the final model. We have not done an imputation for missing values. The information how we dealt with missing values was clarified in the subsection statistical analysis (page 7).

4. Please provide all variables of the logistic regression analysis and also report those that were included in the model.

We have stated that in logistic regression we used all factors which were significant in the univariate analysis as shown in Table 2. To clarify the issue for the reader we now have listed the factors in the “methods” section (page 7).

5. Please clarify which kind of analysis was performed: an intent-to-treat analysis (which should be preferred) or an analysis of complete cases.

We are reporting the results as a cohort study comparing post hoc those who received acupuncture with those who did not. Since patients were not randomized to receive acupuncture; we cannot report an intention-to-treat analysis. As noted in the section “strengths and limitations” we do not know how many patients had been offered acupuncture (intention-to-treat) and declined to give it a try.

Results
1. Please add the time period of patient recruitment.

Patients were recruited from November 2002 to March 2003; the follow up of the latest enrolled patients lasted until February 2004. Each practice had a time frame of 8 weeks to recruit patients. To distribute the phone interviews evenly, practices
started in subsequent waves to recruit patients. This has now been clarified in the manuscript (page 5, methods, subsection patients).
2. Please add the disease duration of patient if available.

Average duration of pain was given in Table 2.

3. Please clarify whether the acupuncture treatments were included in GP consultation (does each acupuncture session equal a visit?). Same for the consultations at specialists. Presentation is a bit confusing here and acupuncture visits should be reported separately.

We asked patients specifically how frequently patients consulted GPs and other health care providers. The number of acupuncture session was a separate question (see below). This is now clarified in the manuscript (page 6 "methods", subsection "instruments and data collection").

4. Please add the mean number of acupuncture treatments that the patients received.

We asked how often patients got acupuncture. The number of acupuncture sessions ranged from 1 to 47 during the follow up period (mean 12 sessions). This has now been added in the manuscript in the result section (page 9 “results”, subsection "patients").

5. Is there any information about diagnostic procedures and treatments that the patients had received before study entry? If so please add this information. It seems that patients in different stages of treatment were included into this study, and information about resource use before study entry does affect resource use after study entry.

As inclusion criteria patients had to consult for back pain. As shown in Table 2, they were in different stages. The baseline data collection about use of health-care resources was done 4 weeks after inclusion and asked 6 months backwards. This has now been clarified (page 8 "results", subsection "patients"). In addition we adjusted the data shown in Table 3 for chronicity and other factors as described in the methods section. We have also added a section in the discussion stating that half of the patients receiving acupuncture did not meet the criterion chronicity (page 9, 11).

6. It seems that the HFAQ is the main outcome parameter, because the follow up results are presented in Table 2. Although there are relevant HFAQ differences at baseline between the patients receiving acupuncture and the patients receiving no acupuncture this factor was not considered in the regression analysis and there was no adjustment for these baseline values. It is known that the baseline value of an outcome parameter could be a relevant effect modifier so it must be included in the model.

The HFAQ was the main outcome concerning the three-armed intervention study. As stated in the section “methods” subsection “study design” (page 4). The present study aims at a different research question, namely to explore variation in care and factors related to it. In Table 2 we have shown the functional capacity score (HFAQ)
at baseline and after 6 and 12 months to demonstrate that on average patients who received acupuncture were more disabled by LBP than those who didn’t throughout the whole follow up period. It is stated in the methods section that the baseline functional capacity is included in the predictive model, but it was not significant (this has now been clarified in the methods section (page 7).

The trial was not designed to evaluate the effect of acupuncture on functional capacity. However, we reported the results of the repeated measure ANOVA comparing the average improvement in functional capacity over time, which was not significantly different. We have now dropped the follow-up data on HFAQ and statistical remarks relating to it following a suggestion of reviewer 2 (Daniel Cherkin).

**7. Only one eights of the contacted practices agreed to participate. Is there any information from/about the declining practices to get an idea of the representativeness of the participating practices?**

We have compared the baseline demographic data of the participating GPs (age and gender) to the national average, which is not meaningfully different. We would also like to point out the size of our cohort. A more detailed answer to the concern that the practices might not be representative is given below for Reviewer 3 (Suzanne Parsons).

**8. Could you provide information of patients insured in one of the statutory health insurance funds who participated at a model project and did cover acupuncture? This might be a strong predictor for receiving acupuncture.**

We have no data on patients’ situation concerning statutory health insurance. To answer your question we have contacted 24 of the 25 GPs providing acupuncture in our study (one GP died from cancer in the meantime). Only 2 of them provided acupuncture within the frame of the model project. The impact of the model project on our study participants is therefore negligible concerning the GPs. We cannot exclude that some specialists provided care covered partly by the model project. However, we have no data about the specialists apart from their speciality. One can only imagine one way how this could have affected our trial: Being member of one of the participating statutory health insurances and consulting a physician who participated in the trial might have lowered the threshold to obtain acupuncture due to lower fees for the patient. We agree that this might be a predictor, but it would have no influence on other health services patients received. A respective caveat has now been added in the discussion (page 12).

**9. The applied prediction model for receiving acupuncture and the way how the results are presented seems confusing. The results of all predictors including gender, age, HFAQ etc should be presented clearer.**

All factors which were included in the model are now listed in the “methods” section (page 7) and as legend within table 3. For better readability, we only report the ORs and CIs for significantly associated factors and omitted the ORs and CIs of non-significant factors.

**Discussion**
1. The authors conclude that their results are representative for Germany. Such a conclusion for the present study could be supported by information about representativeness, but this is missing in the manuscript.

Please see comment 7 in the section above and response to reviewer 3 (Suzanne Parsons).

2. A proportion of 13% of the patients receiving acupuncture appears high to the authors. If the study would have been performed during the same time period as the model projects it would probably have been even more.

We have no reliable data about how many patients with LBP receive acupuncture in Germany. Based on our clinical experience as practising GPs (JFC, AB, NDB, EB, MMK) we were surprised how many people tried acupuncture for LBP unlike our colleagues working in a pain clinic (MP, JH). Virtually all patients with chronic disabling pain seen in a pain clinic have tried acupuncture. In primary care where our study patients were recruited, most patients have acute, recurrent or tolerable chronic back pain and are less likely to try acupuncture. Assumptions about whether this is a high or low proportion depend essentially upon one’s perspective.

3. The discussion of the limitations should be generally more self-critical, and also expanded to include facts like the post hoc analysis, the selection of GP’s and patients, etc.

We have expanded the “limitations” section and stated clearly that we are doing a post hoc analysis in the “summary” and the “discussion” (pages 2 and 11-12).

4. The authors discuss cost-effectiveness and suggest the acupuncture for chronic low back pain might be not cost-effective. This conclusion is not supported by their study, because they did not perform a cost-effectiveness-analysis. The present study might show that there is more resource use in the acupuncture group and less benefit, but it is a non-randomised study and results could be biased.

We agree and have clarified this in the discussion; see also response to reviewer 2 (Daniel Cherkin) who raised the same concern. The value of our study is to give an estimate about how many patients will use acupuncture outside clinical trials and to have information about other health-care resources used during the follow up period.

Conclusion
The conclusion should be weighted by shortcomings of this study.

We have expanded the section “limitations” and in the discussion.

Tables and Figures
1. All boxes in Figure 1 are empty!
We apologize for the technical difficulties. The content of the flow diagram disappeared during uploading. A data set including the content of the boxes will be sent to the editor.
Minor Essential Revisions

The Hanover Functional Disability Questionnaire is normally abbreviated as ‘HFAQ’ twice in the manuscript ‘HFDQ’ is used (page 5 and Table 2).

We now use the corrected abbreviation.

2. If data from other countries is quoted it would be better to also report the country, because health systems in other countries differ from the German health system.

We assume this refers to reference [12]:
We have clarified that this study was done in the UK (page 3)

3. Please give all p values even if not significant

We have provided all p-values for comparing proportions and continuous data, except for the ORs since we believe that the 95 % confidence intervals are more relevant. To clarify what we are writing about. We have added the abbreviation CI in front of all confidence intervals, or OR in front of all odds ratios. We also added the missing p-value e.g. for the comparison of sick leave days.
Reviewer 2 (Daniel Cherkin)

Major Compulsory Revisions

1. Revise the Summary/Abstract-Background, the last paragraph of the Background and the first and last paragraphs of the Discussion sections to make the goals and results of the study more consistent. Specifically, the Abstract Background does not explain why exploring "factors associated with acupuncture treatment ...." is important to do. In the last paragraph of the Background, the two research questions that are mentioned as the special focus of the study (last two sentences of paragraph) do not clearly derive from the broader aims of the study mentioned earlier in the paragraph. The summary of the main findings in the Discussion, should then directly summarize the findings relevant to the newly clarified aims.

In most European countries, acupuncture is not covered by the regular health insurance, e.g. France and Belgium. Recent studies claim an effectiveness on pain, quality of life and even cost effectiveness at least for chronic low back pain. This will increase the pressure to decide whether acupuncture should or should not be part of the general coverage by health insurances. An important aspect is costs. Several times it has been suggested that offering acupuncture will reduce the use of other health services. Our study shows that it is unlikely that health care cost will go down due to the offset of other health services even if acupuncture is cost-effective with regard to functional capacity and quality of life. We have clarified the aims in the background section (pages 2-4) and adapted the summary to the changes made.

2) Sentence 3 of the last paragraph on page 11, states: "Our data suggest that this [the cost-effectiveness of acupuncture] might not be the case outside clinical trials." I don't believe that the data from this study suggest anything about the cost-effectiveness of acupuncture. While the data clearly show that patients who used acupuncture also used lots of other services, this does not suggest that acupuncture is not cost-effective. This would require a different study design where the costs and effectiveness of care with acupuncture is compared with similar care without acupuncture for comparable patient populations (ideally through randomization). The last sentence in the Conclusion of the Summary/Abstract also needs to be changed for the same reason.

We agree that we did not perform a cost-effectiveness analysis of acupuncture; therefore we rephrased the sentence as suggested in the discussion (page 12) and the summary. Our study does not allow us to draw conclusions on effectiveness. We have clarified in the summary, in the background and the discussion that any statement which could be understood as if we are drawing conclusions to cost effectiveness, is only referring to differences in the use of health-care resources.
Minor Essential Revisions

1) Page 10, paragraph 2, line 5: Please clarify why you "overestimate the proportion of GPs' contribution for receiving acupuncture."

Unfortunately, we do not know whether acupuncture was provided by the GP or a specialist. From 179 patients who received acupuncture, as many as 66 had a GP who offered acupuncture services. It is likely that some of these patients received acupuncture from a specialist like the other 113 patients, which could lead to some degree of overestimation of GP's contribution to the amount of acupuncture. This was clarified in the discussion (page 12).

2) Page 11, middle paragraph: Given that this "study was not designed to assess effectiveness of acupuncture" (last sentence), I don't think there is any point of mentioning that patients receiving acupuncture had lower levels of functional capacity. Clearly, receiving acupuncture was associated with several other negative factors, so this difference likely has little to do with acupuncture per se.

We agree and have dropped the follow-up data on the HFAQ from Table 2 and removed comments on the statistical analysis performed with regard to the follow up data.

3) Reference #1 (page 14) Waddell has two d's and two l's.

This was corrected.
Reviewer 3 (Suzanne Parsons)

Major Compulsory

The prospective cohort study described was embedded within a randomised controlled trial of an educational intervention which consisted of quality circles for general practitioners and training of practice nurses in motivational counselling. Could the authors reflect a little more on the impact of this patient data coming from practices who have elected to become involved in a randomised controlled trial to improve quality of care? What influence will this have on the generalisability of your findings to a wider general practice population.

There is always an assumption of bias with any subject who agrees to be part of a study. We needed to contact a large number of practices due to the complicating fact that in addition to the GP also practice nurses had to agree to participate in the trial, since they were part of the intervention in one study arm. This is now more clearly mentioned in the methods section and the discussion of the limitations of our study (pages 5 and 11).

Most trials in primary care are done within existing research networks, which was not the case in our study since we contacted all registered GPs. However, more than half of the practices have previously participated in research projects or medical education in cooperation with the local Dept. of General Practice. There is no reason to believe that patients recruited in research practices are different from patients in practices. Hammersley et al. have shown that there were differences in other practice structure and some aspects of performance, but no important differences in the demography of registered patients, nor in morbidity, mortality, or access to or use in secondary care of patients recruited from practices participating in research networks.


I have added the average age and the proportion of women practising in general practice in Germany from the statistics published by the federal board of medicine in 2001 to allow a comparison of our sample as suggested by Wetzel et. al. (page 5). Although our GPs are slightly younger and our sample has a slightly higher proportion of females, the differences are minor, which suggest that our sample of GPs is representative.


Finally, the sample of 116 practices is fairly large for a trial in a primary care setting. We have no reason to believe that the services provided to patients with LBP are meaningfully different from what is done by the majority of GPs in Germany.
Minor Essential Revisions

Some more proof reading is needed in places, there are a few letters missed off words and decimal points in places were there should be commas.

We apologise for these errors and have intensified proof reading.

It would be useful for the authors to present a few more details of the Hanover Functional Disability questionnaire, in particularly to give an example of some of the items within the questionnaire, so that the reader can ascertain the domains measured.

The Hanover Functional Ability Questionnaire (HAFQ) is comparable to the Roland & Morris scale which is more commonly used in Anglo-American countries as mentioned in the section instruments and data collection (page 6). The HAFQ is used in virtually all German back pain trials. It consists of 12 questions relating to everyday activities like can you lift an object from the ground, can put on you socks etc. There are three answer categories: yes, yes with some effort and no. We have checked publication in other international journals referring to HAFQ which gave about the same information. We have added an explanation in parenthesis behind the extreme values to clarify the meaning of the numbers to the reader (Methods, subsection Instruments and data collection, page 6). We are now only showing the baseline data of the HAFQ responding to a suggestion from reviewer 2 to drop the follow-up data. Therefore, we propose to leave the section on HAFQ as limited as it is.

Could the authors provide another copy of Figure one, as the copy submitted was blank and therefore no information was provided on participant flow and exclusion criteria.

We have included a copy with filled boxes and apologise again for this mishap. We mentioned the inclusion criteria (page 5). The reasons for exclusion after inclusion in the trial are listed in Figure 1, which you could not see. The main reason for exclusion was missing consent.