Author's response to reviews

Title: Yoga for breast cancer patients and survivors: a systematic review and meta-analysis

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Author's response to reviews: see over
Response to the Editor’s and the Reviewer’s comments:

Dear editor, dear reviewers,

Thank you very much indeed for your valuable comments and efforts while reviewing this manuscript. We have found your comments helpful and addressed them accordingly.

Reply to reviewer 1:

1. *I think this is a thorough review and was written in a comprehensive manner. Just minor essential revisions should be made.*

   HC: Thank you very much. Changes are highlighted in grey.

2. *English writing should be checked to make the manuscript more clear.*

   HC: We have again checked the manuscript for language issues and corrected grammar and typos.

3. Please follow the author’s instruction of this journal about the format of the tables.

   HC: We have again checked the tables’ format. Horizontal lines were inserted in table 4 and 5.

4. *Table 3 and Figure 4 Provide the same information, I suggest removing Figure 4.*

   HC: We have removed figure 4 as suggested.

Reply to reviewer 2:

HC: Changes are highlighted in grey.

1. *page 9 "...1 article did assess neither quality of life nor psychological health but natural killer cell counts [37]..." ...eliminate the double negative for clarity (neither/nor)...unclear as written.*

HC: It has been corrected as suggested.

1. *Not so much a revision as an observation of the process of review. The way the study is undertaken is technically correct but given that it is about yoga, I wonder if it might be good to be even more clear about how assumptions made in the criteria about what constitutes yoga ultimately bias the results, perpetuating a misunderstanding of yoga? Specifically p. 6, "3) Types of interventions. Studies that compared yoga with no treatment or any active treatment were eligible. Studies were excluded if yoga was not the main intervention but a part of a multimodal intervention, such as mindfulness-based stress reduction. Since in North America and Europe, physical exercise is perceived as a main component of yoga [10], studies examining yogic relaxation or meditation without physical component were not included in the review." So do we as researchers really want to say, "Well it appears we misunderstand what yoga really is (asana being a small portion of the rich practice) and since we’ve been doing that, let’s just continue in our reporting because it would confuse the western reading audience."*


MBSR is called MBSR for precisely this reason from Jon Kabat-Zinn's comments vs Buddhism/Yoga/Meditation, and yet the practice consists of at least 5 of the 8 limbs of yoga. So we shouldn't include it because of the label? From an axiological perspective (what research is worth doing), my personal concern is by presenting the data the way it is, we miss an important opportunity to inform the readership and future researchers about what yoga really is and the inherent bias/misrepresentation of what yoga is. And what would the results be if we chose not to misrepresent yoga as exercise (asana), but did include the relaxation (savasana being the "king" of asana) and MBSR being technically what yoga is with asana, concentration, non-reactivity, meditation, and a self reflection on the niyamas/yamas? So that's my concern and I hope this platform of inclusion of reviewers comments might spark further reflection by not only the authors, but those in the future that access this article. Thank you.

HC: Thank you very much for bringing up this topic. I really appreciate your reflections and totally agree with you that yoga is far more than just asanas. After careful consideration, we have decided to drop the inclusion criterion of having asanas in the yoga program. We now include all yoga interventions. However, as MBSR is a highly standardized US American intervention program that has been developed for relief of stress and illness (unlike the more spiritual goals of traditional yoga), I still believe it is appropriate not to include MBSR in the review. I have added a citation of another meta-analysis on MBSR for women with breast cancer that is currently in press in Current Oncology.

Reply to reviewer 3:

HC: Changes are highlighted in grey.

1. 1st paragraph - the search term ‘Yoga’ has been used to extract papers on Yoga and breast cancer along with other terms of health related QOL or Psychological health. Why only yoga has been put as a key word? They could have obtained many more recent articles after Lin’s work if they had used other words such as meditation, mindfulness based stress reduction etc which are also yoga practices.

HC: Thank you very much for this argument. I totally agree with you that meditation is at least as important in yoga as physical activity. After careful consideration, we decided to drop this inclusion criterion. We now include every yoga intervention with and without physical component.

2. In types of intervention, physical exercise of yoga has been considered as main component of yoga, whereas studies on meditation and relaxation (excluding physical exercises) have not been included. Yoga includes meditation & relaxation as the main component and hence the search is not exhaustive.

HC: Thank you very much for this argument. I totally agree with you that meditation is at least as important in yoga as physical activity. After careful consideration, we decided to drop this inclusion criterion. We now include every yoga intervention with and without physical component.

3. Earlier meta-analysis review has followed the criteria where I2 was fixed to be >75% with P<0.05 but the current study has I2 >50% with P<0.1. This shows that the assessment of heterogeneity in current meta-analysis is not as strong as earlier study.
HC: I guess, the meta-analysis of Lin et al. is meant with “earlier study”? This is a misunderstanding. The alpha level of <0.1 was chosen in accordance with the recommendations of the Cochrane Collaboration. As the chi-squared test has relatively low power when only a few studies are included in a meta-analysis, a higher p-value than the common 0.05 is recommended. A higher p-value means that a meta-analysis is judged to be heterogeneous earlier. The same for the I-squared test: while there is no strict convention of when an I-squared value indicates heterogeneity, it is clear that a lower I-squared cut-off is more conservative than a higher one. This means that a meta-analysis will be judged to be heterogeneous earlier if a cut-off of 50% is used than if a cut-off of 75% is used. Therefore, the assessment of heterogeneity in the current meta-analysis is “stronger” than the one used in Lin et al.

4. Results of the current review states the same result as it has been stated in earlier review.
No additional information has been added to scientific literature.

HC: I do not agree on this point. Lin et al. analyzed the effects of yoga (including MBSR) on cancer (including breast cancer). MBSR is not normally included in meta-analyses on yoga (see e.g. Smith et al., 2009, Psychooncology; Büsing et al., 2012, J Pain; Posadzki & Ernst, 2012, Complement Ther Med etc.). The present meta-analysis focused on the effects of yoga (without MBSR) on women with breast cancer. Therefore, both, interventions and participants were more homogeneous in our meta-analysis. Lin et al. concluded that there was an effect of yoga on psychological health for people with cancer but that there was none on health-related quality of life. On the other hand, our meta-analysis concludes that there is an effect on psychological health and on health-related quality of life. But, the effects on quality of life are possible biased and there is no effect when only studies on breast cancer survivors are considered. Here again, when considering only more homogeneous studies, the results are different from when a more heterogeneous sample of studies is considered. In my opinion, both approaches – using broad inclusion criteria without subgroup analyses vs. using narrow inclusion criteria with subgroup analyses - have their own right and can answer unique research questions. But one cannot substitute the other.

5. There are errors in grammar that need correction.

HC: We have again checked the manuscript for language issues and corrected grammar and typos.

6. The authors say that articles in references no. 24 and 26 were excluded in Meta analyses. But these are quoted in many places under results and discussion.

HC: The 2 RCTs were included in qualitative analysis but not in meta-analysis. As they offer additional information, this information was assessed as far as possible. This is in line with PRISMA guidelines and the recommendations of the Cochrane Collaboration.

Reply to reviewer 4:

This manuscript presents a meta-analysis and systematic review to determine whether or not yoga shows efficacy for improving health-related quality of life and psychological health in women diagnosed with breast cancer. Strengths of the manuscript include that the authors followed PRISMA and Cochrane Collaboration recommendations and explored the differential efficacy of yoga during versus after active treatment. This manuscript has many strengths in addition to those mentioned, however, there are some limitations to be considered.

HC: Thank you very much. Changes are highlighted in grey.
1. Inclusion criteria state that studies examining yogic relaxation or meditation without a physical component were not included in the review. Reference [29], Kovacic & Kovacic (2011 in the References/2010 in the Figure) does not seem to include the physical component of yoga (only relaxation training) and it is combined with “physiotherapy.” It seems inappropriate to include this study and necessary to know if the results are different when it is not included. Especially since the SMDs for this study are large and may be driving the effects.

HC: You are totally right, the RCT does not meet our initial inclusion criteria. However, after careful consideration of the other reviewers comments, we have decided to no longer use the inclusion criterion that a physical activity component had be included in the yoga program. The reference in the figure has been corrected.
We conducted another subgroup analysis that excludes the RCT without physical activity component. The results were not changed substantially without this RCT.

2. The conclusion that yoga can be recommended to patients who “suffer from psychological problems” is not accurate. These studies did not specifically target women with elevated levels of psychological symptoms. Instead, this review shows that yoga can be recommended as an intervention to manage or improve psychological health during breast cancer treatment.

HC: The conclusion has been changed as you suggested.

3. The terms quality of life and health-related quality of life were used interchangeably. It would be preferable to have one term used consistently throughout the manuscript.

HC: We now constantly use the term “health-related quality of life”.

4. Similarly, it is necessary to distinguish between cancer patients and cancer survivors. It would be useful to define these terms and use them consistently. For example, it was unclear in the background if reference [3] is “breast cancer patients” were undergoing treatment or not and reference [12] includes survivors in the reference, but only patients are mentioned.

HC: We now use the term “patient” only when women under active cancer treatment are considered. Elsewise we use the term “survivor”. When all study participants are considered, we use the term “participants”.

5. Yoga is referred to as an “alternative” treatment in the Background on p.4, which implies that it is used instead of allopathic medicine. Yoga in the studies referenced is considered “complementary”.

HC: Changed to “complementary”.

6. It was not clear how studies were categorized into high vs. low risk of bias form the Sensitivity Analysis. It would be helpful to clarify this in the Methods section and include a column on Table 3 that states the overall category for the study.

HC: We did not use an overall category. As selection bias is commonly considered most important, we based our sensitivity analyses on selection bias and compared trials with inadequate or unclear randomization and/or allocation concealment versus trials with adequate randomization and allocation concealment. We now explain this in more detail in the methods section.
7. In the Data Analysis section, it says that effect sizes were calculated if two studies were available on a specific outcome. Please clarify if outcomes had to be the same measure or the same construct.

HC: They had to be the same construct. We clarified this.

8. The list of which QOL measures were used in the text on p. 10 was confusing for the FACT-G and FACT-B because [30] was listed twice. Since the FACT-G is part of the FACT-B, this could be explained more clearly.

HC: We have deleted the double listing.

9. It should be highlighted in the text that only two studies are included in the analyses of effect sizes for outcomes after active treatment.

HC: We have included this information in the text.

10. Other minor edits:
    Abstract – Results, effectiveness -> “efficacy”
    Types of interventions – missing “a” before physical component
    Study selection – capitalize Yoga of Awareness
    Results - The word “neither” is used incorrectly twice on the top of p. 9.
    Setting and participant characteristics – add “and” before newspaper and for the phrase “2 studies did include” -> remove “did” and change to “included”
    Conclusions – first line, yoga “is” -> “has been”

HC: Changed as suggested.

Discretionary Revisions

11. It may be of more interest to readers to know the effect size of yoga as compared to any active control either in addition or instead of yoga compared to each type of active control separately.

HC: We now report subgroup analyses for yoga compared to active control interventions.

12. It would be useful to explain in the text why a p-value of <.10 is used for heterogeneity rather than p<.05 so the reader does not have to seek out the reference.

HC: We have included an explanation.

13. It would strengthen the section on the publication bias to include a Fail Safe N calculation.

HC: As the fail safe n test is not undisputed in the literature, we have decided to follow the recommendations of the Cochrane Collaboration and to not include this test.

14. More discussion of why there is no significant effect of yoga after completion of active treatment would be of interest. For example, perhaps women in these studies do not have elevated levels of the outcomes addressed to begin with and have little room for change. Studies that target one symptom and select for post-treatment cancer survivors with elevated levels of that symptom may be more likely to demonstrate efficacy. In addition, these results are different than that found by Moadel 2007 who reported that those not receiving chemotherapy showed more favorable results. This may also be worthy of discussion.

HC: We now include a discussion of this topic.
15. The discussion on meta-analyses of “exercise” would be more inclusive of yoga if called “physical activity.” It would be of interest to know if yoga interventions were included in those reviews.

HC: Thanks a lot for this hint. Changed as suggested.

16. It may be considered a limitation to some that dissertations and unpublished studies were not included in the analysis and could be mentioned in the discussion.

HC: We have included this point as a limitation.

17. The discussion of external validity is missing a comment on the socioeconomic status and resulting access to healthcare of the participants. Other than Moadel 2007, it is important to know if the studies represent people with lower SES.

HC: We have included a comment on socioeconomic status.

Once again, we would like to thank the editor and the reviewers for their efforts, encouraging comments and constructive criticism.

Sincerely yours,

Holger Cramer

(on behalf of the authors)