Author’s response to reviews

Title: The EKSPECT Study: The influence of Expectation modification in Knee arthroplasty on Satisfaction of Patients: study protocol for a Randomized Controlled Trial.

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Author’s response to reviews:

Dear editor,

Thank you for the thorough revision and the chance to submit an improved version of the manuscript.

Please find a point-wise response to the reviewers’ questions below:

Reviewer reports:

Reviewer #1: Trials-D-18-00373

The manuscript is a protocol for a randomized clinical trial designed to align patient expectations with expected total knee replacement outcomes (using an educational intervention) with an outcome of a greater rate of satisfaction in the experimental arm relative to the control arm. Secondary aims relate to whether the intervention modifies preoperative and postoperative achievement of expectations. Finally, additional analyses will determine if the effect of the experimental intervention varies based on participant age, gender, severity of symptoms, symptoms of depression and coping mechanisms. The concept for the trial seems sound and the idea is novel and potentially important. However, I found several credibility issues that appear to need attention and these are identified below.

Page 4, Trial Objectives: It is not clear to me how potential participants can be naïve to the purpose of the study. A standard part of any human subjects consent form is the purpose of the
trial and a description of the different arms. How can patients consent to something in which they are not made aware of the interventions?

Patients are informed that the study compares two methods of pre-operative education before TKA. To blind the patient; we will not report specifically about what will be the index intervention and what the control intervention. By this method we aim to blind the patient for the hypothesis of the study as this knowledge might affect the study results. The patients consent to undergo an education module, but are unaware of the difference in content between these educational modules. The procedure is clarified in paragraph 3.5 of the manuscript. These study procedures are explicitly addressed in the study protocol that has been reviewed and approved by the Máxima Medical Centre Medical Ethics Committee (registration code NL54671.015.15).

Page 5, Study population (sample): The inclusion and exclusion criteria do not specify whether unicompartmental arthroplasty will be excluded. Also not mentioned is whether bilateral or staged knee arthroplasty will be included and whether potential participants planning a future hip or knee arthroplasty in the upcoming year will be excluded. It is likely that near future arthroplasty of the knee or hip could influence satisfaction with the index knee.

We only include patients that were indicated for total knee arthroplasty, unicompartmental arthroplasty patients are therefore not eligible. This has been clarified in the revised manuscript.

Patients of whom at baseline it is evident that they will undergo contralateral TKA during the study procedure (either bilateral or staged) are excluded. When patient do have a contralateral TKA during the study period, this will be recorded. This has been clarified in the manuscript.

Page 7, Experimental Intervention: I would encourage the investigators to provide an appendix with the written materials provided to the participants. This is really the only way to judge the content of the intervention and the readers should be able to see the content of the material you are using in the trial.

The leaflet summarizing the information in the additional module on realistic expectations for long-term recovery has been included as an appendix (translated English version, the original leaflet is in Dutch). Referral added in the manuscript.

Page 7: The investigators suggest that expectations are strongly linked to placebo effects and in my view this extrapolation should be deleted. Evidence for this association in knee arthroplasty does not exist, in my opinion, and extrapolation from other literature to knee arthroplasty is far too premature.

We agree the link with the placebo effect has not been established in TKA patients, this is mentioned in the manuscript as well (line 226-229). In the manuscript it is clearly described that the potential positive influence of utilizing the placebo effect is a hypothesis. The current study would provide supporting evidence for the presence or absence of this positive effect. With the explanation of the potential working mechanism we included in the manuscript, we aimed to describe the rationale for the intervention under study. Deleting this explanation would in our view reduce the interpretability.
Reliance on the HSS expectation survey to guide module development seems quite risky because the data used to inform the HSS expectation survey is approximately 20 or more years old. Please address this concern.

The HSS expectation survey has been designed based on what patients think are important expectations for TKA and was first published in 2001. What patient consider important might indeed change over time. In a recent report Smith et al explored if patients had other concerns, not addressed by the HSS expectation survey (Smith et al. J Arthroplasty, 2016 Apr;31(4):786-92), this did not result in new insights or large omissions in the original survey. To our knowledge recently no further extensive efforts have been made to indicate that what TKA patients consider important has changed. Therefore, to the authors opinion the framework for the development of the education module is up to date.

There is an abundance of much more recent evidence to inform prognostic estimates of outcome. Reliance on expert opinion to inform the educational module is discouraged. This approach is not defensible. To be grounded in science (not experience), evidence-based guidance should be the sole source for informing the module.

The HSS survey has only been used as a framework summarizing the expectations that are most important to TKA patients. Answers to these questions are evidence based, and rely on data from recent reports. To make this more clear in the manuscript, the order of the text describing the intervention arm has been altered.

Page 8: I see on page 8 that a variety of sources of evidence are used to inform the module which is appropriate but this seems inconsistent with other parts of the text as mentioned above.

Description in the manuscript has been altered for clarification, see above.

Page 11: A major concern is the use of the numeric rating scale for satisfaction. There is no reference provided, the wording of the question is not provided and the cutoff of 8 or greater to create a dichotomous judgement is arbitrary and reduces utility of what would otherwise be a continuous scale.

The NRS satisfaction scale is a widely used measure of postoperative satisfaction after TKA, and is actually the second most used method of measuring satisfaction scores according to a recent systematic review by Kahlenberg et al (HSSJ (2018) 14:192-201). This measure has indeed not been validated, but it is the preferred method of measuring postoperative satisfaction advocated by the Dutch orthopaedic society and the Dutch arthroplasty registry. For this reason this measure was chosen to analyze postoperative satisfaction.

To answer our primary research question, a ordinal scale would not suffice. A cutoff point had to be defined to determine which patients are considered very satisfied. Indeed this can be seen as arbitrary, but in the authors’ opinion the cutoff point of 8 is the most adequate option.

The wording of the question has been added to the manuscript.
Page 11: the secondary outcome measures are mislabeled. Age and sex, for example are not outcomes.

Labeling has been corrected.

Page 12: Of note, the factorial validity of the HSS expectation scale is unknown so one cannot be sure that this is actually a unidimensional scale with a single summary score and there are likely multiple dimensions captured with the scale. Secondly, the modifications made by Tilbury et al have not been validated and this needs to be made clear.

Clarified in the manuscript.

Reasons for using the EQ5D are not made clear and seem to be overlapping with other measures. Why are you using this scale? The reader should be informed of the rationale for choosing each scale.

The EQ-5D was added as a measure of generic health status, in addition to the joint specific PROMs used (KOOS-ps and OKS). To emphasize this distinction knee specific has been added to the description of the KOOS-PS.

Page 13: A 12-month anchor type question carries substantial bias and error. Patients are greatly influenced by current status when trying to recall baseline state. It is unclear why you are using this problematic scale. I am unclear on why this scale is used in the study.

We agree that current physical status and recall bias have important influence on this measure. On the other hand, when analyzing the effect of expectation fulfillment, the possible discordance between actual and perceived change in functional status is of interest. This can only be addressed by asking patients their perceived change by the means of an anchor question.

Power analysis: Power was based on a very small sample study of 44 persons and the likert type scale that asked a very broad-based question “How satisfied are you with the results of the surgery?” I am unaware of the validity of this scale and with the very small sample from approximately a decade ago, this seems like a very crude method for estimating power in your study, particularly since you are not measuring satisfaction with the same scale and you are only dichotomizing your scale. Please explain and clarify. I would strongly encourage more contemporary and more impactful data using an appropriate satisfaction scale and not the one you are currently proposing.

Most studies reporting on satisfaction after TKA use an ordinal scale (e.g., very satisfied, somewhat satisfied, dissatisfied, very dissatisfied), similar to the study we based our sample size on. The distribution of satisfaction rates after TKA are reported very consistently (Dunbar et al. BJJ 2013;95-B, Supple:148–52). For example Noble et al report on satisfaction rate in 253 TKA patient: satisfied 18%, very satisfied 57%, neutral 11%, dissatisfied (3%) or very dissatisfied 11% (Noble et al, CORR 2006;452:35-43). As the results from other studies in the field show similar results, we feel the choice of this specific study for sample size calculation should not be seen as a limitation.
Choice of the primary outcome measure is mainly based on the advice of the Dutch orthopaedic society, as has been discussed in response to a previous question of this reviewer.

Statistical analysis: The approach is dated and does not handle missing data. A more contemporary approach to the analyses is encouraged. In addition, missing data estimates should be provided and methods for handling missing data should be reported.

Missing data will be handled using multiple imputation. This has been added to the manuscript.

Safety: I found no mention of adverse event monitoring and while this appears to be a low risk study, adverse events should be monitored and reported.

Added to the manuscript.

Reviewer #2:

There is a great need for research investigating the impact of patient expectation modification on postoperative outcomes. I commend the authors for taking the time to perform a RCT on this topic. Overall, I am satisfied with the trial methodology. I do however, have some comments surrounding the study objective and choice of primary outcomes that I hope the authors will take into consideration.

RE: 112-114: The effect of pre-operative expectation management on post-operative expectation fulfilment and ultimately better post-operative satisfaction after TKA has not yet been studied.

Is expectation fulfilment and satisfaction with surgery the most appropriate and meaningful outcome to be assessing? If a patient expects a poor outcome after surgery, they are much more likely to have this expectation met or exceeded, and be satisfied with the surgical outcome. This however, does not mean they are satisfied with their function, QOL, knee symptoms etc. Considering the positive relationship between expectations and outcome in the literature, reducing one’s positive expectations has potential to negatively impact outcome. I would argue that it is very important to evaluate surgical outcome (e.g. activity limitation/function/symptoms/pain) not only surgical satisfaction and fulfilment of expectations.

The evidence on the relation between height of expectations and outcome is conflicting. Increasing pre-operative expectations potentially leads to higher outcome by utilizing the placebo effect, but on the other hand this increases the chance of unfulfilled expectations and subsequent dissatisfaction. Therefore, this approach was not chosen for the present study.

Because the strongest association described in literature is between expectation fulfillment and satisfaction, we chose satisfaction as the main outcome. The functional outcome will be evaluated in the current study as well, but not as primary outcome parameter.

RE: lines 103-104: These findings suggest that more realistic expectations potentially lead to higher post-operative satisfaction.
Is there evidence to suggest that lowering 'optimistic' patient expectations to align with what is deemed more 'realistic', is likely to improve postoperative outcome? The literature shows that higher patient expectations are associated with better postoperative outcomes than lower expectations, even if those expectations may be deemed unrealistically optimistic. I would argue that this is one of the key reasons why research is needed to determine the impact of altering expectations on post-operative outcomes.

To our knowledge there is no evidence available on the effect of altering expectations on outcome. We agree that functional outcome and pain scores have to be evaluated as well, these are included in the study protocol as secondary outcome parameters.

RE: lines 211-226.

You have provided a clear overview of the evidence regarding the relationship between positive expectations and improved outcome, and highlight that 'there are no intervention studies available on the effect of increasing expectations to improve treatment outcome in TKA patients.' I agree that this research is needed, this evidence reiterates the importance of evaluating surgical outcome. Notably, you are collecting appropriate measures (e.g. KOOS-PS, OKS, EQ-5D and NRS Pain), however, it is not clear how you intend to use these measures? Will you evaluate the relationship between expectation education and one or more of these outcomes?

Yes. The primary outcome that will be assessed is the effect on the intervention on satisfaction. For the secondary outcome parameters similar analysis will be performed as described in paragraph 3.11.

I support the decision to include LOT-R, PCS, as these may be important mediators of expectation education on outcome.

We agree.

Line 118-119 RE: realistic expectations for long-term recovery of symptoms, physical functioning and psychological issues (intervention group) What is considered a realistic expectation? For some, a very high expectation will be realistic. The 'average' outcome of a sample is not a 'realistic' outcome for all patients. Is this reflected in the education given? Lowering a patient's expectations may negatively impact their outcome, whereas providing information about the distribution of outcome, whilst not dampening ones optimism, (i.e. you may be in the minority who do extremely well after surgery, and the fact that you expect to do so, increases your likelihood of doing so) may be of greater value to the patient.

In the education module it is emphasized that the details addressed are an average. Patients are informed that individual outcome is likely to be either higher or lower, and modifying factors are addressed that predict higher or lower outcome are specifically addressed.
Line 126-128: RE: Additionally, an explorative analysis will be performed on the effect of the additional education module in subgroups of patients, depending on age, gender, severity of symptoms, symptoms of depression and coping mechanisms.

I suggest performing an exploratory analysis on the effect of modifying high vs. low expectations on outcome

The suggestion that an analysis on the effect of modifying high vs. low expectations and the effect this results in on outcome is a welcome addition. We have added this to the manuscript.

Line 158: RE: Symptomatic and radiographic knee osteoarthritis indicated for a primary TKA How will this be defined?

The Dutch national guideline for TKA will be followed. This recommends considering TKA in patient with radiological knee OA Kellgren and Lawrence ≥2 and pain and functional impairment with influence on quality of life, work and/or social life. The amount of impairment or pain is not further defined in this guideline.

This has been added to the manuscript.

Line 235. RE: 'Therefore, to the authors' opinion an education module should not result in overly optimistic expectations to be most effective.'

This statement is unclear, please clarify and re-phrase.

Rephrased.

RE: Additionally, modifying factors are addressed that predict higher or lower outcome for an individual patient; age, medical co-morbidity, body mass index (BMI), psychosocial factors, pain severity and pre-operative functional status.[33,34] I think the relationship between positive/optimistic expectations and better outcome should also be included here, explained in lay language that patients can easily understand.

The evidence on the height of expectations and outcome is not straightforward. The evidence supports that higher expectations lead to better outcome. But, this is only true for patients that already have high expectations. It is uncertain if increasing expectations would lead to higher outcome.

Stating the height of expectations as a modifier of outcome in the education module would possibly trigger patients to expect more of their TKA. This subsequently poses the risk of more unmet expectations. Given the aim of the education module under study (achieving realistic expectations), we chose not to mention this modifier.

Lines 275-289:
Some of this material is phrased with a negative bias. Example, '..only 43% is reported to return to high-impact sports' instead of '..57% of patients return to high impact sports'. Such phrasing is likely to lower patient expectations, and make patients less likely to engage in such activities or attempt such activities as 'kneeling' or 'walking longer distances.' Since they might, after receiving this information, expect that they will not be able to perform these activities. This in turn, has potential to negatively impact outcome, further highlighting the importance of evaluating postoperative outcome.

The education module itself has a generally positive tone. Numbers/percentages of patients that can do a certain activity or have no complaints are mentioned first.

RE: Table 1 column heading: 'Pre-operative, at admission'

Please re-phrase this heading to make it clearer that this is referring to pre-operative, but post education intervention

Rephrased

Lines 269-273: Why was there no patient involvement when developing the expectations education material? This was largely developed by surgeons whose experience of surgery is likely to differ greatly from that of the patient. Why not work with patients who have undergone TKA to inform the design of the materials?

The design of the module was shaped around a set of expectations that have been identified as most important by patients. The questions answered are identified in previous research with patients, and not based on expert opinion. The same goes for answers to these questions in the education module, this was mainly based on literature presenting patient reported outcome. Therefore, although we did not involve patients in the design, the education module is shaped around what patients think are important expectations, and patients experiences with the treatment result. This has been added to the discussion section.

Reviewer #3:

Thank you for submitting this interesting study protocol to Trials. Please find below some minor suggestions to improve the reporting of your protocol:

General: Please could the English and grammar be checked and improved throughout the manuscript

Checked by native speaker, corrections were made as indicated in the manuscript.

Methods - did PPI inform the design of this trial? If not, please discuss this as a limitation in the discussion section
Although we did not include public and patient involvement in the design of the study, the design is patient oriented. See the answer to the last question of reviewer #2 as well. This has been added to the discussion section.

Methods - please clarify which clinical and trial staff are blinded

Added specification to the manuscript.

Methods - please clarify the use of the NRS pain - does it ask about pain over the past 24 hours, past week, past month?

Past week. Manuscript corrected.

Discussion - please include a section discussing the limitations of this research including the single centre design, the lack of qualitative work and the lack of a cost-effectiveness analysis

The limitations section in the discussion has been extended with comments on the single-center design and patient involvement in the intervention design.

In the authors’ view a qualitative approach is not really appropriate in answering the primary research question at hand. Therefore, we do not see this as a limitation of this study.

Cost-effectiveness is not really an issue. As the intervention is not costly at all, justification for its use by a cost-effectiveness analysis does not provide additional support for the intervention. In the authors’ view, such an analysis would not provide interesting additional information and therefore we do not see its absence as a limitation of the proposed study.

SPIRT checklist item 8: Please add to the manuscript the type of trial, allocation ratio and framework

Added to the manuscript.

SPIRT checklist item 11a: Please provide sufficient information to allow replication of the intervention. For example is the lecture delivered in a group-based setting? How many patients are in each group? How is this only delivered to patients in the intervention group? What steps have been taken to limit or assess contamination between the intervention and usual care group? It may be easier to summarise the content of the lecture in a Table, rather than the main text.

Added the missing items described above to the manuscript text.

The leaflet summarizing the information in the additional module on realistic expectations for long-term recovery has been included as an appendix. Reference added in the manuscript.

SPIRT checklist item 11c - please state in the manuscript how attendance at the intervention is recorded
Added to the manuscript. Attendance is measured blinded for group allocation. Attendance is recorded by patients at the same time as completing the HSS questionnaire at the ‘pre-operative, post-education’ timepoint.

SPIRT checklist item 20c - please provide details on how missing data will be handled in the analysis

Missing data will be handled using multiple imputation. Details have been added to the manuscript, paragraph 3.11.

SPIRT checklist item 21a - please provide justification on why a TSC and DMC are not required for this trial

Explanation added; end of paragraph 3.10

SPIRT checklist item 25 - Protocol amendments should be updated on the Trial Registry record. Please amend

Added to the revised manuscript.