Author's response to reviews

Title: Functional outcome of total knee replacement: a study protocol for a prospective, doubleblinded, parallel-group randomized, clinical controlled trial of novel, personalized and conventional implants

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Functional outcome of total knee replacement: a study protocol for a prospective, double-blinded, parallel-group randomized, clinical controlled trial of novel and conventional implants

BMC Musculoskeletal Disorders

Dear Dr. Gao

We want to thank you for giving us the opportunity to revise the manuscript entitled:”Functional outcome of total knee replacement: a study protocol for a prospective, double-blinded, parallel-group randomized, clinical controlled trial of novel and conventional implants”. The manuscript has been revised based on the comments of the reviewers. We want to thank the reviewers for their constructive and important comments and these comments helping us to improve our manuscript.

Below we have listed all comments with a point-by-point response.

Reviewer #1:
This is a well written protocol for an important RCT. It is good to see appropriate outcomes and long-term follow up.

Concern: Reading the title and abstract and paper, I don't know what the interventions are. If they are all cruciate retaining, cemented, fixed bearings, why is one "novel". There must be a way of describing the key features of each implant. I know that protocols/ articles are published comparing Product A with Product B, but many readers would like to know the features that differ between the them.

Title: "novel and conventional implants" does not provide enough information on the implants. If I was researching a particular group of implants, I would expect this to be identified in the title and abstract.

Similarly, in the abstract, it would be good to briefly describe the implants beyond the product name.

Reply: Thank you for this comment. We have now added a brief description of the novel implant into the manuscript. Please see: Title (novel, personalized) Background, page 1, paragraph 1 (new personalized TKR design), Methods, page 1, paragraph 2 (novel personalized TKR design)

Concern: There is no need to mention hip replacement - the cited articles include hip replacement but report outcomes separately for knee replacement.

"Functional outcome after total knee replacement is, however, considered to be the least favorable measure of these two." I do not think this is necessary but if it stays, a reference is needed.

Line 18. The hip replacement figures are unnecessary

Reply: We appreciate the comments. We omitted all sentences regarding hip replacement. Please see: Background, Paragraph 1

Concern: Page 4 Paragraph 2. It would be good to have a brief description of the implants being evaluated. "new" "improved" "new generation" "redesigned" are not enough.

Reply: Thank you for this comment. We have added personalized to (new, personalized and hopefully improved). Please see: Background, page 4 paragraph 2, line 39. (A more anatomically accurate implant, finer sizing increments and full continuum of bearing constraints is redefining personalization.)

Concern: Study objective. Again, it would be good to have the implant described. The product name could be in brackets

Reply: Thank you for the comment. Please, see response to the previous concern. The product name has now been added in brackets.
Concern: Line 25. 28 is the wrong reference. Should be 33?

Line 41. Throughout, check product names are consistent

Page 7. Line 13. Reference for 15D.

Page 7. Line 54. As elsewhere describe the implants.

Reply: Thank you for your accuracy. References and product names have been corrected as suggested. The description has also been made. Please, see our previous response

Concern: Patient recruitment. It would be good to have some information on methods of informed consent

There is no information on the methods of the cost-effectiveness analysis - what perspective will be used?

Reply: Written informed consent was obtained. In cost-effectiveness analysis, cost of surgery, hospitalization, out-patient visits and physiotherapy visits are calculated. Cost per quality-adjusted life-years will be analyzed. Please see: Patient recruitment, page 8, Methods, Paragraph 2, page 7

Reviewer #2

This protocol described a scientific design of a double-blinded RCT for evaluating the functional outcome and patient satisfaction levels after receiving TKA with three types of bearing with a novel design and two additional conventional design. This work will be beneficial to fill the void of the functional evaluation to this new-designed implant, which may guide the surgeons to select the most proper implants to a patient. The design of this RCT have been fully considered and discussed by the researchers, but there still are some points requiring further detailed.

Concern: 1) The primary outcome measures are mostly based on self-administered PROMs. Although the patient satisfaction levels are an important and primary part of this protocol, the absence of a professional measure from medical staffs may lead to lose of some professional informations on the functional outcomes. Whether a professional objective examination or evaluation should be added to the pre- or post-operative measures needs further consideration. By the way, if the objective functional examinations are needed, whether the training for the sanitation workers are needed, who are the primary researchers during the follow-up trials?

Reply: Thank you very much - we are pleased to hear that. Our routine preoperative outpatient work of orthopedic surgeons includes professional objective examination and evaluation consisting e.g. knee range of motion, knee stability and patellar tracking. At the follow-up visits, these same measurements are performed and recorded by highly experienced physiotherapists, who routinely also see knee arthroplasty patients at the follow-up visits.
Thus, any additional training of the outpatient clinic staff was not needed to implement this study. These persons are not trial researchers. To conclude, even though primary outcome measures are PROMs, also traditional clinical outcome measures (knee ROM, stability etc.) will also be recorded and reported.

Concern: 2) The protocol only mentioned that this is a single-center trial to avoid potential interests relationship in different centres. Actually, many countries have offered many criterias for diagnosis it is known that the surgical skill of the surgeons will lead to different outcomes, so if the surgeons who participate for performing the surgery should be confirmed and recorded as well. If the samples are enough, it could be better to only include the patients receiving the surgery from a same team of surgeons.

Reply: We appreciate the concerns of the reviewer. We emphasized only the independency of the study center not to be biased by the interests of implant manufactures. For sure, the surgical skills of the surgeons will lead to different outcomes, and in this case single-center trial ensures that patients receive the surgery from a same team of surgeons. Every participating surgeon is an experienced knee arthroplasty surgeon. Moreover, PROM analysis between different surgeons will be made.

Concern: 3) Page 12 Line 28-29. Individual surgeon's preferences should be detailed. A unified procedure of the surgery should be defined in a RCT of which the potential bias should be avoided. A systematic training maybe helpful before the trial begin.

Reply: Thank you for the comment. The surgical procedures will be performed by experienced knee arthroplasty surgeons and unified procedure is described in details, please see: Operative treatment, Page 10

Concern: 4) The blinded methods based primarily on an envelope methods, which have plenty of potential risk factors which may lead to unblinded and also easily to be interfered by artificial factors. A more scientific blinded procedure could be better, especially during the grouping procedure, which is connected to the practice of randomised grouping directly, as the surgeon who preforms the surgeries is hardly keep blinded during the surgery procedure finished

Reply: Thank you for this comment. Maintaining blinding is challenging and especially successful blinding of the physiotherapists carrying the follow-up visits are discussed in page 13, paragraph 4. In this case blinding of surgeons performing arthroplasties is impossible

Concern: 5) Considering the probably loss rate to follow-up, no matter what the reasons are, whether the sample size should be enlarged a little for eliminating this probable bias?

Reply: We appreciate the concerns of the reviewer. We think that we have taken drop-outs into account. Please see: Sample size calculations, page 11. Moreover, based on our preliminary analysis drop out rate has been below 10%.