## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Hip Fracture Evaluation with ALternatives of Total Hip Arthroplasty versus Hemi-Arthroplasty (HEALTH): Protocol for a Multi-Centre Randomized Trial |
| **AUTHORS** | Bhandari, Mohit; Devereaux, P.J.; Einhorn, Thomas; Thabane, Lehana; Schemitsch, Emil; Koval, Kenneth; Frihagen, Frede; Poolman, Rudolf; Tetsworth, Kevin; Guerra-Farfán, Ernesto; Madden, Kim; Sprague, Sheila; Guyatt, Gordon |

## VERSION 1 - REVIEW

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| **REVIEWER** | You-Shui Gao<br>Department of Orthopaedic Surgery, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China |
| **REVIEW RETURNED** | 01-Sep-2014 |

- The reviewer completed the checklist but made no further comments

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| **REVIEWER** | Jiri Gallo, MD, PhD<br>Department of Orthopedics, Faculty of Medicine and Dentistry, Palacky University Olomouc, Czech Republic |
| **REVIEW RETURNED** | 06-Sep-2014 |

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| **GENERAL COMMENTS** | Reading this manuscript was a pleasure time: It is focused on familiar topic, planned study design/methods are excellent, and the manuscript is well written. However, I have several remarks on the ideas and concept:<br><br>1) Page 4, lines 50-53: I respect the data from Bhandari et al international survey (JBJS 2005), however, at least in my country the decision to HA is thoroughly thought in each particular patient. In fact, HA is the method of choice only in minority of cases (those who are older than 75 y., with limited time of survival, with inappropriate acetabulum on radiographic examination etc.). In addition, recent survey data suggests small changes in favor of THA comparing to HA also in the USA (Miller, Callaghan et al. 2014).<br><br>2) Page 5, lines 8-26: Interestingly, so-called secondary objectives contains of events that are also included among the primary objectives (unplanned secondary procedures at two years) such as periprosthetic fractures, dislocations (at least some of them), implant failure, soft-tissue problems, heterotopic ossifications (at least some of them). On the other hand, one would expect that implant failure, wear and corrosion, osteolysis, aseptic loosening are typical for later period after the surgery than is proposed two year follow-up (my own experience, individual studies, registry based data). Accepting that these are not typical early complications they should be associated |

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| | either with a mistake in the choice of a particular implant or to a surgical mistake but generally they should not handicap the THA as a therapeutic method.<br>On the other hand, I miss in the list of secondary objectives those that are related to brain dysfunction (esp. development of a postoperative delirium in older patients), (Lee, Mears et al. 2011, Daniels, Daiello et al. 2014).<br><br>3) Page 5, lines 30-39: I do not see a clinically significant difference between surgeons specializing only on HA and those specializing only on THA because those orthopedic surgeons are not available in my country.<br><br>4) Page 5, lines 43-44: Age is very important variable because the main difference between HA and THA could lie in the long-term outcomes with the HA being “vulnerable” to reoperations due to degeneration of acetabular cartilage occurring at least in some cases (Dalldorf, Banas et al. 1995, Li, Hua et al. 2014). That’s why we offer generally the patients younger than 70 years THA instead of HA. In addition, we can offer some of them wear-resistant bearings (either HXLPE liners or COC pair). In this line, the randomization could prevent these patients from getting the modern THA implants shifting at least some of them towards harm in the long-term perspective. Being fair at least one study demonstrate excellent long-term survival of cemented HA, however, this study is focused on patients 75 years and older (Viberg, Overgaard et al. 2013).<br><br>5) Page 6, lines 3-17: Perhaps, ethylic and drug abuse might be included in the inclusion/ exclusion criteria because they might influence on compliance of the patient and on the rate of early complications. At least some patients with femoral neck fractures are those with ethylic (drug) history. Therefore, the outcomes of the proposed study will not address this particular group of patients. In addition, simple tool ascribing cognitive functions might be included in the study protocol. Again, I feel that distinguishing only frank dementia is not enough for such study level.<br><br>6) Page 6, lines 42-47: Perhaps, gender might be included in the list of prognostic factors. Recently, the difference between men and women outcomes was revealed among the patients undergoing THA (Inacio, Ake et al. 2013).<br><br>7) Page 6, lines 51-57: The most frequent early complication of THA is dislocation. It is associated with the size of the head and surgical approach.<br><br>8) Page 7, lines 13-37: Some centers (surgeons) use routinely oral anticoagulation drugs in the thromboprophylaxis. These are not included in the Standardization of Procedures and Peri-Operative Care.<br><br>9) Page 8, line 34-39: It is not clear whether all grades of heterotopic ossifications will be collected. As well as, it is not clear how the abductor weakness will be examined and collected.<br><br>10) Page 10, lines 10-27: I do not think that performing at least 50 procedures in a career and at least 5 procedures per year are appropriate criteria for expertise in THA/HA surgery. In my opinion, these numbers are too low to reduce significantly occurrence of a |

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| | surgeon-induced complication.<br><br>11) Page 16, lines: 28-39: I understand very well the goals of the proposed study; they are attractive and clinically useful. However, this study design will focus only on a list of early complications that are known in majority. It will not give an answer on what is the best choice for the patient of a particular age, gender, activity (mental)-level, health status etc. with a dislocated femoral neck fracture especially in relation to more than 5-year follow-up.<br><br>References:<br>Dalldorf, P. G., M. P. Banas, D. G. Hicks and V. D. Pellegrini, Jr. (1995). "Rate of degeneration of human acetabular cartilage after hemiarthroplasty." J Bone Joint Surg Am 77(6): 877-882.<br>Daniels, A. H., L. A. Daiello, C. R. Lareau, K. A. Robidoux, W. Luo, B. Ott, R. A. Hayda and C. T. Born (2014). "Preoperative cognitive impairment and psychological distress in hospitalized elderly hip fracture patients." Am J Orthop (Belle Mead NJ) 43(7): E146-152.<br>Inacio, M. C., C. F. Ake, E. W. Paxton, M. Khatod, C. Wang, T. P. Gross, R. G. Kaczmarek, D. Marinac-Dabic and A. Sedrakyan (2013). "Sex and risk of hip implant failure: assessing total hip arthroplasty outcomes in the United States." JAMA Intern Med 173(6): 435-441.<br>Lee, H. B., S. C. Mears, P. B. Rosenberg, J. M. Leoutsakos, A. Gottschalk and F. E. Sieber (2011). "Predisposing factors for postoperative delirium after hip fracture repair in individuals with and without dementia." J Am Geriatr Soc 59(12): 2306-2313.<br>Li, J., X. Hua, Z. Jin, J. Fisher and R. K. Wilcox (2014). "Influence of clearance on the time-dependent performance of the hip following hemiarthroplasty: A finite element study with biphasic acetabular cartilage properties." Med Eng Phys.<br>Miller, B. J., J. J. Callaghan, P. Cram, M. Karam, J. L. Marsh and N. O. Noiseux (2014). "Changing Trends in the Treatment of Femoral Neck Fractures: A Review of the American Board of Orthopaedic Surgery Database." J Bone Joint Surg Am 96(17): e149.<br>Viberg, B., S. Overgaard, J. Lauritsen and O. Ovesen (2013). "Lower reoperation rate for cemented hemiarthroplasty than for uncemented hemiarthroplasty and internal fixation following femoral neck fracture: 12- to 19-year follow-up of patients aged 75 years or more." Acta Orthop 84(3): 254-259. |

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| **REVIEWER** | Anders Enocson<br>Section of Trauma and Orthopaedics<br>Karolinska Institute at<br>South Hospital<br>Stockholm<br>Sweden |
| **REVIEW RETURNED** | 11-Sep-2014 |

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| **GENERAL COMMENTS** | have reviewed the study protocol for the proposed HEALTH study. In general I think the study is well designed and it will definitely provide important knowledge on how to treat this patient population. The large number of included patients will make the study unique, and I look forward to see the results in the future. However, I have a few questions listed below.<br><br>• In the Abstract Introduction line 9-11 I think the sentence |

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| | ”*The optimal approach for the surgical management of femoral neck fractures remains unknown. Current evidence suggests the use of arthroplasty.*.” should be clarified that this applies to displaced fractures.<br><br>• Page 4, line 55. I just want to make a comment on the dislocation issue. If this is to be discussed one has to mention the surgical approach used, as an increased risk for dislocation of THA compared to HA probably only exist if a posterior surgical approach is used. We have previously reported in a large series including 713 femoral neck fracture patients operated upon with THA that the dislocation rate was 2% if an anterolateral approach was used (Enocson et al. ACTA Orthop. 2009).<br><br>• Page 5, line 46. Although classification systems, such as the Garden classification, have their limitations, I think that you will get a significant variety in the fracture pattern of the included patients if you choose not to use one. The “*Displaced fracture that is not, in the judgment of the attending surgeon, optimally managed by reduction and internal fixation*” definition seems quite vague.<br><br>• Page 6, line 12. How do you define “*frank dementia*”? As a substantial number of these patients display some degree of impaired cognitive function, a validated and easy to use instrument should be used. I would suggest the SPMSQ (Short Portable Mental Status Questionnaire) (Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients*. J Am Geriatr Soc* 1975).<br><br>• Page 6, line 26. “*If a patient lacks capacity and is deemed unable to consent, study personnel may obtain informed consent from the patient's legally authorized representative*” This seem a bit odd to me. Do you actually mean patients with dementia or other cognitive impairment? If so, the distinction between these patients and the one mentioned above will be difficult to make. Including patients without their consent, in this kind of study, does not correspond with good scientific practice in my opinion.<br><br>• Page 8. Again, if you include patients that cannot consent for themselves you will run into problems with the self-administered questionnaires that you are planning to use. How will you asses pain for example in a non-compliant patient?<br><br>• Page 11, line 24. “…a*rthroscopy…*” should be changed to “…*arthroplasty…*”. |

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| | • Page 15, line 14. "*All patients included in this study will sign a consent form…"* Please see above, and clarify. |

**VERSION 1 – AUTHOR RESPONSE**

Reviewer: 1
There are no comments

Reviewer: 2
Reading this manuscript was a pleasure time: It is focused on familiar topic, planned study design/methods are excellent, and the manuscript is well written. However, I have several remarks on the ideas and concept:

1) Page 4, lines 50-53: I respect the data from Bhandari et al international survey (JBJS 2005), however, at least in my country the decision to HA is thoroughly thought in each particular patient. In fact, HA is the method of choice only in minority of cases (those who are older than 75 y., with limited time of survival, with inappropriate acetabulum on radiographic examination etc.). In addition, recent survey data suggests small changes in favor of THA comparing to HA also in the USA (Miller, Callaghan et al. 2014).

In addition to the survey data by Bhandari et al (2005), in our experience with recruiting sites for the HEALTH trial, we have found that there is a large variation in practice between countries. Several countries have standard of care guidelines that conflict with the standard of care guidelines of other countries. Additionally, in many countries, patients over 75 years constitute the majority of patients with femoral neck fractures with mean ages of 82-86 years and few patients below 70 years. For example, in Norway 81% of adult hip fracture patients were over 75 years old (Stoen RO, Nordsletten L, Meyer HE, Frihagen JF, Falch JA, Lofthus CM. Hip fracture incidence is decreasing in the high incidence area of Oslo, Norway. Osteoporos Int. 2012 Oct;23(10):2527-34.) The results of the HEALTH trial will benefit surgeons and patients in all countries for more standardized care.

2) Page 5, lines 8-26: Interestingly, so-called secondary objectives contains of events that are also included among the primary objectives (unplanned secondary procedures at two years) such as periprosthetic fractures, dislocations (at least some of them), implant failure, soft-tissue problems, heterotopic ossifications (at least some of them). On the other hand, one would expect that implant failure, wear and corrosion, osteolysis, aseptic loosening are typical for later period after the surgery than is proposed two year follow-up (my own experience, individual studies, registry based data). Accepting that these are not typical early complications they should be associated either with a mistake in the choice of a particular implant or to a surgical mistake but generally they should not handicap the THA as a therapeutic method.

We thank the reviewer for raising a good point. All re-operations and secondary procedures will be adjudicated by an independent, blinded central adjudication committee. The committee will make determinations regarding the appropriateness of technique and cause of the secondary procedure.

On the other hand, I miss in the list of secondary objectives those that are related to brain dysfunction (esp. development of a postoperative delirium in older patients), (Lee, Mears et al. 2011, Daniels, Daiello et al. 2014).

While we are collecting safety data for all adverse events, including brain dysfunction like delirium, we have elected to focus on hip-related complications for the secondary outcomes.

3) Page 5, lines 30-39: I do not see a clinically significant difference between surgeons specializing only on HA and those specializing only on THA because those orthopedic surgeons are not available in my country.

In many countries, including Canada and the United States, performing THA is a very specialized role, while most orthopaedic surgeons can perform HA. In the Netherlands, one of the countries involved in this trial, trauma surgeons perform HA and orthopaedic surgeons perform THA.

4) Page 5, lines 43-44: Age is very important variable because the main difference between HA and THA could lie in the long-term outcomes with the HA being “vulnerable” to reoperations due to degeneration of acetabular cartilage occurring at least in some cases (Dalldorf, Banas et al. 1995, Li, Hua et al. 2014). That’s why we offer generally the patients younger than 70 years THA instead of HA. In addition, we can offer some of them wear-resistant bearings (either HXLPE liners or COC pair). In this line, the randomization could prevent these patients from getting the modern THA implants shifting at least some of them towards harm in the long-term perspective. Being fair at least one study demonstrate excellent long-term survival of cemented HA, however, this study is focused on patients 75 years and older (Viberg, Overgaard et al. 2013).

As previously mentioned, standard of care varies widely by country. The HEALTH trial is essential because much of the evidence on which surgeons base their treatment decisions comes from retrospective observational studies.

5) Page 6, lines 3-17: Perhaps, ethylic and drug abuse might be included in the inclusion/ exclusion criteria because they might influence on compliance of the patient and on the rate of early complications. At least some patients with femoral neck fractures are those with ethylic (drug) history. Therefore, the outcomes of the proposed study will not address this particular group of patients.

We exclude patients who are not expected to be able to maintain follow-up for the full two duration of the trial. Patients with alcohol abuse issues may be included in this criterion. We have clarified this point in the eligibility section.

In addition, simple tool ascribing cognitive functions might be included in the study protocol. Again, I feel that distinguishing only frank dementia is not enough for such study level.

The intention of the criterion to exclude patients with frank dementia is to exclude patients who, in the judgement of the enrolling surgeon, it would be difficult to determine re-operation status at two years. We allow patients with mild to moderate dementia (in the judgment of the enrolling surgeon) to be enrolled in the trial provided local regulations allow it, and a legally authorized representative provides consent, and the patient provides assent, and a supportive family member is available to assist. Family members are not permitted to complete questionnaires (i.e. SF-12, EQ5D, and WOMAC) for the patient, but adverse events and re-operations can still be determined. Our approach is consistent with the pragmatic or practical philosophy of the trial.

6) Page 6, lines 42-47: Perhaps, gender might be included in the list of prognostic factors. Recently, the difference between men and women outcomes was revealed among the patients undergoing THA (Inacio, Ake et al. 2013).

We thank the reviewer for their suggestion. Although our primary analysis will be unadjusted, we plan to incorporate gender as one of the key prognostic factors in a secondary adjusted analysis and have specified this in the revised submission.

7) Page 6, lines 51-57: The most frequent early complication of THA is dislocation. It is associated with the size of the head and surgical approach.

We agree with the reviewer. We are collecting data on head size and surgical approach. Although our primary analysis will be unadjusted, we plan to incorporate head size and surgical approach into the data analysis and we have specified this in the revised submission.

8) Page 7, lines 13-37: Some centers (surgeons) use routinely oral anticoagulation drugs in the thromboprophylaxis. These are not included in the Standardization of Procedures and Peri-Operative Care.

We thank the reviewer for the suggestion. We are collecting data on the use of oral anticoagulation drugs so we have added this to the list of examples of thromboprophylaxis in the Standardization of Procedures and Peri-Operative Care section.

9) Page 8, line 34-39: It is not clear whether all grades of heterotopic ossifications will be collected. As well as, it is not clear how the abductor weakness will be examined and collected.

An independent, blinded central adjudication committee is reviewing all cases of heterotopic ossification and will be documenting the grade.

10) Page 10, lines 10-27: I do not think that performing at least 50 procedures in a career and at least 5 procedures per year are appropriate criteria for expertise in THA/HA surgery. In my opinion, these numbers are too low to reduce significantly occurrence of a surgeon-induced complication.

We thank the reviewer for this observation. These numbers are meant to be a guide. We are taking into account various thresholds for expertise from around the world. We are documenting the numbers of each type of arthroplasty that participating surgeons have performed in the past. Our criteria are based on a consensus of the large number of participating surgeons and are based on considerations of optimal experience, feasibility, and the pragmatic philosophy of the trial.

11) Page 16, lines: 28-39: I understand very well the goals of the proposed study; they are attractive and clinically useful. However, this study design will focus only on a list of early complications that are known in majority. It will not give an answer on what is the best choice for the patient of a particular age, gender, activity (mental)-level, health status etc. with a dislocated femoral neck fracture especially in relation to more than 5-year follow-up.

We thank the reviewer for this observation. We understand that a limitation of this trial is that we are not focusing on longer-term outcomes. Like almost all trials, we will not be powered for the level of sub-group analysis implied in the reviewers' comments. In the discussion, we have clarified that these are limitations.

References:

Dalldorf, P. G., M. P. Banas, D. G. Hicks and V. D. Pellegrini, Jr. (1995). "Rate of degeneration of human acetabular cartilage after hemiarthroplasty." J Bone Joint Surg Am 77(6): 877-882.
Daniels, A. H., L. A. Daiello, C. R. Lareau, K. A. Robidoux, W. Luo, B. Ott, R. A. Hayda and C. T. Born (2014). "Preoperative cognitive impairment and psychological distress in hospitalized elderly hip fracture patients." Am J Orthop (Belle Mead NJ) 43(7): E146-152.
Inacio, M. C., C. F. Ake, E. W. Paxton, M. Khatod, C. Wang, T. P. Gross, R. G. Kaczmarek, D. Marinac-Dabic and A. Sedrakyan (2013). "Sex and risk of hip implant failure: assessing total hip arthroplasty outcomes in the United States." JAMA Intern Med 173(6): 435-441.
Lee, H. B., S. C. Mears, P. B. Rosenberg, J. M. Leoutsakos, A. Gottschalk and F. E. Sieber (2011).

"Predisposing factors for postoperative delirium after hip fracture repair in individuals with and without dementia." J Am Geriatr Soc 59(12): 2306-2313.
Li, J., X. Hua, Z. Jin, J. Fisher and R. K. Wilcox (2014). "Influence of clearance on the time-dependent performance of the hip following hemiarthroplasty: A finite element study with biphasic acetabular cartilage properties." Med Eng Phys.
Miller, B. J., J. J. Callaghan, P. Cram, M. Karam, J. L. Marsh and N. O. Noiseux (2014). "Changing Trends in the Treatment of Femoral Neck Fractures: A Review of the American Board of Orthopaedic Surgery Database." J Bone Joint Surg Am 96(17): e149.
Viberg, B., S. Overgaard, J. Lauritsen and O. Ovesen (2013). "Lower reoperation rate for cemented hemiarthroplasty than for uncemented hemiarthroplasty and internal fixation following femoral neck fracture: 12- to 19-year follow-up of patients aged 75 years or more." Acta Orthop 84(3): 254-259.

Reviewer: 3
Reviewer Name Anders Enocson
Institution and Country Section of Trauma and Orthopaedics
Karolinska Institute at
South Hospital
Stockholm
Sweden
Please state any competing interests or state ‘None declared’: None declared

I have reviewed the study protocol for the proposed HEALTH study. In general I think the study is well designed and it will definitely provide important knowledge on how to treat this patient population. The large number of included patients will make the study unique, and I look forward to see the results in the future. However, I have a few questions listed below.

• In the Abstract Introduction line 9-11 I think the sentence ”The optimal approach for the surgical management of femoral neck fractures remains unknown. Current evidence suggests the use of arthroplasty..” should be clarified that this applies to displaced fractures.

We thank the reviewer for the suggestion. We have clarified in the abstract that this applies to displaced femoral neck fractures.

• Page 4, line 55. I just want to make a comment on the dislocation issue. If this is to be discussed one has to mention the surgical approach used, as an increased risk for dislocation of THA compared to HA probably only exist if a posterior surgical approach is used. We have previously reported in a large series including 713 femoral neck fracture patients operated upon with THA that the dislocation rate was 2% if an anterolateral approach was used (Enocson et al. ACTA Orthop. 2009).

According to a recent meta-analysis (Burgers 2012), dislocation rates were 9% after THA and 3% after HA (OR 2.53; 95% CI 1.05-6.10). The quality of the meta-analysis is good, however the trials included have some methodological flaws and the heterogeneity was moderately high (I2=30%). Therefore, the HEALTH trial is still relevant. The authors of the meta-analysis did not evaluate the influence of surgical approach.

• Page 5, line 46. Although classification systems, such as the Garden classification, have their limitations, I think that you will get a significant variety in the fracture pattern of the included patients if you choose not to use one. The “Displaced fracture that is not, in the judgment of the attending surgeon, optimally managed by reduction and internal fixation” definition seems quite vague.

We have chosen to include a variety of fracture patterns to improve generalizability and practicality.

• Page 6, line 12. How do you define “frank dementia”? As a substantial number of these patients display some degree of impaired cognitive function, a validated and easy to use instrument should be used. I would suggest the SPMSQ (Short Portable Mental StatusQuestionnaire) (Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. J Am Geriatr Soc 1975).

We leave the decision of whether to include patients with dementia up to the clinical judgement of the attending surgeon. Sites are instructed to follow all local ethics requirements and to exclude patients with frank dementia that will interfere with collecting the primary outcome at 2 years, based on the attending surgeon’s clinical judgment or according to local regulations. It is of course possible that frailer patients, in this case with mild or moderate dementia, have other functional demands and/or a higher risk of complications that could influence choice of implant. We are collecting data on baseline comorbidities, including mild to moderate dementia. This may be a point of a secondary analysis.

• Page 6, line 26. “If a patient lacks capacity and is deemed unable to consent, study personnel may obtain informed consent from the patient’s legally authorized representative” This seem a bit odd to me. Do you actually mean patients with dementia or other cognitive impairment? If so, the distinction between these patients and the one mentioned above will be difficult to make. Including patients without their consent, in this kind of study, does not correspond with good scientific practice in my opinion.

Patients with mild to moderate dementia are included provided the consent process can be completed according to local regulations. If permissible by local regulations, a legally authorized representative may provide consent for the patient to participate, and the patient should provide assent, if this is allowed by local ethics boards. Surgeons are asked to use their clinical judgment when deciding to include or exclude patients with dementia.

• Page 8. Again, if you include patients that cannot consent for themselves you will run into problems with the self-administered questionnaires that you are planning to use. How will you asses pain for example in a non-compliant patient?

We tell sites that it is acceptable to have a supportive family member or friend available to assist with filling out questions about medical history and events so patients with mild or moderate dementia can be included if possible. We do not allow family members and friends to answer questionnaires on behalf of the patient, so some secondary outcomes will only apply to patients who are not cognitively impaired. We have added this as a study limitation. Our group has conducted several studies on patients with dementia in hip fracture trials and we have concluded that excluding patients with dementia biases results, so it is preferable to include them.

References: 1) Hebert-Davies J, Laflamme GY, Rouleau D; HEALTH and FAITH investigators. Bias towards dementia: are hip fracture trials excluding too many patients? A systematic review. Injury. 2012 Dec;43(12):1978-84. 2) Mundi S, Chaudhry H, Bhandari M. Systematic review on the inclusion of patients with cognitive impairment in hip fracture trials: a missed opportunity? Can J Surg. 2014 Aug;57(4):E141-5.

• Page 11, line 24. “…arthroscopy…” should be changed to “…arthroplasty…”.

We thank the reviewer. We have corrected the error.

• Page 15, line 14. “All patients included in this study will sign a consent form…” Please see above, and clarify.

If permissible by local regulations, a legally authorized representative may provide consent for the patient to participate, and the patient should provide assent, if this is allowed by local ethics boards. We have clarified that all patient or legally authorized representatives will sign the consent form.

**VERSION 2 – REVIEW**

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| **REVIEWER** | Anders Enocson<br>Section of Trauma and Orthopaedics<br>Karolinska Institute at<br>South Hospital<br>Stockholm<br>Sweden |
| **REVIEW RETURNED** | 31-Oct-2014 |

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| **GENERAL COMMENTS** | No further comments, other than that I look forward to see the results in the future. |

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| **REVIEWER** | You-Shui Gao<br>Shanghai Sixth People's Hospital, Shanghai Jiao Tong University |
| **REVIEW RETURNED** | 31-Oct-2014 |

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| **GENERAL COMMENTS** | I think the manuscript merits publication in its current form. It is well performed. |

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| **REVIEWER** | Prof. Jiri Gallo, MD, PhD<br>Department of Orthopedics, Faculty of Medicine and Dentistry, Palacky University Olomouc, University Hospital Olomouc, Czech Republic |
| **REVIEW RETURNED** | 08-Nov-2014 |

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| **GENERAL COMMENTS** | I read this version with a pleasure, the authors included majority of comments and responded well on the remaining ones.<br><br>I have the following comments:<br><br>Page 5, Study objectives: Again, I emphasize that wear-related problems and osteolysis are unlikely during the first 2 years after surgery except the surgeon mistake and/or using inappropriate implants which should be prevented by the trial protocol.<br><br>Page 9, Study follow Up: In my practice I do not see the increased rate of reoperation of THA in patients with dislocated femoral neck fractures treated with THA (except those experiencing dislocation) in comparison to those operated for osteoarthritis. I think that study of Ravikumar et al does not cover the recent progress in surgical techniques (for instance we reconstruct meticulously the joint capsule in HA, we use 36 mm implants in case of THA etc.). Please use a newer citation if possible.<br><br>Page 10, Surgeon expertise. I think still that criterion of at least 5 procedures per year does not have the power to distinguish between |

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| | experienced hip surgeons and those who are less experienced therefore the outcomes may be biased by this fact. I suggest increasing the threshold for demonstration of experience to at least 12 procedures per year.<br><br>Page 16, Discussion, final paragraph: I do not see this point of trial in relation to clinical practice improvements especially with regard to age of the target group of patients. I would appreciate enrolment of patients of age 60 and above. The younger patients will be indicated to THA and the older ones will get HA regardless of the trial outcomes at least in some countries and in some hands. The reason for that lies in worries on the longer follow-up in the case of HA. In addition, nobody can estimate now the balance between promising early clinical outcomes and later ones (including the risk for reoperation for instance after 5 – 7 years postop). Therefore, I would recommend the authors to include some uncertainty and probability thinking into this part of Discussion. |

**VERSION 2 – AUTHOR RESPONSE**

Reviewer 1: I think the manuscript merits publication in its current form. It is well performed.

We thank the reviewer for the comments.

Reviewer 2: Page 5, Study objectives: Again, I emphasize that wear-related problems and osteolysis are unlikely during the first 2 years after surgery except the surgeon mistake and/or using inappropriate implants which should be prevented by the trial protocol.

The central adjudication committee will make determine the appropriateness of technique, the reason for each secondary procedure, and whether or not the procedure meets the established criteria as a study event. In order to make the results of the trial as generalizable as possible, we have not dictated the type of implant or other aspects of the surgical technique.

Page 9, Study follow Up: In my practice I do not see the increased rate of reoperation of THA in patients with dislocated femoral neck fractures treated with THA (except those experiencing dislocation) in comparison to those operated for osteoarthritis.

Burgers et al (2012) published a meta-analysis of THA versus HA studies for femoral neck fractures. The proportion of revision surgeries was not significantly different in THA vs HA and mortality was similar. However, dislocation rates were 9% after THA versus 3% after HA and pain and patient-important outcomes were better in the THA group. This shows that the question of whether THA or HA is superior in this population is not yet settled.

I think that study of Ravikumar et al does not cover the recent progress in surgical techniques (for instance we reconstruct meticulously the joint capsule in HA, we use 36 mm implants in case of THA etc.). Please use a newer citation if possible.

Ravikumar shows that most of the re-operations occur before two years for the early complications that we are looking at. We realize our trial will be generalizable to only those events that occur within two years, but we believe that it will still provide important information given that event rates are not small in the first few years. Our choice of a two year follow up is a trade-off between feasibility and pragmatic expectations for early complications.

Page 10, Surgeon expertise. I think still that criterion of at least 5 procedures per year does not have

the power to distinguish between experienced hip surgeons and those who are less experienced therefore the outcomes may be biased by this fact. I suggest increasing the threshold for demonstration of experience to at least 12 procedures per year.

We thank the reviewer for this observation. We are taking into account various thresholds for expertise from around the world, based on conversations with our steering committee members and investigators in other countries. Additionally, we are attempting to keep the trial feasible for enrollment. We are documenting the numbers of each type of arthroplasty that participating surgeons have performed in the past. If necessary we may be able to look at the actual expertise numbers in the final analysis.

Page 16, Discussion, final paragraph: I do not see this point of trial in relation to clinical practice improvements especially with regard to age of the target group of patients. I would appreciate enrolment of patients of age 60 and above.

For the first 555 patients only 19 are under the age of 60. We include patients aged 50-59 because we aim to be pragmatic. We will fully describe the age of the included population in the results paper.

The younger patients will be indicated to THA and the older ones will get HA regardless of the trial outcomes at least in some countries and in some hands. The reason for that lies in worries on the longer follow-up in the case of HA. In addition, nobody can estimate now the balance between promising early clinical outcomes and later ones (including the risk for reoperation for instance after 5 – 7 years postop). Therefore, I would recommend the authors to include some uncertainty and probability thinking into this part of Discussion.

Since we are focusing on earlier clinical outcomes in this trial, we understand that our results apply in the short-term only; up to two years following the initial surgery. We have expanded upon our discussion of this limitation in the discussion section. Since randomized trials are so costly, it may be more feasible to use registry data rather than randomized trial data when considering long term outcomes.