Femoroacetabular Impingement Randomised controlled Trial (FIRST) - a multi-centre randomized controlled trial comparing arthroscopic lavage and arthroscopic osteochondroplasty on patient important outcomes and quality of life in the treatment of young adult (18–50 years) femoroacetabular impingement: a statistical analysis plan

Nicole Simunovic², D. Heels-Ansdell¹, L. Thabane¹,²,³, O. R. Ayeni²* and on behalf of the FIRST Investigators

Abstract

Background: The research objectives of the Femoroacetabular Impingement Randomised controlled Trial (FIRST) are to assess whether surgical correction of the hip impingement morphology (arthroscopic osteochondroplasty) with or without labral repair, in adults aged 18–50 years diagnosed with non-arthritic femoroacetabular impingement (FAI), provides decreased pain and improved health-related quality of life at 12 months compared to arthroscopic lavage of the hip joint. This article describes the statistical analysis plan for the FIRST trial.

Methods/design: FIRST is an ongoing multi-centre, blinded randomised controlled trial of 220 patients who have been diagnosed with FAI and are optimized for surgical intervention. This article describes the overall analysis principles, including how participants will be included in each analysis, the presentation of the results, adjustments for covariates, the primary and secondary outcomes and their respective analyses. In addition, we will present the planned sensitivity and subgroup analyses.

Discussion: Our rationale for FIRST is based upon (1) an epidemic of FAI surgery with resultant increased healthcare costs over that last decade, (2) worldwide disparity in perceptions about its utility, and (3) consensus that definitive evidence for or against surgical approaches is lacking.

Trial registration: ClinicalTrials.gov, NCT01623843. Registered on 20 June 2012.

Keywords: Statistical analysis plan, Randomised controlled trial, Femoroacetabular impingement, Lavage, Osteochondroplasty

* Correspondence: ayenif@mcmaster.ca
²Department of Surgery, Division of Orthopaedic Surgery, McMaster University, 1200 Main St W, 4E15, Hamilton, ON L8N 3Z5, Canada
Full list of author information is available at the end of the article
Background

The Femoroacetabular Impingement Randomised controlled Trial (FIRST) is a multi-centre, concealed randomized controlled trial (RCT) evaluating the effect of arthroscopic lavage (i.e. washing out the hip joint) versus osteochondroplasty (i.e. surgical correction of the hip impingement morphology) in adults aged 18–50 years diagnosed with non-arthritic femoroacetabular impingement (FAI). The protocol for the FIRST trial has been previously published [1] and provides more detail on the trial rationale, eligibility criteria, interventions, data management, and methods for limiting bias.

FAI is a condition that causes hip pain in the young adult as a result of a size and shape mismatch between the femoral head and the acetabulum. FAI is typically classified into two sub-types; cam type (a misshaped femoral head) or pincer type (an over-covered or deep socket). Most patients have a combination of both types of impingement. With FAI, the femoral head (ball) and acetabular rim (socket) of the hip joint collide during hip flexion and rotation. This collision results in an impingement of the femoral head/neck/column on the acetabular rim, and patients experience hip pain. This pain can be a precursor to early hip damage such as cartilage delamination and labral tears of the hip. As the condition progresses, the resulting hip damage may lead to osteoarthritis of the hip [1].

The rationale for the FIRST trial is based upon (1) an exponential increase in FAI surgery with resultant increased healthcare costs over that last decade, (2)
worldwide disparity in perceptions about its utility, and (3) consensus that definitive evidence for or against surgical approaches is lacking. Therefore, the primary objective of the trial is to assess whether surgical correction of the impingement morphology (arthroscopic osteochondroplasty) with or without labral repair, in adults aged 18–50 years diagnosed with non-arthritic FAI, provides decreased pain at 12 months compared to arthroscopic lavage of the hip joint. Secondary objectives include measuring outcomes associated with the intervention and control groups (osteochondroplasty versus lavage) related to improved lifestyle, emotional health, and physical health.

### Table 1 Statistical analysis plan summary

| Objective | Outcome Name | Hypothesis | Method of analysis |
|-----------|--------------|------------|-------------------|
| Primary objective | To compare pain levels at 1 year | Pain (VAS) | Continuous | Osteochondroplasty will reduce pain compared to lavage | Multiple linear regression |
| Secondary objectives 1 | To compare patient-reported health-related quality of life | Hip function (HOS) | Continuous | Osteochondroplasty will improve health-related quality of life, function, and utility compared to lavage | Multiple linear regression |
| Secondary objectives 1 | | Hip-specific disease on hip function (iHOT-12) | Continuous | | |
| Secondary objectives 1 | | Physical health (SF-12 PCS) | Continuous | | |
| Secondary objectives 1 | | Mental health (SF-12 MCS) | Continuous | | |
| Secondary objectives 1 | | Health Utility (EQ-5D) | Continuous | | |
| Secondary objective 2 | To compare hip complications | Hip-related complications (e.g. re-operation) | Binary | Osteochondroplasty will reduce rate of re-operations compared to lavage | Multiple logistic regression |
| Subgroup analysis | Hip impingement severity: mild (alpha angle < 60 – > 50 degrees), moderate (alpha angle > 60 – < 83°), severe (alpha angle > 83°) | Pain (VAS) | Continuous | Patients with severe impingement at baseline will have the greatest improvement with the osteochondroplasty procedure compared with those with moderate to mild impingement | Multiple linear regression |
| Subgroup analysis | Gender: male, female | Pain (VAS) | Continuous | The osteochondroplasty procedure will perform better in males | Multiple linear regression |
| Subgroup analysis | Cartilage status (based on Tonnis and Heinecke classification): grades 3 and 4, grades 1 and 2 | Pain (VAS) | Continuous | Osteochondroplasty will perform worse in patients with worse cartilage status (i.e. grades 3 and 4) | Multiple linear regression |
| Subgroup analysis | Treatment of the labrum: labral repair, resection | Pain (VAS) | Continuous | Patients receiving a labral repair will perform better than those receiving a resection as part of the osteochondroplasty procedure | Multiple linear regression |
| Sensitivity analysis | Trial site (centre-effects) | Pain (VAS) | Continuous | We do not expect the effect to change substantially when centre-effects are removed from the primary analysis | Multiple linear regression with centre-effects removed |
| Sensitivity analysis | Missing data effect | Pain (VAS) | Continuous | We do not expect the effect to change substantially without imputation for missing data | Multiple linear regression with complete cases only |
| Sensitivity analysis | Potential baseline imbalance | Pain (VAS) | Continuous | Results will remain robust after adjusting for potential baseline imbalance on age, any comorbidities, onset of symptoms, and presence of labral tears at initial surgery | Multiple linear regression with complete cases only |

*All regression analyses will be controlled for centre as a stratification variable. VAS: Visual Analogue Scale, SF: Short Form, PCS: Physical Component Summary, MCS: Mental Component Summary, HOS: Hip Outcome Score, iHOT: International Hip Outcome Tool, EQ-5D: Euroqol-5 Dimensions*
This trial is a parallel multi-centre, blinded randomised controlled trial (RCT) of 220 patients who have been diagnosed with FAI, to determine the superiority of arthroscopic osteochondroplasty to arthroscopic lavage. Briefly, participants were recruited from experienced hip surgeons practicing at 10 participating sites based in Canada, Finland, and Denmark. Patients were allocated to one of two treatment arms using an online centralized 24-h computerised randomisation system. The randomisation system follows a computer-generated randomisation schedule in random block sizes of 4 and 8. Randomisation was stratified by impingement sub-type (cam versus mixed) and clinical centre. Study personnel monitor critical aspects of perioperative care and rehabilitation. We are assessing subject pain within 12 months using a visual analogue scale (VAS) after surgery as the primary outcome. Secondary outcomes include function, health-related quality of life, post-operative complications, and costs. Quality of the surgery and complications, including re-operations, will be reviewed by an independent adjudication committee. Outcome assessors and data analysts are blinded to treatment allocation. The full study process is shown in Fig. 1.

In this article, we present our planned statistical analyses for the FIRST trial. The statistical analysis plan was finalized and approved on 29 November 2017 (Version 1.0) for the FIRST trial protocol (20 April 2016, Version 3.0) and in accordance with the trial Masterfile, including the Data Management Plan (June 4, 2014, Version 1.0). Ethics approval was granted at the Methods Centre at McMaster University (Hamilton Integrated Research Ethics Board #12–396) and at each participating site (as per their local ethics board). The trial is registered at ClinicalTrials.gov (NCT01623843).

Methods

Outcomes

Primary outcome

The FIRST primary outcome is pain at 12 months as measured by the VAS. The primary analysis is to assess whether surgical correction of the impingement morphology (arthroscopic osteochondroplasty) with/without labral repair, in adults aged 18–50 years diagnosed with FAI, provides decreased pain at 12 months compared to arthroscopic lavage of the hip joint with/without labral repair, as measured by the VAS. The VAS is a validated uni-dimensional scale that is easy to use, requires no verbal or reading skills, and is sufficiently versatile to be employed in a variety of settings [2–4].

Secondary outcomes

Secondary outcomes include:

1. Hip function as measured by the Hip Outcome Score (HOS).
2. Generic physical and mental health as measured by the Short Form-12 (SF-12).
3. Impact of hip-specific disease on function and lifestyle in the young, active patient as measured by the International Hip Outcome Tool (iHOT-12).
4. Health utility as measured by the EuroQol (EQ-5D).
5. Complications, including additional surgery and other serious and non-serious adverse events. Reasons for reoperations for the randomized hip typically include, but are not limited to re-injury of the labrum/cartilage, hip dislocation, hip instability, infection (deep or superficial), wound healing problem, soft tissue problem, and unresolved hip pain. Other hip-related adverse events to be reported include, but are not limited to, hip instability, tendinopathy, re-injury of the labrum/cartilage, hip osteoarthritis post-surgery, and infection (superficial or deep).

The HOS is a self-administered hip score that was designed to capture hip function and outcomes following surgical therapies such as arthroscopy [5]. The HOS has been shown to have the greatest clinimetric evidence for use in patients with FAI or labral tears [6, 7]. The SF-12 may be self-completed or interview-administered and will help document general health status and the burden of illness that FAI presents [8]. The iHOT-12 is a shorter version of the iHOT-33 designed to be easier to complete in routine clinical practice to measure both health-related quality of life and changes after treatment in young, active patients with hip disorders [9]. This questionnaire has been shown to be valid, reliable, and responsive to change [9]. The EQ-5D is a standardized instrument for use as a measure of health outcome [10]. The EQ-5D comprises five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). The EQ-5D has been used in previous studies involving patients with hip pain and has been extensively validated [11, 12].

Discussion

Analysis plan

This statistical analysis plan follows the JAMA Guidelines for the content of statistical analysis plans in clinical trials [13]. A summary of all planned analyses is provided in Table 1.

Blinded analyses

All statistical analyses will first be completed using blinded treatment groups (i.e. treatment X and Y). Interpretations for the effect of the surgical interventions will be documented based upon blinded X versus Y treatment [14].

Presentation of data

The trial results will be presented according to the Consolidated standards of reporting trials (CONSORT) guidelines.
The baseline demographic characteristics and a description of the surgical and peri-operative management characteristics of the patients will be summarized by group, reported as mean (standard deviation (SD)) or median (first
Table 3 Surgical and peri-operative management

| Division                                    | Treatment X | Treatment Y |
|--------------------------------------------|-------------|-------------|
| Duration of procedure, mean (SD)           | n =         | n =         |
| Duration of traction, mean (SD)            |             |             |
| Total saline used in procedure, mean (SD)  |             |             |
| Type of surgical prep solution, n (%)      |             |             |
| Iodine                                      |             |             |
| Chlorhexidine                               |             |             |
| Alcohol                                     |             |             |
| Etc... (as per available data)             |             |             |
| Labral tears, n (%)                        |             |             |
| None                                        |             |             |
| Partial                                     |             |             |
| Complete                                    |             |             |
| Labrum injected, n (%)                     |             |             |
| No                                          |             |             |
| Yes                                         |             |             |
| Focal                                       |             |             |
| Diffuse                                     |             |             |
| Outerbridge intra-operative cartilage classification, n (%) | | |
| Grade 0                                    |             |             |
| Grade 1                                    |             |             |
| Grade 2                                    |             |             |
| Grade 3                                    |             |             |
| Grade 4                                    |             |             |
| Beck intra-operative cartilage classification, n (%) | | |
| Grade 0                                    |             |             |
| Grade 1                                    |             |             |
| Grade 2                                    |             |             |
| Grade 3                                    |             |             |
| Grade 4                                    |             |             |
| Beck intra-operative labral classification, n (%) | | |
| Grade 0                                    |             |             |
| Grade 1                                    |             |             |
| Grade 2                                    |             |             |
| Grade 3                                    |             |             |
| Grade 4                                    |             |             |
| Capsulotomy performed, n (%)               |             |             |
| No                                         |             |             |
| Yes                                        |             |             |
| Partial                                    |             |             |
| Complete                                   |             |             |
| Capsular closure performed, n (%)          |             |             |
| Yes                                        |             |             |
| No                                         |             |             |
| Anchors used for labrum repair, n (%)      |             |             |

| Table 3 Surgical and peri-operative management (Continued) |
|-----------------------------------------------------------|
| Not applicable (no repair)                                |
| 0                                                         |
| 1                                                         |
| 2                                                         |
| 3                                                         |
| 4                                                         |
| 5                                                         |
| 6                                                         |
| Antibiotic prophylaxis, n (%)                             |
| No                                                        |
| Yes                                                       |
| Cefazolin                                                 |
| Cefuroxime                                                |
| Vancomycin                                                |
| Other                                                     |
| Thromboprophylaxis, n (%)                                 |
| No                                                        |
| Yes                                                       |
| Aspirin                                                   |
| Heparin                                                   |
| Warfarin                                                  |
| Mechanical                                                |
| LMWH                                                      |
| Other                                                     |
| Patient discharge location, n (%)                         |
| Home                                                      |
| Rehabilitation facility                                  |
| Other hospital                                            |
| Weightbearing, n (%)                                      |
| Non-weightbearing                                         |
| Partial weightbearing                                     |
| Full weightbearing                                        |
| Patient aids at discharge, n (%)                          |
| None (ambulatory)                                         |
| Wheelchair                                                |
| Walker                                                    |
| Two crutches                                              |
| One crutch                                                |
| Cane                                                      |
| Other                                                     |

**LMWH** low molecular-weight heparin

quartile, third quartile) for continuous variables and count (percent) for categorical variables (Tables 2 and 3). All statistical tests will be two-tailed with $\alpha = 0.05$. 
**Primary outcome analysis**

Our hypotheses for the primary analysis are as follows:

- Null hypothesis: there is no difference in reported pain between groups at 12 months measured using the VAS score.
- Alternative hypothesis: there is a difference in reported pain between groups at 12 months measured using the VAS score.

The primary analysis will be an analysis to compare the mean pain scores (VAS) at 12 months post-surgery adjusting for baseline VAS score (Table 4). This analysis will be a multiple linear regression with VAS as the dependent variable and the following independent variables: treatment, baseline VAS score, impingement subtype, and clinical centre (all centres with fewer than 10 patients enrolled will be collapsed into a single centre for the independent variable entered into the primary analysis model). Assuming that data would be missing at random, we will use multiple imputation that will be stratified by trial arm and will include baseline demographic or prognostic variables for which we have complete data to handle missing data to enable intention-to-treat analysis [16]. The treatment effect will be reported as an absolute difference in rate of pain reduction with the associated 95% confidence interval and \( p \) value. We will not perform a per-protocol analysis given the cross-over rate at the time of final enrollment was less than 0.5%. We will not exclude cross-overs in the final analysis. We will examine residuals to assess the model assumptions for the multiple linear regression model. All analyses will be performed using SAS version 9.4 (Cary, NC, USA).

**Secondary outcomes analysis**

We will estimate the effect of arthroscopic osteochondroplasty (intervention) versus lavage (control) on FAI patient quality of life (SF-12 mental component summary (MCS) and physical component summary (PCS)), function HOS, iHOT-12, and health utility (EQ-5D) at 12 months (Table 4). Similar to the primary analysis, we will perform multiple linear regressions that include treatment, baseline score, impingement sub-type and centre as independent variables. The results will be reported as mean differences with 95% confidence intervals. We will also estimate the effect of arthroscopic osteochondroplasty (intervention) versus lavage (control) on re-operation using logistic regression that includes treatment and impingement sub-type as independent variables. If we observe enough events, we will also include centre as an independent variable. The results will be presented as the odds ratio (OR) with the 95% confidence interval. Other hip-related adverse events that were not treated operatively will be presented by randomised group. The \( p \) values for treatment effects for these outcomes will not be adjusted given that the secondary analyses will be exploratory. We will also report hip measurements pre-surgery/post-surgery and 12 months post-surgery by treatment group (Table 5). Analyses for secondary outcomes will be complete-case analyses only.

**Sensitivity analyses**

We will perform sensitivity analysis of centre-effects, where we will repeat the primary analysis where clinical centre is not included in the model. We will also perform sensitivity analysis in regards to missing data where we include only complete cases (i.e. no imputation for missing data) [17, 18]. We will also conduct an adjusted analysis, which will adjust for baseline demographics, which we reasonably expect to have an impact on our trial outcomes. We will add the following to the primary analysis as independent variables: (1) age (under 40 years vs. 40 years and older), (2) any comorbidities reported at baseline, (3) onset of symptoms (acute, subacute, insidious, traumatic, non-traumatic), and (4) presence of labral tears at initial surgery. This will address any potential baseline imbalance between randomised groups.

**Subgroup analyses**

At the onset of the FIRST trial, we identified 4 important subgroups, which will be reported according to standard
We will add a main effect for the subgroup variable and the treatment by subgroup interaction to our primary model described above to assess whether the magnitude of the treatment effect is significantly different between subgroups (Fig. 2). This will be repeated for each subgroup variable. We will perform these subgroup analyses with the primary endpoint as the outcome:

1. Severe versus moderate versus mild baseline impingement - impingement will be classified as follows: severe (alpha angle greater than 83°), moderate (alpha greater than 60°), and mild (alpha angle less than 60°). We hypothesize that patients with severe impingement at baseline will have the greatest improvement with the osteochondroplasty procedure compared with those with moderate to mild impingement [20–22].

2. Gender - we hypothesize that the osteochondroplasty procedure will perform better in men [23, 24].

3. Cartilage status (grades 3 and 4 vs 1 and 2) - based on the Tonnis and Heinecke cartilage classification, we hypothesize that osteochondroplasty will perform worse in patients with worse cartilage status (i.e. grades 3 and 4) [25–27].

4. Treatment of the labrum - we hypothesize that patients receiving a labral repair will perform better than those receiving a resection as part of the osteochondroplasty procedure [28].

If a statistically significant subgroup effect is found, we will further explore the impact of the subgroup on the secondary outcomes. No interim analyses are planned.
due to our desire to avoid spuriously inflated estimates of treatment effect \[29, 30\]. The Data Safety and Monitoring Committee (DSMC) meet regularly to monitor the study data for safety.

**Dissemination**

Upon trial completion, the primary manuscript with the 12-month follow-up results, whether positive, negative or neutral, will be submitted for peer-reviewed publication in a top medical journal. The final dataset will be shared through an open access data repository once all analyses are completed.

**Trial status**

The trial began as a pilot of 50 patients in November 2012. Upon demonstrating feasibility and securing additional funding (January 2015), these participants were rolled into the definitive trial \(N = 220\). For the definitive trial, full participant recruitment was achieved in November 2017 and the final 12-month follow-up is expected to be completed in December 2018.

**Abbreviations**

- EQ-5D: EuroQol-5 Dimensions
- FAI: Femoroacetabular impingement
- FIRST: Femoroacetabular impingement randomised controlled trial
- HOS: Hip Outcome Score
- iHOT-12: International Hip Outcome Tool-12
- MCS: Mental component summary
- OR: Odds ratio
- PCS: Physical component summary
- RCT: Randomised controlled trial
- SD: Standard deviation
- SF-12: Short Form-12
- VAS: Visual analogue scale

**Acknowledgements**

Full authorship list for the FIRST Investigators:

- Steering Committee: Olufemi R, Ayeni (Chair, McMaster University), Mohit Bhandari (Co-Chair, McMaster University), Asheesh Bedi (University of Michigan), Teppo Järvinen (University of Helsinki), Volker Musahl (University of Pittsburgh), Douglas Naudie (University of Western Ontario), Matti Seppänen MD (Turku University), Gerard Slobogean (University of Maryland, Baltimore), Lehana Thabane (McMaster University).
- Methods Centre: Olufemi R. Ayeni (Principal Investigator); Nicole Simunovic (Research Manager); Andrew Duong, Matthew Skelly (Project Management); Sheila Sprague (Research Methodologist); Diane Heels-Ansdell, (Statistical Analysis); Lisa Buckingham (Data Management) (McMaster University).
- Data and Safety Monitoring Committee: Tim Ramsay (Chair, Ottawa Hospital Research Institute), John Lee (University of Toronto), Petteri Kousa (Sports Clinic Hospital Dextra).
- Adjudication Committee: Sasha Carsen (University of Ottawa), Hema Choudur (Hamilton Health Sciences), Yan Sim (McMaster University), Kelly Johnston (University of Calgary).

**Funding**

Research grants were received from the following: Canadian Institutes of Health Research (CIHR) (PI: OR Ayeni), American Orthopaedic Society for Sports Medicine (PI: OR Ayeni), Canadian Orthopaedic Foundation.
Authors’ contributions
NS drafted the manuscript, incorporated all author edits, and has given final approval of the version to be published. DHA drafted the majority of the initial statistical analysis plan, reviewed the manuscript critically for important intellectual content, and has given final approval of the version to be published. LT provided important intellectual content to the initial statistical analysis plan, reviewed the manuscript critically for important intellectual content, and has given final approval of the version to be published. ORA made substantial contributions to the conception and design of the intellectual content, and has given final approval of the version to be published. ORA drafted the manuscript, incorporated all author edits, and has given final approval of the version to be published. ORA provided important intellectual content to the initial statistical analysis plan, reviewed the manuscript critically for important intellectual content, has agreed to be accountable for all aspects of the work, and has given final approval of the version to be published. The FIRST Investigators contributed to the design, conduct, and overall data collection for the FIRST trial. All authors have read and approved the final manuscript.

Ethics approval and consent to participate
Ethics approval, including consent form approval, was granted at the Methods Centre at McMaster University (Hamilton Integrated Research Ethics Board #12–396) and at each participating site (as per their local ethics board).

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
1Department of Health Research Methods, Evidence and Impact, McMaster University, 1200 Main St W, 2C, Hamilton, ON L8S 4K1, Canada. 2Department of Surgery, Division of Orthopaedic Surgery, McMaster University, 1200 Main St W, 4E15, Hamilton, ON L8N 3Z5, Canada. 3Biostatistics/FORSC, 3rd Floor, H325, St. Joseph’s Healthcare, 50 Charlton Ave. E, Hamilton, ON L8N 4A6, Canada.

Received: 11 June 2018 Accepted: 4 October 2018

Published online: 29 October 2018

References
1. FIRST Investigators. A multi-centre randomized controlled trial comparing arthroscopic osteochondroplasty and lavage with arthroscopic lavage alone on patient important outcomes and quality of life in the treatment of young adult (18-50) femoroacetabular impingement. BMC Musculoskelet Disord. 2015;16:64.
2. Jensen MP, Karczy P. The measurement of clinical pain intensity: a comparison of six methods. Pain. 1986;27:17–26.
3. Collins S, Moore A, McQuay H. The visual analog pain intensity scale: what is moderate pain in millennials? Pain. 1999;72:95–7.
4. Ho K, Spence J, Murphy M. Review of pain measurement tools. Ann Emerg Med. 1996;27:427–31.
5. Schenker ML, Martin R, Weiland DE, Philpippon MJ. Current trends in hip arthroscopy: a review of injury diagnosis, techniques and outcome scoring. Curr Opin Orthopedics. 2005;16:89–94.
6. Thorborg K, Roos EM, Barkel EM, Petersen J, Hølmich P. Validity, reliability and responsiveness of patient-reported outcome questionnaires when assessing hip and groin disability: a systematic review. Br J Sports Med. 2010;44:1186–96.
7. Mohtadi NGH, Griffin DR, Pedersen ME, Chan D, Safran MR, Parsons N, Sekiya JK, Kelly BT, Werle JR, Leunig M, JC MC, Martin HD, Byrd T, Philpippon MJ, Martin RL, Guanche CA, Clohisy JC, Sampson TG, Kocher MS, Larson CM, for the Multicenter Arthroscopy of the Hip Outcomes Research Network (MAHORN). The development and validation of a self-administered quality-of-life outcome measure for young, active patients with symptomatic hip disease: the International Hip Outcome Tool (iHOT-33). Arthroscopy. 2012;28:595–610.
8. Ware J Jr, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34:220–33.
9. Griffin DR, Parsons N, Mohtadi NGH, Safran MR, on behalf of the Multicenter Arthroscopy of the Hip Outcomes Research Network (MAHORN). A short version of the International Hip Outcome Tool (iHOT-12) for use in routine clinical practice. Arthroscopy. 2013;29:611–8.
10. EuroQol Group. The EQ-SD. Available at: http://www.euroqol.org/home.html. Accessed 10 Jan 2018.
11. Bosch JL, Hunink MG. Comparison of the Health Utilities Index Mark 3 (HUI3) and the EuroQol EQ-SD in patients treated for intermittent claudication. Qual Life Res. 2000;9:591–601.
12. Hurst NP, Kind P, Ruta D, Hunter M, Stubbing S. Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-SD). Br J Rheumatol. 1997;36:551–9.
13. Gamble C, Krishan A, Stocken D, Lewis S, Juszczak E, Dore C, Williamson PR, Altman DG, Montgomery A, Lin P, Berlin J, Senn S, Day S, Barbachano Y, Loder E. Guidelines for the content of statistical analysis plans in clinical trials. JAMA. 2017;318(23):2337–43.
14. Javineen TL, Silvonen R, Bhandari M, Strygge S, Malmivaara A, Paavola M, Schunemann HJ, Guyatt GH. Blinded interpretation of study results can feasibly and effectively diminish interpretation bias. J Clin Epidemiol. 2014;67(7):769–72.
15. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340:c332.
16. Yang Z, Alyass A, Varniwaysingam T, Sadeghihrad B, Floresz ID, Pickha SC, Kennedy SA, AbdulKarimova U, Zhang Y, Ilton T, Mongao GP, Colunga Lozano LE, Aloweni FAB, Lopes LC, Yepes-Nunez JJ, Fei Y, Wang L, Kahale LA, Meyre D, Aki EA, Thabane L, Guyatt GH. A systematic survey of the methods literature on the reporting on reporting and optimal methods of handling participants with missing outcome data for continuous outcomes in randomized controlled trials. J Clin Epidemiol. 2017;88:67–80.
17. Chu R, Thabane L, Ma J, Holbrook A, Pullenayegum E, Devereaux PJ. Comparing methods to estimate treatment effects on a continuous outcome in multicentre randomized controlled trials: a simulation study. BMC Med Res Methodol. 2011;11:21.
18. Thabane L, Mbuaqabw B, Zhang S, Samaan Z, Marucci M, Ye C, Thabane M, Giangregorio L, Dennis B, Kosa D, Borg Debono V, Dillenburg R, Fruci V, Bavor M, Lee J, Wells G, Goldsmith CH. A tutorial on sensitivity analyses in clinical trials: the what, why, when and how. BMC Med Res Methodol. 2013;13:92.
19. Wang R, Lagakos SW, Ware JH, Hunter DJ, Dazem JM. Statistics in medicine – reporting of subgroup analyses in clinical trials. N Engl J Med. 2007;357:2189–94.
20. Agricola R, Heijboer MP, Biema-Zeinstra SM, Verhaar JA, Wehans H, Waarsing JH. Cam impingement causes osteoarthritis of the hip: a nationwide prospective cohort study (CHECK). Ann Rheum Dis. 2013;72:919–23.
21. Agricola R, Waarsing JH, Thomas GE, Cair AJ, Raeman M, Biema-Zeinstra SM, Glyn-Jones S, Wehans H, Arden NK. Cam impingement: defining the presence of a cam deformity by the alpha angle: data from the CHECK cohort and Chingford cohort. Osteoarthr Cartil. 2014;22:218–25.
22. Agricola R, Waarsing JH, Arden NK, Cair AJ, Biema-Zeinstra SM, Thomas GE, Wehans H, Glyn-Jones S. Cam impingement of the hip-a risk factor for hip osteoarthritis. Nat Rev Rheumatol. 2013;9:630–4.
23. Thomas DD, Bernhardson AS, Bernstein E, Dewing CB. Hip arthroscopy for hip arthroscopy according to sex and age: a comparative matched-group analysis. J Bone Joint Surg Am. 2016;98(10):797–804.
24. Tomnis D, Heinecke A. Current concepts review – acetabular and femoral anteversion: relationship with osteoarthritis of the hip. J Bone Joint Surg Am. 1999;81:1747–70.
25. Horner NS, Ekhtiari S, Simunovic N, Safran MR, Philpippon MJ, Ayeni OR. Hip arthroscopy in patients age 40 or older: a systematic review. Arthroscopy. 2017;33(2):464–75.
27. Egerton T, Hinman RS, Takla A, Bennell KL, O'Donnell J. Intraoperative cartilage degeneration predicts outcome 12 months after hip arthroscopy. Clin Orthop Relat Res. 2013;471(2):593–9.

28. Ayeni OR, Adamich J, Farokhyar F, Simunovic N, Crouch S, Philippon MJ, Bhandari M. Surgical management of labral tears during femoroacetabular impingement surgery: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2014;22(4):756–62.

29. Briel M, Lane M, Montori VM, Bassler D, Glasziou P, Malaga G, Aki EA, Ferreira-Gonzalez I, Alonso-Coello P, Unruh G, Kunz R, Culebro CR, da Silva SA, Flynn DN, Elamir MB, Strahim B, Murad MH, Djulbegovic B, Adhikari NKJ, Mills EJ, Gwadry-Sridhar F, Kirpalani H, Soares HP, Ehouri NOA, You JI, Karanikolas PJ, Bucher HC, Lampropoulos JF, Nordmann AJ, Burns KEA, Mull SJ, Raatz H, Sood A, Kaur J, Blandhead CR, Mullan RJ, Neerenberg KA, Vandvik PO, Coto-Yglesias F, Schunemann H, Tuche F, Chrispim PPM, Cook DJ, Lutz K, Ribic CM, Vale N, Ervin PJ, Perera R, Zhou Q, Heels-Ansdell D, Ramsay T, Walter SD, Guyatt GH. Stopping randomized clinical trials early for benefit: a protocol of the study of trial policy of interim truncation-2 (STOPIT-2). Trials. 2009;10:49.

30. Montori VM, Devereaux PJ, Adhikari NK, Burns KE, Eggert CH, Briel M, Lacchetti C, Leung TW, Darling E, Bryant DM, Bucher HC, Schunemann HJ, Meade MO, Cook DJ, Ervin PJ, Sood A, Sood R, Lo B, Thompson CA, Zhou Q, Mills E, Guyatt GH. Randomized trials stopped early for benefit: a systematic review. JAMA. 2005;294:2203–9.