The Journal of Rheumatology

# Outcome measures used in arthroplasty trials: Systematic review of the 2008 and 2013 literature

| | |
|---|---|
| Journal: | *The Journal of Rheumatology* |
| Manuscript ID | 2016-1477.R1 |
| Manuscript Type: | Manuscript |
| Date Submitted by the Author: | n/a |
| Complete List of Authors: | Richards, Bethan; Institute of Rheumatology and Orthopaedics, Royal Prince Alfred Hospital, Sydney, Australia and Sidney Medical School, University of Sydney,<br>Wall, Peter; Warwick Clinical trials Unit, University of Warwick, Orthopaedics<br>Sprowson, Andrew; Warwick Clinical trials Unit, University of Warwick, Orthopaedics<br>Singh, Jasvinder; University of Alabama Medical Center, Medicine<br>Buchbinder, Rachelle; Cabrini Hospital and Monash University, |
| Keywords: | arthroplasty trials, systematic review, outcome measures |
| | |

## Title

Outcome measures used in arthroplasty trials: Systematic review of the 2008 and 2013 literature

**Running Title:** Outcome measures in arthoplasty RCTs

## Authors


| | | |
|---|---|---|
| Bethan L Richards[1,2], | FRACP, MClinEpi, MSportsMed | |
| | Bethan.Richards@sswahs.nsw.gov.au | |
| Peter DH Wall[3] | MBChB (Hons), MRCS (Edin), PhD | |
| | pdhwall@gmail.com | |
| Andrew Sprowson[3*] | MD, FRCS | |
| | A.P.Sprowson@warwick.ac.uk | |
| Jasvinder A Singh[4,5], | MD, MPH | |
| | jassingh@uab.edu | |
| Rachelle Buchbinder[6,7] | FRACP, MD | |
| | rachelle.buchbinder@monash.edu | |

[*]Dr Sprowson died March 13th, 2015


## Affiliations


1. Institute of Rheumatology and Orthopaedics, Royal Prince Alfred Hospital, Sydney, Australia
2. Sydney Medical School, University of Sydney, Sydney, Australia

3. Birmingham Veterans Affairs Warwick Orthopaedics, University of Warwick, Coventry, UK.
4. Medical Center and University of Alabama at Birmingham, Birmingham, Alabama, USA
5. Mayo Clinic College of Medicine, Rochester, MN, USA
6. Department of Epidemiology and Preventive Medicine, School of Public Health & Preventive Medicine, Monash University, VIC Australia
7. Monash Department of Clinical Epidemiology, Cabrini Hospital, Melbourne, VIC, Australia.



**Conflict of interest statement**

Each author certifies that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article

**Word Count**: 3282 (excluding Abstract)

**Corresponding Author:**

Dr Bethan L Richards

Bethan.Richards@sswahs.nsw.gov.au

**Abstract**

**Background/objective**: Previously published literature assessing the reporting of outcome measures used in joint replacement randomised controlled trials (RCTs) has revealed disappointing results. It remains unknown as to whether international initiatives have led to any improvement in the quality of reporting and/or a reduction in the heterogeneity of outcome measures used. Our objective was to systematically assess and compare primary outcome measures and risk of bias of joint replacement RCTs published in 2008 and 2013.

**Methods**: We searched MEDLINE, EMBASE and CENTRAL for RCTs investigating adult patients undergoing joint replacement surgery. Two authors independently identified eligible trials, extracted data and assessed risk of bias using the Cochrane tool.

**Results**: Seventy RCTs (30 in 2008; 40 in 2013) met the eligibility criteria. There was no significant difference in the number of trials judged to be at low overall risk of bias (N=6, 20%) in 2008 compared with six (15%) in 2013 ($\chi^2$=0.302, P=0.75). Significantly more trials published in 2008 did not specify a primary outcome measure (N=25, 83%) compared with 18 (45%) trials in 2013, $\chi^2$= 10.6316, P=0.001). When specified, there was significant heterogeneity in the measures used to assess primary outcomes.

**Conclusion**: While less than a quarter of trials published in both 2008 and 2013 were judged to be at low overall risk of bias, significantly more trials published in 2013 specified a primary outcome. Although this might represent a temporal trend towards improvement, the overall frequency of primary outcome reporting and the wide heterogeneity in primary outcomes reported remain suboptimal.

## Introduction

With an expanding and aging population, an escalating prevalence of obesity and a rising need for both initial and joint revision surgery, the incidence and associated economic burden of joint replacement surgery has been projected to increase exponentially(1). For many patients, joint replacement surgery is an effective management option to reduce pain, restore function and improve quality of life. However, individuals who undergo joint replacement are also at risk for a variety of adverse events associated with both the anaesthetic and the surgery. With expanding indications for joint replacement and the continuing evolution of surgical techniques and implants, many important research questions need to be answered. To address these issues there is an ongoing need for high quality trials within this field of orthopaedics.

Randomised controlled trials (RCTs) are widely acknowledged to be the best type of trial design to evaluate the effectiveness and safety of health care interventions.(2-5) However, the RCT's ability to answer important clinical questions will always be limited by its design and the outcome measures used. To draw meaningful conclusions from individual RCTs, relevant, robust and validated outcomes measures are required. In addition, these outcomes should be pre-specified and clearly reported as to whether they are primary or secondary. This enables readers to assess whether the RCT is adequately powered and avoids the perception of selective reporting bias.

In the field of joint replacement surgery, previously published literature assessing the reporting frequency, relevance and homogeneity of outcome measures used has revealed disappointing results(6). Specifically, primary outcomes were often not specified, and when they were, there

was significant heterogeneity in the types of outcomes measures used to assess the same endpoint. To address this on a large scale, several multi-national collaborations and initiatives have been established. For example, following the poor findings in their systematic review, Riddle and colleagues proposed that consensus from an international group of experts involved in the care of these patients was needed(7). In 2008 a working group within Outcome Measures in Rheumatology (OMERACT) and Osteoarthritis Research Society International (OARSI) was established with the aim of improving the reporting of relevant, evidence based health outcome domains within joint replacement trials(8). In addition, to facilitate accurate, complete, and transparent reporting of all clinical trials, in 2008 the EQUATOR (Enhancing the Quality and Transparency of Health Research) Network was launched and in 2010 the Consolidated Standards of Reporting Trials (CONSORT) Statement (first published in 1996) was published to provide researchers with a check list of 25 items to facilitate complete and transparent reporting of trial findings(9).

It remains unknown as to whether these international initiatives have led to any improvement in the quality of joint replacement trial reporting and/or a reduction in the heterogeneity of outcome measures used. To investigate this question and inform the OMERACT 2014 Working Group meeting (which aimed to define an internationally agreed upon core set of domains and outcome measures that should be reported in every joint replacement clinical trial)(10), we performed a systematic review of outcomes that had been reported in joint replacement trials published in 2008 and 2013. This paper reports the risk of bias of included trials and assesses and compares their primary outcomes. A separate paper will report the extent to which all reported outcomes

met the OMERACT criteria of truth, discrimination, and feasibility and map the reported outcomes to OMERACT Filter 2.0(11).

## Methods

### Search Strategy and Criteria

This systematic review was performed in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) format(12) and the protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO) Registration number: CRD42014009216. This study did not require ethics committee approval , since it does not involve any human or animals and is a systematic review of published articles in the medical literature.

All randomised or quasi-randomised (where allocation not strictly random) controlled trials investigating adult patients undergoing joint replacement surgery (defined as substitution of any joint surface with a prosthesis) were identified. Trials were included if the comparator was another type of joint implant, surgical placebo or sham, usual care, physical therapy or other active treatment and at least one outcome had been reported. Studies were excluded if they evaluated spinal joint replacement surgery, had a primary intervention of interest that was not the insertion of a joint prosthesis (e.g. trials investigating pre-operative education, peri-operative analgesia or post-operative care) or were not published as a full report in English.

An electronic literature search for articles published in 2008 and 2013 was performed in MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL)

using a comprehensive search strategy (**Supplementary Table 1**). We also performed a hand search of reference lists of relevant articles to identify additional relevant trials.

Two authors (BR and PW) independently screened the titles and abstracts of all studies identified by the search strategy and then independently reviewed the full text of all potentially eligible studies to identify studies that fulfilled inclusion criteria. Any disagreement in study selection was resolved by consensus or by discussion with a third reviewer (RB).

The same two authors independently extracted data from the included using predetermined forms. Differences in data extraction were resolved by referring back to the original articles and establishing a consensus. A third reviewer (RB) was consulted to help resolve differences as necessary. The information extracted included study site, funding, enrolment date, size, design, population, interventions, and outcome measures (and whether they were pre-specified). Each outcome was recorded as either primary or secondary. An outcome was recorded as primary if it was reported as a "primary outcome" in the manuscript or registered protocol or was used to calculate the sample size. More than one primary outcome could be recorded provided these criteria were met.

Two authors (BR and PW) independently assessed risk of bias for all included studies using methods recommended by the Cochrane Collaboration,(13) which assess the following key criteria: random sequence generation, allocation concealment, blinding of participants, care provider and outcome assessor for each outcome measure, incomplete outcome data, selective outcome reporting and other sources of bias. Other sources of bias that were considered included

whether or not co-interventions and adherence to treatment (e.g. for analgesics and physical therapy programs) were assessed and reported to be equal between groups, and sources of funding. Each criterion was rated as low risk of bias, high risk of bias, or unclear risk (indicating either lack of information or uncertainty over the potential for bias). Information to inform the risk of bias rating was sourced from searching trial registries and the published papers.

An assessment of overall risk of bias was made where low overall risk of bias indicated plausible bias unlikely to seriously alter the results (low risk of bias for all key domains), unclear overall risk of bias indicated plausible bias that raises some doubt about the results (unclear risk of bias for one or more key domains) and high overall risk of bias indicating plausible bias seriously weakens confidence in the results (high risk of bias for one or more key domains)(13). A third reviewer (RB) was consulted to resolve differences as necessary.

**Data Analysis**

A descriptive analysis of the primary outcomes was performed which compared frequency and description of primary outcome measures by site of joint replacement and year. Comparison of 2008 and 2013 results for overall risk of bias and number of trials reporting primary outcomes was made using Pearson chi-squared tests. We also used the Pearson chi-squared test to determine whether an association might exist between overall risk of bias and reporting of primary outcomes.

**Results**

The search strategy identified 1635 studies. Of these 70 randomised controlled trials (30 with 2,789 participants published in 2008 and 40 with 4253 participants published in 2013), met the

eligibility criteria and were included in the review. A PRISMA flow diagram of the searches through to the final inclusion is shown in **Figure 1**. The summary characteristics of the included trials according to their year of publication are shown in **Table 2**.

***Study characteristics of trials published in 2008***

Eighteen (60%) of the 30 trials published in 2008 were conducted in Europe (14-26), six (20%) in the USA(27-32), two (7%) each in Asia(33, 34) and Canada (35, 36) and one (3%) each in Australia(37) and New Zealand(38). Twenty (67%) trials were independently funded(14-17, 19, 20, 22-24, 26-28, 30-32, 34, 35, 37-39) , 9 (30%) had industry funding(17, 18, 21, 29, 31, 36, 40-42) and in one trial the source of funding was unclear(25). The year of first recruitment ranged from 1994 to 2007 (median, 2001). The most common joint evaluated was the knee (N= 19, 63%)(17-24, 26, 29, 30, 33-37, 39, 42, 43), followed by the hip (N=10, 33%)(14-16, 27, 28, 31, 32, 38, 40, 41), and one trial (3%) evaluated the shoulder(25). There were no trials evaluating joint replacement surgery of the elbow, wrist, hand, ankle or foot. Fifteen (50%) trials evaluated two or more different prostheses or components(14, 16-19, 25, 26, 30, 31, 38-43), 13 (43%) evaluated the same prosthesis but used differing surgical techniques(20-24, 27-29, 33-37) and two (1%) evaluated joint replacement versus other joint surgeries(15, 32).

***Study Characteristics of trials published in 2013***

Twenty (50%) of the 40 trials published in 2013 were conducted in Europe(44-63), nine (23%) in Asia(64-71), five (13%) in the USA(72-76), four (10%) in Canada(77-80), and one (3%) each in Australia(81) and the Middle East(82). Twelve (30%) trials were industry funded(45, 52, 54-56, 59, 62, 63, 70, 73, 77, 80), 15 (38%) had independent funding(44, 46, 48, 50, 51, 53, 57, 60,

64, 65, 69, 72, 78, 81, 82) and in 13 (33%) trials the source of funding was not specified(47, 49, 58, 61, 66-68, 70, 71, 74-76, 79). The year of first recruitment ranged from 1996 to 2011 (median, 2007). The knee (n= 20, 50%)(45, 48, 49, 54, 55, 57, 61, 64-66, 68-71, 73-76, 81) and hip (N=17, 43%)(44, 46, 47, 51-53, 56, 58-60, 62, 63, 67, 72, 77, 79, 80) were again the most commonly studied joints, with two trials (5%) studying the shoulder(78, 82) and one (3%) studying the wrist(50). There were no trials evaluating joint replacement surgery of the elbow, hand, ankle or foot. Eighteen (43%) trials evaluated two or more different prostheses or components(44, 45, 47-50, 52, 54, 56, 57, 61-64, 67, 73, 79, 80), 20 (50%) evaluated the same prosthesis but used differing surgical techniques(53, 55, 58-60, 65, 66, 68-72, 74-78, 81, 82) and two (5%) evaluated joint replacement versus other joint surgeries(46, 51).

***Risk of Bias***

Of the 30 trials published in 2008, 6 (20%) were judged to be at low overall risk of bias, and the remainder were all judged to be at high or unclear overall risk of bias (**Figure 2**). Four (21%) of the 19 knee trials(36, 39, 42, 43), and 2 (20%) of the 10 hip trials were judged to be low risk of bias(40, 41). In the one shoulder joint trial(25), the risk of bias was deemed unclear.

Of the 40 trials published in 2013, only six (15%) were judged to be at low overall risk of bias (**Figure 3**). Three (15%) of the 20 knee trials were judged to be at low overall risk of bias(56, 58, 77), 11 (55%) were deemed unclear(48, 57, 64, 66, 68-70, 73, 76, 81) and 6 (30%) were judged to be at high risk of bias(49, 54, 61, 71, 74, 75). Three (21%) of the 17 hip trials were judged to be at low overall risk of bias(56, 58, 77), six (43%) were deemed unclear(46, 47, 59, 60, 62, 80) and eight (57%) were judged to be at high risk of bias(44, 51-53, 63, 67, 72, 79). One shoulder

trial was deemed unclear(82) and one was judged to be at high overall risk of bias(78), while the single wrist trial was also judged to be at high overall risk of bias(50).

**Figure 4** compares the number of trials with low risk of bias for each risk of bias domain and overall low risk of bias according to publication year. There was no difference between years in number of trials judged to be at overall low risk of bias (6/30 in 2008 compared with 6/40 in 2013, $\chi^2$ 0.302, P=0.75). The method used to generate the random sequence was adequately reported in 63% of the 2008 trials and 53% of the 2013 trials, however details of allocation concealment were reported in only 10 (33%) trials in 2008 and 12 (30%) trials in 2013. More trials reported blinding of patients (13, 33%) and outcomes (N=14, 35%) in 2013 in comparison with 2008 (N=17 (23%) and 4 (13%) respectively). Twenty-six (87%) trials in 2008 reported detailed baseline characteristics however this only applied to 22 (55%) of the 2013 trials. Few trials pre-specified or reported the use of relevant co-interventions (N=13, 43%) in 2008; N=9, 22% in 2013), or described how incomplete data were addressed (N=4, 13% in 2008; N=14, 35% in 2013). Several trials also had evidence of selective outcome reporting (N=11, 37% in 2008; N=9, 22% in 2013). These issues may have influenced outcomes.

**Primary Outcomes**

A summary of the primary outcomes reported in the 2008 and 2013 trials is shown in **Table 3**. Compared with trials published in 2008, more trials published in 2013 reported a primary outcome (N=22/40 (55%) compared with N=5/30 (17%), $\chi^2$= 10.6316, P=0.001). Four out of 19 (21%) knee trials specified a primary outcome in 2008 compared with 11/20 (55%) knee trials in 2013. In these 15 knee trials, 17 different primary outcomes were specified despite evaluating

similar questions. Within each time period only two trials reported the same primary outcome (knee range of motion was specified in two trials in 2008 and difference in mechanical axis deviation measured in degrees in the coronal plane on x-ray in two trials in 2013). No primary outcome was used in both time periods. The majority of primary outcomes reported evaluated technical aspects of the procedures (N=12/17, 71%), rather than patient centred outcomes.

Only one out of 10 (10%) hip trials reported a primary outcome in 2008 compared with 8/17 (47%) hip trials in 2013. Similar to the knee trials, the primary outcomes varied widely and were focussed on technical outcomes of the procedure. Primary outcomes used in more than one hip trial included component migration (RSA) (N=3), deviation ≥5 degrees of planned stem shaft angle (x-ray) (N=2), computerized gait assessment (mean gait velocity, stride length) (N=2) and revision rates (N=2). Assessment of component migration was the only primary outcome measure utilised in both time periods.

Two of the three shoulder trials reported a primary outcome. Only the two 2013 trials evaluating shoulder joint replacement surgery reported a primary outcome, and each trial used a different measures to assess "improvement" (post-operative pain on a VAS 0-10mm and healing rate of the subscapularis tendon visualised on MRI). The single wrist trial reported a primary outcome and used RSA to measure component migration in mm.

**Discussion**

We observed a significant difference in the frequency of reporting of primary outcomes in joint replacement trials in 2013 compared with 2008. Only 17% (21% knee and 10% hip) of RCTs

published in 2008 reported a primary outcome measure in comparison with 55% (55% knee and 47% hip) in 2013. Without knowledge of the frequency of reporting before 2008 and between 2008 and 2013 it is not possible to know with certainty whether or not the improved reporting in 2013 reflects a real improvement over time. Nevertheless almost half of all joint replacement trials continue to fail to specify a primary outcome despite widely accepted CONSORT recommendations(9, 83). Similar inadequate reporting of primary outcomes have been shown in other surgical fields including ophthalmic surgery(84), solid organ transplantation(85), plastic surgery(86), urology(87), trauma surgery(88) and neurosurgery(89).

In addition, we found that among trials that did specify one or more primary outcomes, these varied widely despite the trials addressing similar research questions. In both years (2008 and 2013), no primary outcome measure was used in more than two trials despite similar research questions. This heterogeneity in primary outcome reporting is consistent with results from a previous systematic review(6). Heterogeneity in outcome measurement hampers our ability to combine, contrast and accurately interpret the results from multiple RCTs answering the same (and sometimes, similar) research questions. To improve the quality of information available for patients undergoing joint replacement surgery, RCTs evaluating the same clinical questions need to utilise a homogenous set of outcome measures. Further efforts are required to achieve this(10).

Furthermore, the majority of primary outcomes reported were predominantly focussed upon technical aspects of the surgery. Hence, despite the significant investment of time, money and resources in evaluating these important research questions, we found that the majority of trials in

this systematic review were not designed nor powered to evaluate other important core domains of health for both the patient and society.

Few trials published in both 2008 and 2013 were judged to be at low overall risk of bias (20% in 2008 and 15% in 2013). Not surprisingly, the trials at less potential for bias were more likely to report a primary outcome measure. In addition almost a quarter of the trials we included trials (20/70, 23%) were judged to be at unclear risk of bias as they reported insufficient information. While it is often not possible in surgical RCTs to blind the investigators to the group assignments, or standardize surgical techniques, it should be possible to minimise other potential sources of bias. Common areas of potential bias occurring in more than 50% of the studies included failing to describe allocation concealment, participant blinding, how incomplete data were addressed, and selective reporting of outcomes. Lack of adequate reporting of details of randomisation, allocation concealment, blinding, co-intervention use and outcomes is not limited to joint replacement trials or orthopaedic surgery(84, 87-93).

Our study has several limitations. Firstly, while we used a comprehensive systematic search strategy to identify all relevant studies, we excluded foreign language publications. Given the high proportion of papers published in English language journals (80–90%) this is unlikely to affect generalisability(94). Secondly, the majority of joint replacement trials in this review involved hip and knee surgery. There were limited trials evaluating the shoulder, wrist and hand, and no trials evaluating elbow or ankle joint replacement. Therefore our results may or may not be generalisable to joint replacement trials of other joints. Thirdly, in selecting two publication years, there is a possibility that this literature may not have been truly representative of periods

just before, between and after these dates. The five year gap between study years may not have been long enough to capture meaningful change; however we chose the start year as the year of publication of the study that showed poor quality of arthroplasty trials (6). More studies may be needed in the future with a longer interval to look for improvements using the same quality criteria. Our results are however consistent with previous reviews. Finally, we judged risk of bias and specification of primary outcomes on the basis of the published paper. It may be that we overestimated potential for bias and underestimated frequency of primary outcome specification due to poor reporting practices rather than suboptimal trial methodology. However we tried to limit this effect by also searching the trial registries for protocols.

In conclusion, despite an observed increase in frequency of reporting of primary outcome measures in joint replacement trials in 2013 compared with 2008, almost 50% of trials published in 2013 did not report their primary outcomes. In addition among trials that did report primary outcomes, these were heterogeneous, frequently measured technical aspects of surgery rather than patient important endpoints and few trials used the same primary outcome even for similar research questions. In addition the majority of trials published in both years were at high or unclear overall risk of bias and reflect a lack of implementation of quality improvement initiatives such as the CONSORT guidelines (or similar). Further efforts are needed to improve the quality of joint replacement trials and ensure primary outcomes are reported. A standardised, universally accepted core set of outcomes to be used in all joint replacement trials, based upon their clinical relevance would enhance this field.



**Acknowledgement**

Co-author Dr. Andrew P. Sprowson died tragically on March 13, 2015. The authors remember him as an orthopaedic surgeon with immense enthusiasm for research and for robust clinical evidence in the field of joint replacement surgery. He was an integral part of the Working group for joint arthroplasty within OMERACT, and a great friend.

References

1. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007;89:780-5.
2. Britton A, McKee M, Black N, McPherson K, Sanderson C, Bain C. Choosing between randomised and non-randomised studies: a systematic review. Health Technol Assess 1998;2:i-iv, 1-124.
3. Ross S, Grant A, Counsell C, Gillespie W, Russell I, Prescott R. Barriers to participation in randomised controlled trials: a systematic review. J Clin Epidemiol 1999;52:1143-56.
4. Mapstone J, Elbourne D, Roberts I. Strategies to improve recruitment to research studies. Cochrane Database Syst Rev 2007:MR000013.
5. Treweek S, Mitchell E, Pitkethly M, Cook J, Kjeldstrom M, Taskila T, et al. Strategies to improve recruitment to randomised controlled trials. Cochrane Database Syst Rev 2010:MR000013.
6. Riddle DL, Stratford PW, Bowman DH. Findings of extensive variation in the types of outcome measures used in hip and knee replacement clinical trials: a systematic review. Arthritis Rheum 2008;59:876-83.
7. Riddle DL, Stratford PW, Singh JA, Strand CV. Variation in outcome measures in hip and knee arthroplasty clinical trials: a proposed approach to achieving consensus. J Rheumatol 2009;36:2050-6.
8. Gossec L, Paternotte S, Bingham CO, 3rd, Clegg DO, Coste P, Conaghan PG, et al. OARSI/OMERACT initiative to define states of severity and indication for joint replacement in hip and knee osteoarthritis. An OMERACT 10 Special Interest Group. J Rheumatol 2011;38:1765-9.
9. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. Int J Surg 2011;9:672-7.
10. Singh JA, Dohm M, Sprowson AP, Wall PD, Richards BL, Gossec L, et al. Outcome Domains and Measures in Total Joint Replacement Clinical Trials: Can We Harmonize Them? An OMERACT Collaborative Initiative. J Rheumatol 2015;42:2496-502.
11. Boers M, Kirwan JR, Wells G, Beaton D, Gossec L, d'Agostino MA, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. J Clin Epidemiol 2014;67:745-53.
12. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. Open Med 2009;3:e123-30.
13. Higgins JPT, Green S, (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from http://www.cochrane-handbook.org.2011.
14. Hamadouche M, Baque F, Lefevre N, Kerboull M. Minimum 10-year survival of Kerboull cemented stems according to surface finish. Clin Orthop Rel Res 2008;466:332-9.
15. Mouzopoulos G, Stamatakos M, Arabatzi H, Vasiliadis G, Batanis G, Tsembeli A, et al. The four-year functional result after a displaced subcapital hip fracture treated with three different surgical options. Int Orthop 2008;32:367-73.
16. Garcia-Rey E, Garcia-Cimbrelo E, Cruz-Pardos A, Ortega-Chamarro J. New polyethylenes in total hip replacement: a prospective, comparative clinical study of two types of liner. J Bone Joint Surg Br 2008;90:149-53.
17. Breugem SJM, Sierevelt IN, Schafroth MU, Blankevoort L, Schaap GR, Van Dijk CN. Less anterior knee pain with a mobile-bearing prosthesis compared with a fixed-bearing prosthesis. Clin Orthop Rel Res 2008;466:1959-65.
18. Findlay IA, Bowman NK, Miles K, East DJ, Apthorp HD, Butler-Manuel A. The AGC total knee replacement-cemented versus cementless hydroxyapatite fixation. J Bone Joint Surg Br 2008;90-A:Supplement.

19. Hansson U, Ryd L, Toksvig-Larsen S. A randomised RSA study of Peri-Apatite HA coating of a total knee prosthesis. Knee 2008;15:211-6.
20. Karachalios T, Giotikas D, Roidis N, Poultsides L, Bargiotas K, Malizos KN. Total knee replacement performed with either a mini-midvastus or a standard approach: A prospective randomised clinical and radiological trial. J Bone Joint Surg Br 2008;90:584-91.
21. Lutzner J, Krummenauer F, Wolf C, Gunther KP, Kirschner S. Computer-assisted and conventional total knee replacement: a comparative, prospective, randomised study with radiological and CT evaluation. J Bone Joint Surg Br 2008;90:1039-44.
22. Oberst M, Bertsch C, Konrad G, Lahm A, Holz U. CT analysis after navigated versus conventional implantation of TKA. Arch Orthop Trauma Surg 2008;128:561-6.
23. Lozano LM, Segur JM, Macule F, Nunez M, Torner P, Castillo F, et al. Intramedullary versus extramedullary tibial cutting guide in severely obese patients undergoing total knee replacement: a randomized study of 70 patients with body mass index >35 kg/m2. Obesity Surgery 2008;18:1599-604.
24. Luring C, Beckmann J, Haibock P, Perlick L, Grifka J, Tingart M. Minimal invasive and computer assisted total knee replacement compared with the conventional technique: A prospective, randomised trial. Knee Surg Sports Traumatol Arthrosc 2008;16:928-34.
25. Fialka C, Stampfl P, Arbes S, Reuter P, Oberleitner G, Vecsei V. Primary hemiarthroplasty in four-part fractures of the proximal humerus: Randomized trial of two different implant systems. J Shoulder Elbow Surg 2008;17:210-5.
26. Therbo M, Lund B, Jensen KE, Schroder HM. Effect of bioactive coating of the tibial component on migration pattern in uncemented total knee arthroplasty: A randomized RSA study of 14 knees presented according to new RSA-guidelines. J Orthop Traumatol 2008;9:63-7.
27. Meneghini RM, Smits SA, Swinford RR, Bahamonde RE. A Randomized, Prospective Study of 3 Minimally Invasive Surgical Approaches in Total Hip Arthroplasty. Comprehensive Gait Analysis. J Arthroplasty 2008;23:68-73.
28. Pagnano MW, Trousdale RT, Meneghini RM, Hanssen AD. Slower recovery after two-incision than mini-posterior-incision total hip arthroplasty: A randomized clinical trial. J Bone Joint Surg Am 2008;90:1000-6.
29. Lionberger DR, Weise J, Ho DM, Haddad JL. How does electromagnetic navigation stack up against infrared navigation in minimally invasive total knee arthroplasties? J Arthroplasty 2008;23:573-80.
30. Hall J, Copp SN, Adelson WS, D'Lima DD, Colwell CW, Jr. Extensor mechanism function in single-radius vs multiradius femoral components for total knee arthroplasty. J Arthroplasty 2008;23:216-9.
31. Lachiewicz PF, Kelley SS, Soileau ES. Survival of polished compared with precoated roughened cemented femoral components: A prospective, randomized study. J Bone Joint Surg Am 2008;90:1457-63.
32. Macaulay W, Nellans KW, Garvin KL, Iorio R, Healy WL, Rosenwasser MP, et al. Prospective randomized clinical trial comparing hemiarthroplasty to total hip arthroplasty in the treatment of displaced femoral neck fractures: winner of the Dorr Award. J Arthroplasty 2008;23:2-8.
33. Han I, Seong SC, Lee S, Yoo JH, Lee MC. Simultaneous bilateral MIS-TKA results in faster functional recovery. Clin Orthop Relat Res 2008;466:1449-53.
34. Dutton AQ, Yeo S-J, Yang K-Y, Lo N-N, Chia K-U, Chong H-C. Computer-assisted minimally invasive total knee arthroplasty compared with standard total knee arthroplasty. A prospective, randomized study. J Bone Joint Surg Am 2008;90:2-9.
35. Harato K, Bourne RB, Victor J, Snyder M, Hart J, Ries MD. Midterm comparison of posterior cruciate-retaining versus -substituting total knee arthroplasty using the Genesis II prosthesis. A multicenter prospective randomized clinical trial. Knee 2008;15:217-21.

36. Chaudhary R, Beaupre LA, Johnston DWC. Knee range of motion during the first two years after use of posterior cruciate-stabilizing or posterior cruciate-retaining total knee prostheses: A randomized clinical trial. J Bone Joint Surg Am 2008;90:2579-86.
37. Smith AJ, Wood DJ, Li MG. Total knee replacement with and without patellar resurfacing: a prospective, randomised trial using the profix total knee system. J Bone Joint Surg Br 2008;90:43-9.
38. Pitto RP, Bhargava A, Pandit S, Munro JT. Retroacetabular stress-shielding in THA. Clin Orthop Relat Res 2008;466:353-8.
39. Wylde V, Learmonth I, Potter A, Bettinson K, Lingard E. Patient-reported outcomes after fixed- versus mobile-bearing total knee replacement: a multi-centre randomised controlled trial using the Kinemax total knee replacement. J Bone Joint Surg Br 2008;90:1172-9.
40. Glyn-Jones S, Isaac S, Hauptfleisch J, McLardy-Smith P, Murray DW, Gill HS. Does highly cross-linked polyethylene wear less than conventional polyethylene in total hip arthroplasty? A double-blind, randomized, and controlled trial using roentgen stereophotogrammetric analysis. J Arthroplasty 2008;23:337-43.
41. Glyn-Jones S, McLardy-Smith P, Gill HS, Murray DW. The creep and wear of highly cross-linked polyethylene: A three-year randomised, controlled trial using radiostereometric analysis. J Bone Joint Surg Br 2008;90:556-61.
42. Nutton RW, van der Linden ML, Rowe PJ, Gaston P, Wade FA. A prospective randomised double-blind study of functional outcome and range of flexion following total knee replacement with the NexGen standard and high flexion components. J Bone Joint Surg Br 2008;90:37-42.
43. Ladermann A, Lubbeke A, Stern R, Riand N, Fritschy D. Fixed-bearing versus mobile-bearing total knee arthroplasty: a prospective randomised, clinical and radiological study with mid-term results at 7 years. Knee 2008;15:206-10.
44. Bjorgul K, Novicoff WN, Andersen ST, Ahlund OR, Bunes A, Wiig M, et al. High rate of revision and a high incidence of radiolucent lines around Metasul metal-on-metal total hip replacements: Results from a randomised controlled trial of three bearings after seven years. Bone Joint J 2013;95 B:881-6.
45. Breeman S, Campbell MK, Dakin H, Fiddian N, Fitzpatrick R, Grant A, et al. Five-year results of a randomised controlled trial comparing mobile and fixed bearings in total knee replacement. Bone Joint J 2013;95 B:486-92.
46. Cadossi M, Chiarello E, Savarino L, Tedesco G, Baldini N, Faldini C, et al. A comparison of hemiarthroplasty with a novel polycarbonate-urethane acetabular component for displaced intracapsular fractures of the femoral neck: a randomised controlled trial in elderly patients.[Erratum appears in Bone Joint J. 2013 Nov;95-B(11):1582]. Bone Joint J 2013;95-B:609-15.
47. Desmarchelier R, Viste A, Chouteau J, Lerat J-L, Fessy M-H. Metasul vs Cerasul bearings: a prospective, randomized study at 9 years. J Arthroplasty 2013;28:296-302.
48. Fischer M, von Eisenhart-Rothe R, Simank HG. Comparable short-term results seen with standard and high-flexion knee arthroplasty designs in European patients. J Orthop 2013;10:119-22.
49. Hamilton DF, Simpson A, Burnett R, Patton JT, Moran M, Clement ND, et al. Lengthening the moment arm of the patella confers enhanced extensor mechanism power following total knee arthroplasty. J Orthop Res 2013;31:1201-7.
50. Hansen TB, Stilling M. Equally good fixation of cemented and uncemented cups in total trapeziometacarpal joint prostheses. A randomized clinical RSA study with 2-year follow-up. Acta Orthopaedica 2013;84:98-105.
51. Hedbeck CJ, Inngul C, Blomfeldt R, Ponzer S, Tornkvist H, Enocson A. Internal fixation versus cemented hemiarthroplasty for displaced femoral neck fractures in patients with severe cognitive dysfunction: A randomized controlled trial. J Orthop Traumatol 2013;27:690-5.

52. Inngul C, Hedbeck CJ, Blomfeldt R, Lapidus G, Ponzer S, Enocson A. Unipolar hemiarthroplasty versus bipolar hemiarthroplasty in patients with displaced femoral neck fractures. A four-year follow-up of a randomised controlled trial. Int Orthop 2013;37:2457-64.
53. Landgraeber S, Quitmann H, Guth S, Haversath M, Kowalczyk W, Kecskemethy A, et al. A prospective randomized peri- and post-operative comparison of the minimally invasive anterolateral approach versus the lateral approach. Orthop Rev 2013;5:87-92.
54. Nieuwenhuijse MJ, van der Voort P, Kaptein BL, van der Linden-van der Zwaag HM, Valstar ER, Nelissen RG. Fixation of high-flexion total knee prostheses: five-year follow-up results of a four-arm randomized controlled clinical and roentgen stereophotogrammetric analysis study. J Bone Joint Surg Am 2013;95:e1411-.
55. Pandit H, Liddle AD, Kendrick BJ, Jenkins C, Price AJ, Gill HS, et al. Improved fixation in cementless unicompartmental knee replacement: five-year results of a randomized controlled trial. J Bone Joint Surg Am 2013;95:1365-72.
56. Penny JO, Ovesen O, Varmarken J-E, Overgaard S. Similar range of motion and function after resurfacing large-head or standard total hip arthroplasty. Acta Orthop 2013;84:246-53.
57. Radetzki F, Wienke A, Mendel T, Gutteck N, Delank K-S, Wohlrab D. High flex total knee arthroplasty--a prospective, randomized study with results after 10 years. Acta Orthop Belg 2013;79:536-40.
58. Smolders JM, Pakvis DF, Hendrickx BW, Verdonschot N, van Susante JL. Periacetabular bone mineral density changes after resurfacing hip arthroplasty versus conventional total hip arthroplasty. A randomized controlled DEXA study. J Arthroplasty 2013;28:1177-84.
59. Stiehler M, Goronzy J, Hartmann A, Krummenauer F, Gunther K-P. The First SICOT Oral Presentation Award 2011: imageless computer-assisted femoral component positioning in hip resurfacing: a prospective randomised trial. Int Orthop 2013;37:569-81.
60. Vidovic D, Matejcic A, Punda M, Ivica M, Tomljenovic M, Bekavac-Beslin M, et al. Periprosthetic bone loss following hemiarthroplasty: A comparison between cemented and cementless hip prosthesis. Injury 2013;44:S62-S6.
61. Hamilton DF, Clement ND, Burnett R, Patton JT, Moran M, Howie CR, et al. Do modern total knee replacements offer better value for money? A health economic analysis. Int Orthop 2013;37:2147-52.
62. Munzinger U, Guggi T, Kaptein B, Persoon M, Valstar E, Cornelis Doets H. A titanium plasma-sprayed cup with and without hydroxyapatite-coating: A randomised radiostereometric study of stability and osseointegration. Hip Int 2013;23:33-9.
63. Zagra L, Anasetti F, Bianchi L, Licari V, Giacometti Ceroni R. No difference in gait recovery after THA with different head diameters: A prospective randomized study. Clin Orthop Rel Res 2013;471:3830-7.
64. Aggarwal AK, Agrawal A. Mobile vs fixed-bearing total knee arthroplasty performed by a single surgeon. A 4- to 6.5-year randomized, prospective, controlled, double-blinded study. J Arthroplasty 2013;28:1712-6.
65. Chareancholvanich K, Narkbunnam R, Pornrattanamaneewong C. A prospective randomised controlled study of patient-specific cutting guides compared with conventional instrumentation in total knee replacement. Bone Joint J 2013;95-B:354-9.
66. Jung W, Chun C, Lee J, Ha J, Jeong JH. The accuracy of the extramedullary and intramedullary femoral alignment system in total knee arthroplasty for varus osteoarthritic knee. Knee Surg Sports Traumatol Arthrosc 2013;21:629-35.
67. Kim YH, Park JW, Kulkarni SS. A randomised prospective evaluation of ceramic-on-ceramic and ceramic-on-highly cross-linked polyethylene bearings in the same patients with primary cementless total hip arthroplasty. Int Orthop 2013;37:2131-7.

68. Nishizawa Y, Matsumoto T, Kubo S, Muratsu H, Matsushita T, Oka S, et al. The influence of patella height on soft tissue balance in cruciate-retaining and posterior-stabilised total knee arthroplasty. Int Orthop 2013;37:421-5.
69. Roh YW, Kim TW, Lee S, Seong SC, Lee MC. Is TKA using patient-specific instruments comparable to conventional TKA? A randomized controlled study of one system. Clin Orthop Rel Res 2013;471:3988-95.
70. Song EK, Seon JK, Yim JH, Netravali NA, Bargar WL. Robotic-assisted TKA reduces postoperative alignment outliers and improves gap balance compared to conventional TKA knee. Clin Orthop Rel Res 2013;471:118-26.
71. Umrani SP, Cho K-Y, Kim K-I. Patellar eversion does not adversely affect quadriceps recovery following total knee arthroplasty. J Arthroplasty 2013;28:591-4.
72. Barrett WP, Turner SE, Leopold JP. Prospective randomized study of direct anterior vs postero-lateral approach for total hip arthroplasty. J Arthroplasty 2013;28:1634-8.
73. Dennis DA, Heekin RD, Clark CR, Murphy JA, O'Dell TL, Dwyer KA. Effect of implant design on knee flexion. J Arthroplasty 2013;28:429-38.
74. Hamilton WG, Parks NL, Saxena A. Patient-specific instrumentation does not shorten surgical time: A prospective, randomized trial. J Arthroplasty 2013;28:96-100.
75. Jarvis SL, Johnson-Wo AK, Onstot BR, Bhowmik-Stoker M, Shrader MW, Jacofsky MC, et al. Differences between standard and minimally invasive parapatellar surgical approaches for total knee arthroplasty in the tasks of sitting and standing. J Knee Surg 2013;26:249-56.
76. Wegrzyn J, Parratte S, Coleman-Wood K, Kaufman KR, Pagnano MW. The John Insall award: no benefit of minimally invasive TKA on gait and strength outcomes: a randomized controlled trial. Clin Orthop Rel Res 2013;471:46-55.
77. Greidanus NV, Chihab S, Garbuz DS, Masri BA, Tanzer M, Gross AE, et al. Outcomes of minimally invasive anterolateral THA are not superior to those of minimally invasive direct lateral and posterolateral THA hip. Clin Orthop Relat Res 2013;471:463-71.
78. Lapner PLC, Sabri E, Rakhra K, Bell K, Athwal GS. Healing rates and subscapularis fatty infiltration after lesser tuberosity osteotomy versus subscapularis peel for exposure during shoulder arthroplasty. J Shoulder Elbow Surg 2013;22:396-402.
79. Naudie DDR, Somerville L, Korczak A, Yuan X, McCalden RW, Holdsworth D, et al. A Randomized trial comparing acetabular component fixation of two porous ingrowth surfaces using RSA. J Arthroplasty 2013;28:48-52.
80. Vendittoli PA, Riviere C, Lavigne M, Lavoie P, Alghamdi A, Duval N. Alumina on alumina versus metal on conventional polyethylene: a randomized clinical trial with 9 to 15 years follow-up. Acta Orthop Belg 2013;79:181-90.
81. Joseph J, Simpson PMS, Whitehouse SL, English HW, Donnelly WJ. The use of navigation to achieve soft tissue balance in total knee arthroplasty - A randomised clinical study. Knee 2013;20:401-6.
82. Soliman OA, Koptan WMT. Proximal humeral fractures treated with hemiarthroplasty: does tenodesis of the long head of the biceps improve results? Injury 2013;44:461-4.
83. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. Ann Intern Med 2001;134:657-62.
84. Yao AC, Khajuria A, Camm CF, Edison E, Agha R. The reporting quality of parallel randomised controlled trials in ophthalmic surgery in 2011: a systematic review. Eye (Lond) 2014;28:1341-9.
85. Liu LQ, Morris PJ, Pengel LH. Compliance to the CONSORT statement of randomized controlled trials in solid organ transplantation: a 3-year overview. Transpl Int 2013;26:300-6.
86. Agha RA, Camm CF, Doganay E, Edison E, Siddiqui MR, Orgill DP. Randomised controlled trials in plastic surgery: a systematic review of reporting quality. Eur J Plast Surg 2014;37:55-62.

87. Zavitsanos PJ, Bird VG, Mince KA, Neuberger MM, Dahm P. Low methodological and reporting quality of randomized, controlled trials of devices to treat urolithiasis. J Urol 2014;191:988-93.
88. Lee SY, Teoh PJ, Camm CF, Agha RA. Compliance of randomized controlled trials in trauma surgery with the CONSORT statement. J Trauma Acute Care Surg 2013;75:562-72.
89. Kiehna EN, Starke RM, Pouratian N, Dumont AS. Standards for reporting randomized controlled trials in neurosurgery. J Neurosurg 2011;114:280-5.
90. Camm CF, Chen Y, Sunderland N, Nagendran M, Maruthappu M, Camm AJ. An assessment of the reporting quality of randomised controlled trials relating to anti-arrhythmic agents (2002-2011). Int J Cardiol 2013;168:1393-6.
91. Hopewell S, Dutton S, Yu LM, Chan AW, Altman DG. The quality of reports of randomised trials in 2000 and 2006: comparative study of articles indexed in PubMed. Bmj 2010;340:c723.
92. Peters JP, Hooft L, Grolman W, Stegeman I. Assessment of the quality of reporting of randomised controlled trials in otorhinolaryngologic literature - adherence to the CONSORT statement. PLoS One 2015;10:e0122328.
93. Chan AW, Altman DG. Epidemiology and reporting of randomised trials published in PubMed journals. Lancet 2005;365:1159-62.
94. Montgomery S. Of towers, walls, and fields: perspectives on language in science. Science 2004;303:1333-5.

**Title**

Outcome measures used in arthroplasty trials: Systematic review of the 2008 and 2013 literature

**Running Title:** Outcome measures in arthoplasty RCTs

**Authors**


| | | |
|---|---|---|
| Bethan L Richards[1,2], | FRACP, MClinEpi, MSportsMed | |
| | Bethan.Richards@sswahs.nsw.gov.au | |
| Peter DH Wall[3] | MBChB (Hons), MRCS (Edin), PhD | |
| | pdhwall@gmail.com | |
| Andrew Sprowson[3*] | MD, FRCS | |
| | A.P.Sprowson@warwick.ac.uk | |
| Jasvinder A Singh[4,5], | MD, MPH | |
| | jassingh@uab.edu | |
| Rachelle Buchbinder[6,7] | FRACP, MD | |
| | rachelle.buchbinder@monash.edu | |

[*]Dr Sprowson died March 13th, 2015

**Affiliations**

1. Institute of Rheumatology and Orthopaedics, Royal Prince Alfred Hospital, Sydney, Australia
2. Sydney Medical School, University of Sydney, Sydney, Australia

3. Birmingham Veterans Affairs Warwick Orthopaedics, University of Warwick, Coventry, UK.
4. Medical Center and University of Alabama at Birmingham, Birmingham, Alabama, USA
5. Mayo Clinic College of Medicine, Rochester, MN, USA
6. Department of Epidemiology and Preventive Medicine, School of Public Health & Preventive Medicine, Monash University, VIC Australia
7. Monash Department of Clinical Epidemiology, Cabrini Hospital, Melbourne, VIC, Australia.



**Conflict of interest statement**

JAS has received research grants from Takeda and Savient and consultant fees from Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta/Horizon and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology. JAS serves as the principal investigator for an investigator-initiated study funded by Horizon pharmaceuticals through a grant to DINORA, Inc., a 501 (c)(3) entity. JAS is a member of the executive of OMERACT, an organization that develops outcome measures in rheumatology and receives arms-length funding from 36 companies; a member of the American College of Rheumatology's (ACR) Annual Meeting Planning Committee (AMPC); Chair of the ACR Meet-the-Professor, Workshop and Study Group Subcommittee; and a member of the Veterans Affairs Rheumatology Field Advisory Committee. JAS is the editor and Director of the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis.

All other authors certify that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

**Word Count**: 3282 (excluding Abstract)

**Corresponding Author:**

Dr Bethan L Richards

Bethan.Richards@sswahs.nsw.gov.au

**Abstract**

**Background/objective**: Previously published literature assessing the reporting of outcome measures used in joint replacement randomised controlled trials (RCTs) has revealed disappointing results. It remains unknown as to whether international initiatives have led to any improvement in the quality of reporting and/or a reduction in the heterogeneity of outcome measures used. Our objective was to systematically assess and compare primary outcome measures and risk of bias of joint replacement RCTs published in 2008 and 2013.

**Methods**: We searched MEDLINE, EMBASE and CENTRAL for RCTs investigating adult patients undergoing joint replacement surgery. Two authors independently identified eligible trials, extracted data and assessed risk of bias using the Cochrane tool.

**Results**: Seventy RCTs (30 in 2008; 40 in 2013) met the eligibility criteria. There was no significant difference in the number of trials judged to be at low overall risk of bias (N=6, 20%) in 2008 compared with six (15%) in 2013 ($\chi^2$=0.302, P=0.75). Significantly more trials published in 2008 did not specify a primary outcome measure (N=25, 83%) compared with 18 (45%) trials in 2013, $\chi^2$= 10.6316, P=0.001). When specified, there was significant heterogeneity in the measures used to assess primary outcomes.

**Conclusion**: While less than a quarter of trials published in both 2008 and 2013 were judged to be at low overall risk of bias, significantly more trials published in 2013 specified a primary outcome. Although this might represent a temporal trend towards improvement, the overall frequency of primary outcome reporting and the wide heterogeneity in primary outcomes reported remain suboptimal.

## Introduction

With an expanding and aging population, an escalating prevalence of obesity and a rising need for both initial and joint revision surgery, the incidence and associated economic burden of joint replacement surgery has been projected to increase exponentially(1). For many patients, joint replacement surgery is an effective management option to reduce pain, restore function and improve quality of life. However, individuals who undergo joint replacement are also at risk for a variety of adverse events associated with both the anaesthetic and the surgery. With expanding indications for joint replacement and the continuing evolution of surgical techniques and implants, many important research questions need to be answered. To address these issues there is an ongoing need for high quality trials within this field of orthopaedics.

Randomised controlled trials (RCTs) are widely acknowledged to be the best type of trial design to evaluate the effectiveness and safety of health care interventions.(2-5) However, the RCT's ability to answer important clinical questions will always be limited by its design and the outcome measures used. To draw meaningful conclusions from individual RCTs, relevant, robust and validated outcomes measures are required. In addition, these outcomes should be pre-specified and clearly reported as to whether they are primary or secondary. This enables readers to assess whether the RCT is adequately powered and avoids the perception of selective reporting bias.

In the field of joint replacement surgery, previously published literature assessing the reporting frequency, relevance and homogeneity of outcome measures used has revealed disappointing results(6). Specifically, primary outcomes were often not specified, and when they were, there

was significant heterogeneity in the types of outcomes measures used to assess the same endpoint. To address this on a large scale, several multi-national collaborations and initiatives have been established. For example, following the poor findings in their systematic review, Riddle and colleagues proposed that consensus from an international group of experts involved in the care of these patients was needed(7). In 2008 a working group within Outcome Measures in Rheumatology (OMERACT) and Osteoarthritis Research Society International (OARSI) was established with the aim of improving the reporting of relevant, evidence based health outcome domains within joint replacement trials(8). In addition, to facilitate accurate, complete, and transparent reporting of all clinical trials, in 2008 the EQUATOR (Enhancing the Quality and Transparency of Health Research) Network was launched and in 2010 the Consolidated Standards of Reporting Trials (CONSORT) Statement (first published in 1996) was published to provide researchers with a check list of 25 items to facilitate complete and transparent reporting of trial findings(9).

It remains unknown as to whether these international initiatives have led to any improvement in the quality of joint replacement trial reporting and/or a reduction in the heterogeneity of outcome measures used. To investigate this question and inform the OMERACT 2014 Working Group meeting (which aimed to define an internationally agreed upon core set of domains and outcome measures that should be reported in every joint replacement clinical trial)(10), we performed a systematic review of outcomes that had been reported in joint replacement trials published in 2008 and 2013. This paper reports the risk of bias of included trials and assesses and compares their primary outcomes. A separate paper will report the extent to which all reported outcomes

met the OMERACT criteria of truth, discrimination, and feasibility and map the reported outcomes to OMERACT Filter 2.0(11).

## Methods

### Search Strategy and Criteria

This systematic review was performed in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) format(12) and the protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO) Registration number: CRD42014009216. This study did not require ethics committee approval , since it does not involve any human or animals and is a systematic review of published articles in the medical literature.

All randomised or quasi-randomised (where allocation not strictly random) controlled trials investigating adult patients undergoing joint replacement surgery (defined as substitution of any joint surface with a prosthesis) were identified. Trials were included if the comparator was another type of joint implant, surgical placebo or sham, usual care, physical therapy or other active treatment and at least one outcome had been reported. Studies were excluded if they evaluated spinal joint replacement surgery, had a primary intervention of interest that was not the insertion of a joint prosthesis (e.g. trials investigating pre-operative education, peri-operative analgesia or post-operative care) or were not published as a full report in English.

An electronic literature search for articles published in 2008 and 2013 was performed in MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL)

using a comprehensive search strategy (**Table 1)**. We also performed a hand search of reference lists of relevant articles to identify additional relevant trials.

Two authors (BR and PW) independently screened the titles and abstracts of all studies identified by the search strategy and then independently reviewed the full text of all potentially eligible studies to identify studies that fulfilled inclusion criteria. Any disagreement in study selection was resolved by consensus or by discussion with a third reviewer (RB).

The same two authors independently extracted data from the included using predetermined forms. Differences in data extraction were resolved by referring back to the original articles and establishing a consensus. A third reviewer (RB) was consulted to help resolve differences as necessary. The information extracted included study site, funding, enrolment date, size, design, population, interventions, and outcome measures (and whether they were pre-specified). Each outcome was recorded as either primary or secondary. An outcome was recorded as primary if it was reported as a "primary outcome" in the manuscript or registered protocol or was used to calculate the sample size. More than one primary outcome could be recorded provided these criteria were met.

Two authors (BR and PW) independently assessed risk of bias for all included studies using methods recommended by the Cochrane Collaboration,(13) which assess the following key criteria: random sequence generation, allocation concealment, blinding of participants, care provider and outcome assessor for each outcome measure, incomplete outcome data, selective outcome reporting and other sources of bias. Other sources of bias that were considered included

whether or not co-interventions and adherence to treatment (e.g. for analgesics and physical therapy programs) were assessed and reported to be equal between groups, and sources of funding. Each criterion was rated as low risk of bias, high risk of bias, or unclear risk (indicating either lack of information or uncertainty over the potential for bias). Information to inform the risk of bias rating was sourced from searching trial registries and the published papers.

An assessment of overall risk of bias was made where low overall risk of bias indicated plausible bias unlikely to seriously alter the results (low risk of bias for all key domains), unclear overall risk of bias indicated plausible bias that raises some doubt about the results (unclear risk of bias for one or more key domains) and high overall risk of bias indicating plausible bias seriously weakens confidence in the results (high risk of bias for one or more key domains)(13). A third reviewer (RB) was consulted to resolve differences as necessary.

**Data Analysis**

A descriptive analysis of the primary outcomes was performed which compared frequency and description of primary outcome measures by site of joint replacement and year. Comparison of 2008 and 2013 results for overall risk of bias and number of trials reporting primary outcomes was made using Pearson chi-squared tests. We also used the Pearson chi-squared test to determine whether an association might exist between overall risk of bias and reporting of primary outcomes.

**Results**

The search strategy identified 1635 studies. Of these 70 randomised controlled trials (30 with 2,789 participants published in 2008 and 40 with 4253 participants published in 2013), met the

eligibility criteria and were included in the review. A PRISMA flow diagram of the searches through to the final inclusion is shown in **Figure 1**. The summary characteristics of the included trials according to their year of publication are shown in **Table 2**.

***Study characteristics of trials published in 2008***

Eighteen (60%) of the 30 trials published in 2008 were conducted in Europe (14-26), six (20%) in the USA(27-32), two (7%) each in Asia(33, 34) and Canada (35, 36) and one (3%) each in Australia(37) and New Zealand(38). Twenty (67%) trials were independently funded(14-17, 19, 20, 22-24, 26-28, 30-32, 34, 35, 37-39) , 9 (30%) had industry funding(17, 18, 21, 29, 31, 36, 40-42) and in one trial the source of funding was unclear(25). The year of first recruitment ranged from 1994 to 2007 (median, 2001). The most common joint evaluated was the knee (N= 19, 63%)(17-24, 26, 29, 30, 33-37, 39, 42, 43), followed by the hip (N=10, 33%)(14-16, 27, 28, 31, 32, 38, 40, 41), and one trial (3%) evaluated the shoulder(25). There were no trials evaluating joint replacement surgery of the elbow, wrist, hand, ankle or foot. Fifteen (50%) trials evaluated two or more different prostheses or components(14, 16-19, 25, 26, 30, 31, 38-43), 13 (43%) evaluated the same prosthesis but used differing surgical techniques(20-24, 27-29, 33-37) and two (1%) evaluated joint replacement versus other joint surgeries(15, 32).

***Study Characteristics of trials published in 2013***

Twenty (50%) of the 40 trials published in 2013 were conducted in Europe(44-63), nine (23%) in Asia(64-71), five (13%) in the USA(72-76), four (10%) in Canada(77-80), and one (3%) each in Australia(81) and the Middle East(82). Twelve (30%) trials were industry funded(45, 52, 54-56, 59, 62, 63, 70, 73, 77, 80), 15 (38%) had independent funding(44, 46, 48, 50, 51, 53, 57, 60,

64, 65, 69, 72, 78, 81, 82) and in 13 (33%) trials the source of funding was not specified(47, 49, 58, 61, 66-68, 70, 71, 74-76, 79). The year of first recruitment ranged from 1996 to 2011 (median, 2007). The knee (n= 20, 50%)(45, 48, 49, 54, 55, 57, 61, 64-66, 68-71, 73-76, 81) and hip (N=17, 43%)(44, 46, 47, 51-53, 56, 58-60, 62, 63, 67, 72, 77, 79, 80) were again the most commonly studied joints, with two trials (5%) studying the shoulder(78, 82) and one (3%) studying the wrist(50). There were no trials evaluating joint replacement surgery of the elbow, hand, ankle or foot. Eighteen (43%) trials evaluated two or more different prostheses or components(44, 45, 47-50, 52, 54, 56, 57, 61-64, 67, 73, 79, 80), 20 (50%) evaluated the same prosthesis but used differing surgical techniques(53, 55, 58-60, 65, 66, 68-72, 74-78, 81, 82) and two (5%) evaluated joint replacement versus other joint surgeries(46, 51).

***Risk of Bias***

Of the 30 trials published in 2008, 6 (20%) were judged to be at low overall risk of bias, and the remainder were all judged to be at high or unclear overall risk of bias (**Figure 2**). Four (21%) of the 19 knee trials(36, 39, 42, 43), and 2 (20%) of the 10 hip trials were judged to be low risk of bias(40, 41). In the one shoulder joint trial(25), the risk of bias was deemed unclear.

Of the 40 trials published in 2013, only six (15%) were judged to be at low overall risk of bias (**Figure 3**). Three (15%) of the 20 knee trials were judged to be at low overall risk of bias(56, 58, 77), 11 (55%) were deemed unclear(48, 57, 64, 66, 68-70, 73, 76, 81) and 6 (30%) were judged to be at high risk of bias(49, 54, 61, 71, 74, 75). Three (21%) of the 17 hip trials were judged to be at low overall risk of bias(56, 58, 77), six (43%) were deemed unclear(46, 47, 59, 60, 62, 80) and eight (57%) were judged to be at high risk of bias(44, 51-53, 63, 67, 72, 79). One shoulder

trial was deemed unclear(82) and one was judged to be at high overall risk of bias(78), while the single wrist trial was also judged to be at high overall risk of bias(50).

**Figure 4** compares the number of trials with low risk of bias for each risk of bias domain and overall low risk of bias according to publication year. There was no difference between years in number of trials judged to be at overall low risk of bias (6/30 in 2008 compared with 6/40 in 2013, $\chi^2$ 0.302, P=0.75). The method used to generate the random sequence was adequately reported in 63% of the 2008 trials and 53% of the 2013 trials, however details of allocation concealment were reported in only 10 (33%) trials in 2008 and 12 (30%) trials in 2013. More trials reported blinding of patients (13, 33%) and outcomes (N=14, 35%) in 2013 in comparison with 2008 (N=17 (23%) and 4 (13%) respectively). Twenty-six (87%) trials in 2008 reported detailed baseline characteristics however this only applied to 22 (55%) of the 2013 trials. Few trials pre-specified or reported the use of relevant co-interventions (N=13, 43%) in 2008; N=9, 22% in 2013), or described how incomplete data were addressed (N=4, 13% in 2008; N=14, 35% in 2013). Several trials also had evidence of selective outcome reporting (N=11, 37% in 2008; N=9, 22% in 2013). These issues may have influenced outcomes.



**Primary Outcomes**

A summary of the primary outcomes reported in the 2008 and 2013 trials is shown in **Table 3**. Compared with trials published in 2008, more trials published in 2013 reported a primary outcome (N=22/40 (55%) compared with N=5/30 (17%), $\chi^2$= 10.6316, P=0.001). Four out of 19 (21%) knee trials specified a primary outcome in 2008 compared with 11/20 (55%) knee trials in 2013. In these 15 knee trials, 17 different primary outcomes were specified despite evaluating

similar questions. Within each time period only two trials reported the same primary outcome (knee range of motion was specified in two trials in 2008 and difference in mechanical axis deviation measured in degrees in the coronal plane on x-ray in two trials in 2013). No primary outcome was used in both time periods. The majority of primary outcomes reported evaluated technical aspects of the procedures (N=12/17, 71%), rather than patient centred outcomes.

Only one out of 10 (10%) hip trials reported a primary outcome in 2008 compared with 8/17 (47%) hip trials in 2013. Similar to the knee trials, the primary outcomes varied widely and were focussed on technical outcomes of the procedure. Primary outcomes used in more than one hip trial included component migration (RSA) (N=3), deviation ≥5 degrees of planned stem shaft angle (x-ray) (N=2), computerized gait assessment (mean gait velocity, stride length) (N=2) and revision rates (N=2). Assessment of component migration was the only primary outcome measure utilised in both time periods.

Two of the three shoulder trials reported a primary outcome. Only the two 2013 trials evaluating shoulder joint replacement surgery reported a primary outcome, and each trial used a different measures to assess "improvement" (post-operative pain on a VAS 0-10mm and healing rate of the subscapularis tendon visualised on MRI). The single wrist trial reported a primary outcome and used RSA to measure component migration in mm.

**Discussion**

We observed a significant difference in the frequency of reporting of primary outcomes in joint replacement trials in 2013 compared with 2008. Only 17% (21% knee and 10% hip) of RCTs

published in 2008 reported a primary outcome measure in comparison with 55% (55% knee and 47% hip) in 2013. Without knowledge of the frequency of reporting before 2008 and between 2008 and 2013 it is not possible to know with certainty whether or not the improved reporting in 2013 reflects a real improvement over time. Nevertheless almost half of all joint replacement trials continue to fail to specify a primary outcome despite widely accepted CONSORT recommendations(9, 83). Similar inadequate reporting of primary outcomes have been shown in other surgical fields including ophthalmic surgery(84), solid organ transplantation(85), plastic surgery(86), urology(87), trauma surgery(88) and neurosurgery(89).

In addition, we found that among trials that did specify one or more primary outcomes, these varied widely despite the trials addressing similar research questions. In both years (2008 and 2013), no primary outcome measure was used in more than two trials despite similar research questions. This heterogeneity in primary outcome reporting is consistent with results from a previous systematic review(6). Heterogeneity in outcome measurement hampers our ability to combine, contrast and accurately interpret the results from multiple RCTs answering the same (and sometimes, similar) research questions. To improve the quality of information available for patients undergoing joint replacement surgery, RCTs evaluating the same clinical questions need to utilise a homogenous set of outcome measures. Further efforts are required to achieve this(10).

Furthermore, the majority of primary outcomes reported were predominantly focussed upon technical aspects of the surgery. Hence, despite the significant investment of time, money and resources in evaluating these important research questions, we found that the majority of trials in

this systematic review were not designed nor powered to evaluate other important core domains of health for both the patient and society.

Few trials published in both 2008 and 2013 were judged to be at low overall risk of bias (20% in 2008 and 15% in 2013). Not surprisingly, the trials at less potential for bias were more likely to report a primary outcome measure. In addition almost a quarter of the trials we included trials (20/70, 23%) were judged to be at unclear risk of bias as they reported insufficient information. While it is often not possible in surgical RCTs to blind the investigators to the group assignments, or standardize surgical techniques, it should be possible to minimise other potential sources of bias. Common areas of potential bias occurring in more than 50% of the studies included failing to describe allocation concealment, participant blinding, how incomplete data were addressed, and selective reporting of outcomes. Lack of adequate reporting of details of randomisation, allocation concealment, blinding, co-intervention use and outcomes is not limited to joint replacement trials or orthopaedic surgery(84, 87-93).

Our study has several limitations. Firstly, while we used a comprehensive systematic search strategy to identify all relevant studies, we excluded foreign language publications. Given the high proportion of papers published in English language journals (80–90%) this is unlikely to affect generalisability(94). Secondly, the majority of joint replacement trials in this review involved hip and knee surgery. There were limited trials evaluating the shoulder, wrist and hand, and no trials evaluating elbow or ankle joint replacement. Therefore our results may or may not be generalisable to joint replacement trials of other joints. Thirdly, in selecting two publication years, there is a possibility that this literature may not have been truly representative of periods

just before, between and after these dates. The five year gap between study years may not have been long enough to capture meaningful change; however we chose the start year as the year of publication of the study that showed poor quality of arthroplasty trials (6). More studies may be needed in the future with a longer interval to look for improvements using the same quality criteria. Our results are however consistent with previous reviews. Finally, we judged risk of bias and specification of primary outcomes on the basis of the published paper. It may be that we overestimated potential for bias and underestimated frequency of primary outcome specification due to poor reporting practices rather than suboptimal trial methodology. However we tried to limit this effect by also searching the trial registries for protocols.

In conclusion, despite an observed increase in frequency of reporting of primary outcome measures in joint replacement trials in 2013 compared with 2008, almost 50% of trials published in 2013 did not report their primary outcomes. In addition among trials that did report primary outcomes, these were heterogeneous, frequently measured technical aspects of surgery rather than patient important endpoints and few trials used the same primary outcome even for similar research questions. In addition the majority of trials published in both years were at high or unclear overall risk of bias and reflect a lack of implementation of quality improvement initiatives such as the CONSORT guidelines (or similar). Further efforts are needed to improve the quality of joint replacement trials and ensure primary outcomes are reported. A standardised, universally accepted core set of outcomes to be used in all joint replacement trials, based upon their clinical relevance would enhance this field.



**Acknowledgement**

Co-author Dr. Andrew P. Sprowson died tragically on March 13, 2015. The authors remember him as an orthopaedic surgeon with immense enthusiasm for research and for robust clinical evidence in the field of joint replacement surgery. He was an integral part of the Working group for joint arthroplasty within OMERACT, and a great friend.

References

1. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007;89:780-5.
2. Britton A, McKee M, Black N, McPherson K, Sanderson C, Bain C. Choosing between randomised and non-randomised studies: a systematic review. Health Technol Assess 1998;2:i-iv, 1-124.
3. Ross S, Grant A, Counsell C, Gillespie W, Russell I, Prescott R. Barriers to participation in randomised controlled trials: a systematic review. J Clin Epidemiol 1999;52:1143-56.
4. Mapstone J, Elbourne D, Roberts I. Strategies to improve recruitment to research studies. Cochrane Database Syst Rev 2007:MR000013.
5. Treweek S, Mitchell E, Pitkethly M, Cook J, Kjeldstrom M, Taskila T, et al. Strategies to improve recruitment to randomised controlled trials. Cochrane Database Syst Rev 2010:MR000013.
6. Riddle DL, Stratford PW, Bowman DH. Findings of extensive variation in the types of outcome measures used in hip and knee replacement clinical trials: a systematic review. Arthritis Rheum 2008;59:876-83.
7. Riddle DL, Stratford PW, Singh JA, Strand CV. Variation in outcome measures in hip and knee arthroplasty clinical trials: a proposed approach to achieving consensus. J Rheumatol 2009;36:2050-6.
8. Gossec L, Paternotte S, Bingham CO, 3rd, Clegg DO, Coste P, Conaghan PG, et al. OARSI/OMERACT initiative to define states of severity and indication for joint replacement in hip and knee osteoarthritis. An OMERACT 10 Special Interest Group. J Rheumatol 2011;38:1765-9.
9. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. Int J Surg 2011;9:672-7.
10. Singh JA, Dohm M, Sprowson AP, Wall PD, Richards BL, Gossec L, et al. Outcome Domains and Measures in Total Joint Replacement Clinical Trials: Can We Harmonize Them? An OMERACT Collaborative Initiative. J Rheumatol 2015;42:2496-502.
11. Boers M, Kirwan JR, Wells G, Beaton D, Gossec L, d'Agostino MA, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. J Clin Epidemiol 2014;67:745-53.
12. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. Open Med 2009;3:e123-30.
13. Higgins JPT, Green S, (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from http://www.cochrane-handbook.org.2011.
14. Hamadouche M, Baque F, Lefevre N, Kerboull M. Minimum 10-year survival of Kerboull cemented stems according to surface finish. Clin Orthop Rel Res 2008;466:332-9.
15. Mouzopoulos G, Stamatakos M, Arabatzi H, Vasiliadis G, Batanis G, Tsembeli A, et al. The four-year functional result after a displaced subcapital hip fracture treated with three different surgical options. Int Orthop 2008;32:367-73.
16. Garcia-Rey E, Garcia-Cimbrelo E, Cruz-Pardos A, Ortega-Chamarro J. New polyethylenes in total hip replacement: a prospective, comparative clinical study of two types of liner. J Bone Joint Surg Br 2008;90:149-53.
17. Breugem SJM, Sierevelt IN, Schafroth MU, Blankevoort L, Schaap GR, Van Dijk CN. Less anterior knee pain with a mobile-bearing prosthesis compared with a fixed-bearing prosthesis. Clin Orthop Rel Res 2008;466:1959-65.
18. Findlay IA, Bowman NK, Miles K, East DJ, Apthorp HD, Butler-Manuel A. The AGC total knee replacement-cemented versus cementless hydroxyapatite fixation. J Bone Joint Surg Br 2008;90-A:Supplement.

19. Hansson U, Ryd L, Toksvig-Larsen S. A randomised RSA study of Peri-Apatite HA coating of a total knee prosthesis. Knee 2008;15:211-6.
20. Karachalios T, Giotikas D, Roidis N, Poultsides L, Bargiotas K, Malizos KN. Total knee replacement performed with either a mini-midvastus or a standard approach: A prospective randomised clinical and radiological trial. J Bone Joint Surg Br 2008;90:584-91.
21. Lutzner J, Krummenauer F, Wolf C, Gunther KP, Kirschner S. Computer-assisted and conventional total knee replacement: a comparative, prospective, randomised study with radiological and CT evaluation. J Bone Joint Surg Br 2008;90:1039-44.
22. Oberst M, Bertsch C, Konrad G, Lahm A, Holz U. CT analysis after navigated versus conventional implantation of TKA. Arch Orthop Trauma Surg 2008;128:561-6.
23. Lozano LM, Segur JM, Macule F, Nunez M, Torner P, Castillo F, et al. Intramedullary versus extramedullary tibial cutting guide in severely obese patients undergoing total knee replacement: a randomized study of 70 patients with body mass index >35 kg/m2. Obesity Surgery 2008;18:1599-604.
24. Luring C, Beckmann J, Haibock P, Perlick L, Grifka J, Tingart M. Minimal invasive and computer assisted total knee replacement compared with the conventional technique: A prospective, randomised trial. Knee Surg Sports Traumatol Arthrosc 2008;16:928-34.
25. Fialka C, Stampfl P, Arbes S, Reuter P, Oberleitner G, Vecsei V. Primary hemiarthroplasty in four-part fractures of the proximal humerus: Randomized trial of two different implant systems. J Shoulder Elbow Surg 2008;17:210-5.
26. Therbo M, Lund B, Jensen KE, Schroder HM. Effect of bioactive coating of the tibial component on migration pattern in uncemented total knee arthroplasty: A randomized RSA study of 14 knees presented according to new RSA-guidelines. J Orthop Traumatol 2008;9:63-7.
27. Meneghini RM, Smits SA, Swinford RR, Bahamonde RE. A Randomized, Prospective Study of 3 Minimally Invasive Surgical Approaches in Total Hip Arthroplasty. Comprehensive Gait Analysis. J Arthroplasty 2008;23:68-73.
28. Pagnano MW, Trousdale RT, Meneghini RM, Hanssen AD. Slower recovery after two-incision than mini-posterior-incision total hip arthroplasty: A randomized clinical trial. J Bone Joint Surg Am 2008;90:1000-6.
29. Lionberger DR, Weise J, Ho DM, Haddad JL. How does electromagnetic navigation stack up against infrared navigation in minimally invasive total knee arthroplasties? J Arthroplasty 2008;23:573-80.
30. Hall J, Copp SN, Adelson WS, D'Lima DD, Colwell CW, Jr. Extensor mechanism function in single-radius vs multiradius femoral components for total knee arthroplasty. J Arthroplasty 2008;23:216-9.
31. Lachiewicz PF, Kelley SS, Soileau ES. Survival of polished compared with precoated roughened cemented femoral components: A prospective, randomized study. J Bone Joint Surg Am 2008;90:1457-63.
32. Macaulay W, Nellans KW, Garvin KL, Iorio R, Healy WL, Rosenwasser MP, et al. Prospective randomized clinical trial comparing hemiarthroplasty to total hip arthroplasty in the treatment of displaced femoral neck fractures: winner of the Dorr Award. J Arthroplasty 2008;23:2-8.
33. Han I, Seong SC, Lee S, Yoo JH, Lee MC. Simultaneous bilateral MIS-TKA results in faster functional recovery. Clin Orthop Relat Res 2008;466:1449-53.
34. Dutton AQ, Yeo S-J, Yang K-Y, Lo N-N, Chia K-U, Chong H-C. Computer-assisted minimally invasive total knee arthroplasty compared with standard total knee arthroplasty. A prospective, randomized study. J Bone Joint Surg Am 2008;90:2-9.
35. Harato K, Bourne RB, Victor J, Snyder M, Hart J, Ries MD. Midterm comparison of posterior cruciate-retaining versus -substituting total knee arthroplasty using the Genesis II prosthesis. A multicenter prospective randomized clinical trial. Knee 2008;15:217-21.

36. Chaudhary R, Beaupre LA, Johnston DWC. Knee range of motion during the first two years after use of posterior cruciate-stabilizing or posterior cruciate-retaining total knee prostheses: A randomized clinical trial. J Bone Joint Surg Am 2008;90:2579-86.
37. Smith AJ, Wood DJ, Li MG. Total knee replacement with and without patellar resurfacing: a prospective, randomised trial using the profix total knee system. J Bone Joint Surg Br 2008;90:43-9.
38. Pitto RP, Bhargava A, Pandit S, Munro JT. Retroacetabular stress-shielding in THA. Clin Orthop Relat Res 2008;466:353-8.
39. Wylde V, Learmonth I, Potter A, Bettinson K, Lingard E. Patient-reported outcomes after fixed- versus mobile-bearing total knee replacement: a multi-centre randomised controlled trial using the Kinemax total knee replacement. J Bone Joint Surg Br 2008;90:1172-9.
40. Glyn-Jones S, Isaac S, Hauptfleisch J, McLardy-Smith P, Murray DW, Gill HS. Does highly cross-linked polyethylene wear less than conventional polyethylene in total hip arthroplasty? A double-blind, randomized, and controlled trial using roentgen stereophotogrammetric analysis. J Arthroplasty 2008;23:337-43.
41. Glyn-Jones S, McLardy-Smith P, Gill HS, Murray DW. The creep and wear of highly cross-linked polyethylene: A three-year randomised, controlled trial using radiostereometric analysis. J Bone Joint Surg Br 2008;90:556-61.
42. Nutton RW, van der Linden ML, Rowe PJ, Gaston P, Wade FA. A prospective randomised double-blind study of functional outcome and range of flexion following total knee replacement with the NexGen standard and high flexion components. J Bone Joint Surg Br 2008;90:37-42.
43. Ladermann A, Lubbeke A, Stern R, Riand N, Fritschy D. Fixed-bearing versus mobile-bearing total knee arthroplasty: a prospective randomised, clinical and radiological study with mid-term results at 7 years. Knee 2008;15:206-10.
44. Bjorgul K, Novicoff WN, Andersen ST, Ahlund OR, Bunes A, Wiig M, et al. High rate of revision and a high incidence of radiolucent lines around Metasul metal-on-metal total hip replacements: Results from a randomised controlled trial of three bearings after seven years. Bone Joint J 2013;95 B:881-6.
45. Breeman S, Campbell MK, Dakin H, Fiddian N, Fitzpatrick R, Grant A, et al. Five-year results of a randomised controlled trial comparing mobile and fixed bearings in total knee replacement. Bone Joint J 2013;95 B:486-92.
46. Cadossi M, Chiarello E, Savarino L, Tedesco G, Baldini N, Faldini C, et al. A comparison of hemiarthroplasty with a novel polycarbonate-urethane acetabular component for displaced intracapsular fractures of the femoral neck: a randomised controlled trial in elderly patients.[Erratum appears in Bone Joint J. 2013 Nov;95-B(11):1582]. Bone Joint J 2013;95-B:609-15.
47. Desmarchelier R, Viste A, Chouteau J, Lerat J-L, Fessy M-H. Metasul vs Cerasul bearings: a prospective, randomized study at 9 years. J Arthroplasty 2013;28:296-302.
48. Fischer M, von Eisenhart-Rothe R, Simank HG. Comparable short-term results seen with standard and high-flexion knee arthroplasty designs in European patients. J Orthop 2013;10:119-22.
49. Hamilton DF, Simpson A, Burnett R, Patton JT, Moran M, Clement ND, et al. Lengthening the moment arm of the patella confers enhanced extensor mechanism power following total knee arthroplasty. J Orthop Res 2013;31:1201-7.
50. Hansen TB, Stilling M. Equally good fixation of cemented and uncemented cups in total trapeziometacarpal joint prostheses. A randomized clinical RSA study with 2-year follow-up. Acta Orthopaedica 2013;84:98-105.
51. Hedbeck CJ, Inngul C, Blomfeldt R, Ponzer S, Tornkvist H, Enocson A. Internal fixation versus cemented hemiarthroplasty for displaced femoral neck fractures in patients with severe cognitive dysfunction: A randomized controlled trial. J Orthop Traumatol 2013;27:690-5.

52. Inngul C, Hedbeck CJ, Blomfeldt R, Lapidus G, Ponzer S, Enocson A. Unipolar hemiarthroplasty versus bipolar hemiarthroplasty in patients with displaced femoral neck fractures. A four-year follow-up of a randomised controlled trial. Int Orthop 2013;37:2457-64.
53. Landgraeber S, Quitmann H, Guth S, Haversath M, Kowalczyk W, Kecskemethy A, et al. A prospective randomized peri- and post-operative comparison of the minimally invasive anterolateral approach versus the lateral approach. Orthop Rev 2013;5:87-92.
54. Nieuwenhuijse MJ, van der Voort P, Kaptein BL, van der Linden-van der Zwaag HM, Valstar ER, Nelissen RG. Fixation of high-flexion total knee prostheses: five-year follow-up results of a four-arm randomized controlled clinical and roentgen stereophotogrammetric analysis study. J Bone Joint Surg Am 2013;95:e1411-.
55. Pandit H, Liddle AD, Kendrick BJ, Jenkins C, Price AJ, Gill HS, et al. Improved fixation in cementless unicompartmental knee replacement: five-year results of a randomized controlled trial. J Bone Joint Surg Am 2013;95:1365-72.
56. Penny JO, Ovesen O, Varmarken J-E, Overgaard S. Similar range of motion and function after resurfacing large-head or standard total hip arthroplasty. Acta Orthop 2013;84:246-53.
57. Radetzki F, Wienke A, Mendel T, Gutteck N, Delank K-S, Wohlrab D. High flex total knee arthroplasty--a prospective, randomized study with results after 10 years. Acta Orthop Belg 2013;79:536-40.
58. Smolders JM, Pakvis DF, Hendrickx BW, Verdonschot N, van Susante JL. Periacetabular bone mineral density changes after resurfacing hip arthroplasty versus conventional total hip arthroplasty. A randomized controlled DEXA study. J Arthroplasty 2013;28:1177-84.
59. Stiehler M, Goronzy J, Hartmann A, Krummenauer F, Gunther K-P. The First SICOT Oral Presentation Award 2011: imageless computer-assisted femoral component positioning in hip resurfacing: a prospective randomised trial. Int Orthop 2013;37:569-81.
60. Vidovic D, Matejcic A, Punda M, Ivica M, Tomljenovic M, Bekavac-Beslin M, et al. Periprosthetic bone loss following hemiarthroplasty: A comparison between cemented and cementless hip prosthesis. Injury 2013;44:S62-S6.
61. Hamilton DF, Clement ND, Burnett R, Patton JT, Moran M, Howie CR, et al. Do modern total knee replacements offer better value for money? A health economic analysis. Int Orthop 2013;37:2147-52.
62. Munzinger U, Guggi T, Kaptein B, Persoon M, Valstar E, Cornelis Doets H. A titanium plasma-sprayed cup with and without hydroxyapatite-coating: A randomised radiostereometric study of stability and osseointegration. Hip Int 2013;23:33-9.
63. Zagra L, Anasetti F, Bianchi L, Licari V, Giacometti Ceroni R. No difference in gait recovery after THA with different head diameters: A prospective randomized study. Clin Orthop Rel Res 2013;471:3830-7.
64. Aggarwal AK, Agrawal A. Mobile vs fixed-bearing total knee arthroplasty performed by a single surgeon. A 4- to 6.5-year randomized, prospective, controlled, double-blinded study. J Arthroplasty 2013;28:1712-6.
65. Chareancholvanich K, Narkbunnam R, Pornrattanamaneewong C. A prospective randomised controlled study of patient-specific cutting guides compared with conventional instrumentation in total knee replacement. Bone Joint J 2013;95-B:354-9.
66. Jung W, Chun C, Lee J, Ha J, Jeong JH. The accuracy of the extramedullary and intramedullary femoral alignment system in total knee arthroplasty for varus osteoarthritic knee. Knee Surg Sports Traumatol Arthrosc 2013;21:629-35.
67. Kim YH, Park JW, Kulkarni SS. A randomised prospective evaluation of ceramic-on-ceramic and ceramic-on-highly cross-linked polyethylene bearings in the same patients with primary cementless total hip arthroplasty. Int Orthop 2013;37:2131-7.

68. Nishizawa Y, Matsumoto T, Kubo S, Muratsu H, Matsushita T, Oka S, et al. The influence of patella height on soft tissue balance in cruciate-retaining and posterior-stabilised total knee arthroplasty. Int Orthop 2013;37:421-5.
69. Roh YW, Kim TW, Lee S, Seong SC, Lee MC. Is TKA using patient-specific instruments comparable to conventional TKA? A randomized controlled study of one system. Clin Orthop Rel Res 2013;471:3988-95.
70. Song EK, Seon JK, Yim JH, Netravali NA, Bargar WL. Robotic-assisted TKA reduces postoperative alignment outliers and improves gap balance compared to conventional TKA knee. Clin Orthop Rel Res 2013;471:118-26.
71. Umrani SP, Cho K-Y, Kim K-I. Patellar eversion does not adversely affect quadriceps recovery following total knee arthroplasty. J Arthroplasty 2013;28:591-4.
72. Barrett WP, Turner SE, Leopold JP. Prospective randomized study of direct anterior vs postero-lateral approach for total hip arthroplasty. J Arthroplasty 2013;28:1634-8.
73. Dennis DA, Heekin RD, Clark CR, Murphy JA, O'Dell TL, Dwyer KA. Effect of implant design on knee flexion. J Arthroplasty 2013;28:429-38.
74. Hamilton WG, Parks NL, Saxena A. Patient-specific instrumentation does not shorten surgical time: A prospective, randomized trial. J Arthroplasty 2013;28:96-100.
75. Jarvis SL, Johnson-Wo AK, Onstot BR, Bhowmik-Stoker M, Shrader MW, Jacofsky MC, et al. Differences between standard and minimally invasive parapatellar surgical approaches for total knee arthroplasty in the tasks of sitting and standing. J Knee Surg 2013;26:249-56.
76. Wegrzyn J, Parratte S, Coleman-Wood K, Kaufman KR, Pagnano MW. The John Insall award: no benefit of minimally invasive TKA on gait and strength outcomes: a randomized controlled trial. Clin Orthop Rel Res 2013;471:46-55.
77. Greidanus NV, Chihab S, Garbuz DS, Masri BA, Tanzer M, Gross AE, et al. Outcomes of minimally invasive anterolateral THA are not superior to those of minimally invasive direct lateral and posterolateral THA hip. Clin Orthop Relat Res 2013;471:463-71.
78. Lapner PLC, Sabri E, Rakhra K, Bell K, Athwal GS. Healing rates and subscapularis fatty infiltration after lesser tuberosity osteotomy versus subscapularis peel for exposure during shoulder arthroplasty. J Shoulder Elbow Surg 2013;22:396-402.
79. Naudie DDR, Somerville L, Korczak A, Yuan X, McCalden RW, Holdsworth D, et al. A Randomized trial comparing acetabular component fixation of two porous ingrowth surfaces using RSA. J Arthroplasty 2013;28:48-52.
80. Vendittoli PA, Riviere C, Lavigne M, Lavoie P, Alghamdi A, Duval N. Alumina on alumina versus metal on conventional polyethylene: a randomized clinical trial with 9 to 15 years follow-up. Acta Orthop Belg 2013;79:181-90.
81. Joseph J, Simpson PMS, Whitehouse SL, English HW, Donnelly WJ. The use of navigation to achieve soft tissue balance in total knee arthroplasty - A randomised clinical study. Knee 2013;20:401-6.
82. Soliman OA, Koptan WMT. Proximal humeral fractures treated with hemiarthroplasty: does tenodesis of the long head of the biceps improve results? Injury 2013;44:461-4.
83. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. Ann Intern Med 2001;134:657-62.
84. Yao AC, Khajuria A, Camm CF, Edison E, Agha R. The reporting quality of parallel randomised controlled trials in ophthalmic surgery in 2011: a systematic review. Eye (Lond) 2014;28:1341-9.
85. Liu LQ, Morris PJ, Pengel LH. Compliance to the CONSORT statement of randomized controlled trials in solid organ transplantation: a 3-year overview. Transpl Int 2013;26:300-6.
86. Agha RA, Camm CF, Doganay E, Edison E, Siddiqui MR, Orgill DP. Randomised controlled trials in plastic surgery: a systematic review of reporting quality. Eur J Plast Surg 2014;37:55-62.

87. Zavitsanos PJ, Bird VG, Mince KA, Neuberger MM, Dahm P. Low methodological and reporting quality of randomized, controlled trials of devices to treat urolithiasis. J Urol 2014;191:988-93.
88. Lee SY, Teoh PJ, Camm CF, Agha RA. Compliance of randomized controlled trials in trauma surgery with the CONSORT statement. J Trauma Acute Care Surg 2013;75:562-72.
89. Kiehna EN, Starke RM, Pouratian N, Dumont AS. Standards for reporting randomized controlled trials in neurosurgery. J Neurosurg 2011;114:280-5.
90. Camm CF, Chen Y, Sunderland N, Nagendran M, Maruthappu M, Camm AJ. An assessment of the reporting quality of randomised controlled trials relating to anti-arrhythmic agents (2002-2011). Int J Cardiol 2013;168:1393-6.
91. Hopewell S, Dutton S, Yu LM, Chan AW, Altman DG. The quality of reports of randomised trials in 2000 and 2006: comparative study of articles indexed in PubMed. Bmj 2010;340:c723.
92. Peters JP, Hooft L, Grolman W, Stegeman I. Assessment of the quality of reporting of randomised controlled trials in otorhinolaryngologic literature - adherence to the CONSORT statement. PLoS One 2015;10:e0122328.
93. Chan AW, Altman DG. Epidemiology and reporting of randomised trials published in PubMed journals. Lancet 2005;365:1159-62.
94. Montgomery S. Of towers, walls, and fields: perspectives on language in science. Science 2004;303:1333-5.

**Table 1:** Search Strategy for Medline and EMBASE

| Medline | Embase |
|---|---|
| 1. exp Arthroplasty/<br>2. arthroplast$.tw.<br>3. exp Joint Prosthesis/<br>4. (knee and (replace$ or arthroplast$ or prosthe$ or endoprosthe$ or implant)).tw.<br>5. (hip and (replace$ or arthroplast$ or prosthe$ or endoprosthe$ or implant)).tw.<br>6. (elbow and (replace$ or arthroplast$ or prosthe$ or endoprosthe$ or implant)).tw.<br>7. (shoulder and (replace$ or arthroplast$ or prosthe$ or endoprosthe$ or implant)).tw.<br>8. (joint and (replace$ or arthroplast$ or prosthe$ or endoprosthe$ or implant)).tw.<br>9. (tka or tkr or total knee or total hip).tw.<br>10. or/1-9<br>11. randomized controlled trial.pt.<br>12. controlled clinical trial.pt.<br>13. randomized.ab.<br>14. placebo.ab.<br>15. drug therapy.fs.<br>16. randomly.ab.<br>17. trial.ab.<br>18. groups.ab.<br>19. or/11-18<br>20. exp animals/ not humans.sh.<br>21. 19 not 20<br>22. 10 and 21<br>23. limit 22 to "all adult (19 plus years)"<br>24. limit 23 to english<br>25. limit 24 to yr="2008" | #1 arthroplasty'/exp OR 'arthroplasty'<br>#2 total AND knee AND replacement<br>#3 joint AND replacement<br>#4 joint AND prosthesis<br>#5 replacement* OR arthroplast* OR prosthe* OR implant OR endoprosthe* AND knee<br>#6 replacement* OR arthroplast* OR prosthe* OR implant OR endoprosthe* AND hip<br>#7 replacement* OR arthroplast* OR prosthe* OR implant OR endoprosthe* AND elbow<br>#8 replacement* OR arthroplast* OR prosthe* OR implant OR endoprosthe* AND shoulder<br>#9 tka<br>#10 tha<br>#11 total AND hip AND replacement<br>#12 knee AND prosthesis<br>#13 hip AND prosthesis<br>#14 #1 OR #2 OR #3 OR #4 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14<br>#15 randomized AND controlled AND trial<br>#16 randomization<br>#17 double AND blind AND procedure<br>#18 single AND blind AND procedure<br>#19 #15 OR #16 OR #17 OR #18<br>#20 animal NOT human<br>#21 #19 NOT #20<br>#22 #14 AND #19 AND #21<br>#23 #22 AND ([adult]/lim OR [aged]/lim OR [middle aged]/lim OR [very elderly]/lim) AND 2008:py<br>#24 #22 AND ([adult]/lim OR [aged]/lim OR [middle aged]/lim OR [very elderly]/lim) AND 2013:py<br>#25 english:la |

**Table 2:** Characteristics of joint replacement randomised controlled trials published in 2008 and 2013

| | **2008 (N=30)** | **2013 (N=40)** |
|---|---|---|
| Year of first recruitment (Range, (median)) | 1994 – 2007 (2001) | 1996 – 2011 (2007) |
| Number of participants (median, range) | 85 (14-284) | 81 (28-539) |
| Region | N (%) | N (%) |
| Europe | 18 (60) | 20 (50) |
| Asia | 2 (7) | 9 (23) |
| USA | 6 (20) | 5 (13) |
| Canada | 2 (7) | 4 (10) |
| Middle East | 0 (0) | 1 (3) |
| Australia | 2 (7) | 1 (3) |
| Funding | | |
| Independent | 20 (67) | 15 (38) |
| Industry funded | 9 (30) | 12 (30) |
| Not specified | 1 (3) | 13 (33) |

**Figure 1.** PRISMA diagram showing selection of included trials

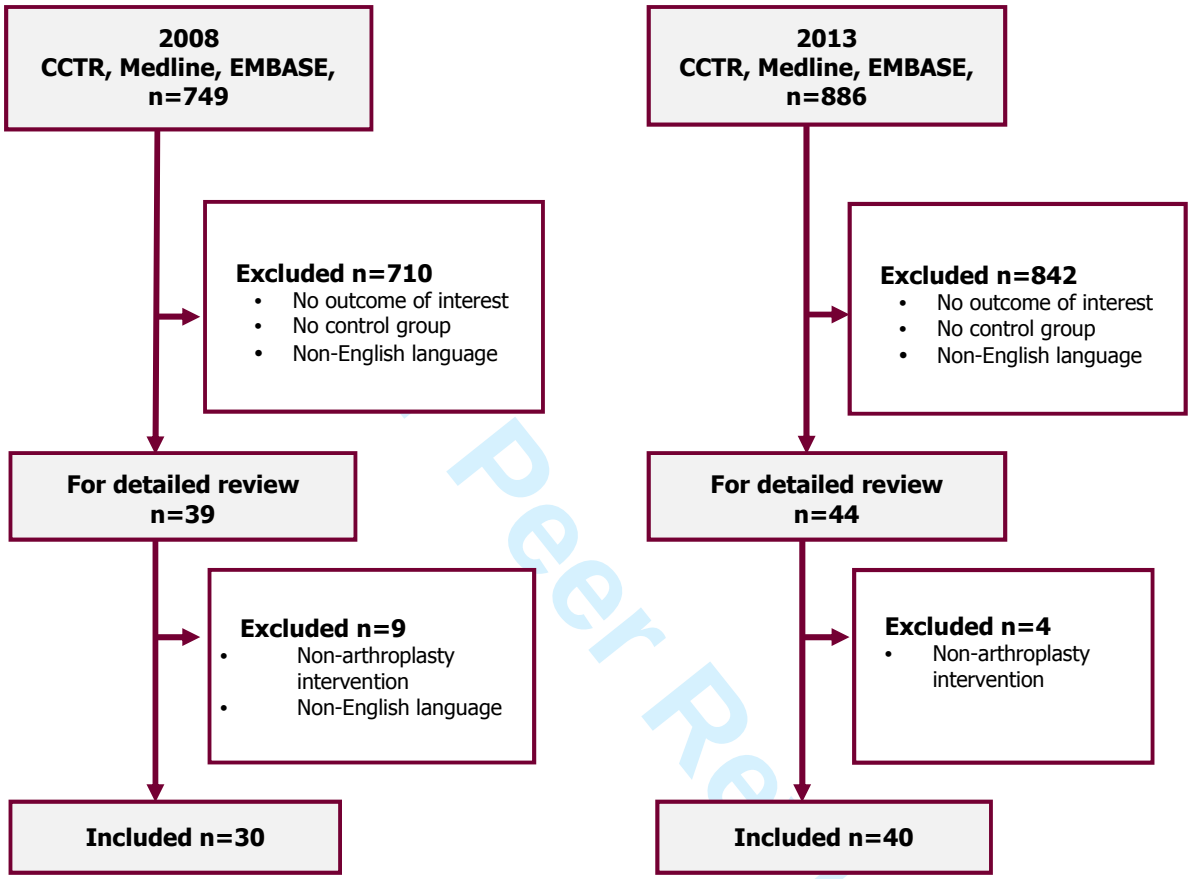


**Figure 2.** The Risk of Bias summary of included joint replacement trials in 2008

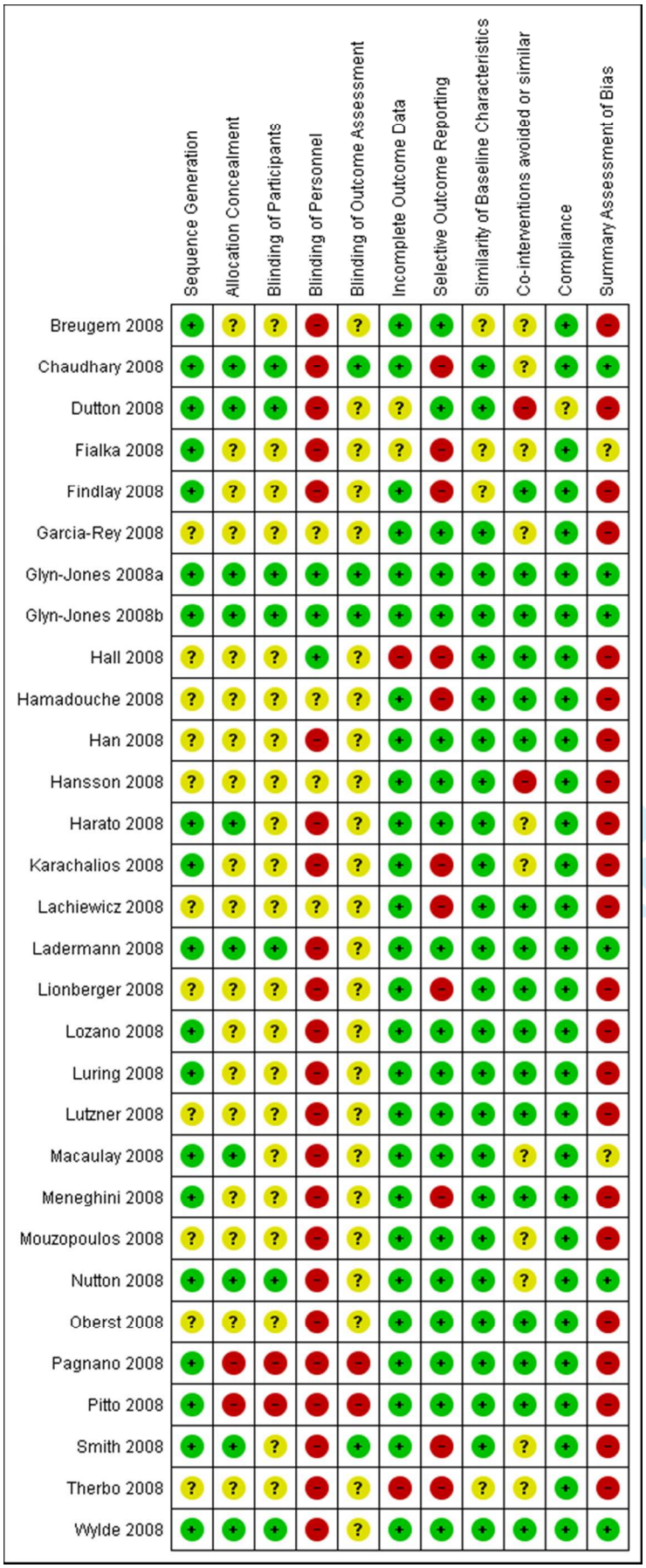
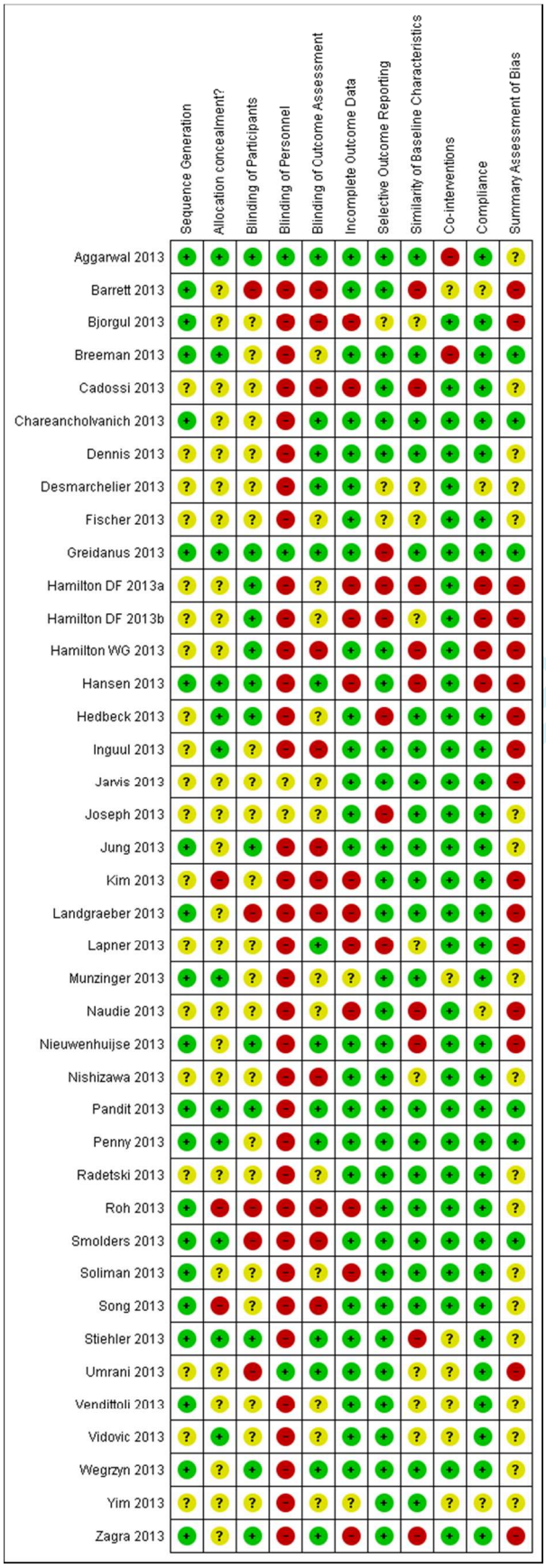


**Figure 3.** The Risk of Bias summary of included joint replacement trials in 2013



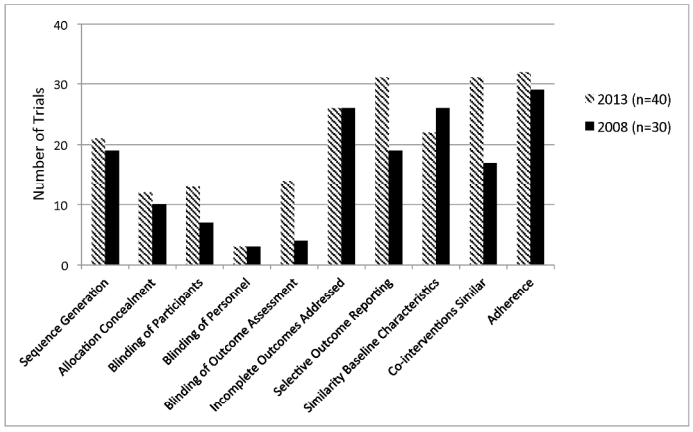



Figure 4: Number of trials with low risk of bias for different criteria in the Cochrane Risk of Bias tool comparing 2008 and 2013 joint replacement randomised controlled trials