RESEARCH ARTICLE

Inconsistent selection of outcomes and measurement devices found in shoulder arthroplasty research: An analysis of studies on ClinicalTrials.gov

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Abstract

Introduction

Recent evidence suggests a lack of standardization of shoulder arthroplasty outcomes. This issue is a limiting factor in systematic reviews. Core outcome set (COS) methodology could address this problem by delineating a minimum set of outcomes for measurement in all shoulder arthroplasty trials.

Methods

A ClinicalTrials.gov search yielded 114 results. Eligible trials were coded on the following characteristics: study status, study type, arthroplasty type, sample size, measured outcomes, outcome measurement device, specific metric of measurement, method of aggregation, outcome classification, and adverse events.

Results

Sixty-six trials underwent data abstraction and data synthesis. Following abstraction, 383 shoulder arthroplasty outcomes were organized into 11 outcome domains. The most commonly reported outcomes were shoulder outcome score (n = 58), pain (n = 33), and quality of life (n = 15). The most common measurement devices were the Constant-Murley Shoulder Outcome Score (n = 38) and American Shoulder and Elbow Surgeons Shoulder Score (n = 33). Temporal patterns of outcome use was also found.

Conclusion

Our study suggests the need for greater standardization of outcomes and instruments. The lack of consistency across trials indicates that developing a core outcome set for shoulder arthroplasty trials would be worthwhile. Such standardization would allow for more effective comparison across studies in systematic reviews, while at the same time consider important
outcomes that may be underrepresented otherwise. This review of outcomes provides an evidence-based foundation for the development of a COS for shoulder arthroplasty.

1 Introduction
Orthopedic shoulder pathology from age-related complications is increasing, due in part to longer lifespans. Osteoarthritis and rotator cuff disease are two degenerative conditions most commonly identified as causing pain and disability in the aging population [1]. While many treatments exist for initial stages of degenerative shoulder diseases, three interventions are most common for treatment of progressive to severe osteoarthritis. Total shoulder arthroplasty (TSA)—replacement of the humeral head and prosthetic resurfacing of the glenoid—is considered the gold standard treatment due to its reliable pain relief, predictable improvement of function, and enhanced quality of life [2–4]. Hemiarthroplasty (HA), which involves replacing the humeral head alone [1], and reverse shoulder arthroplasty (RSA), a modified TSA where the semi-circumference ball is implanted in the glenoid and a stem with a concave polyethylene cap implanted in the humerus, are also viable treatments for advanced shoulder disease. Exponential increases in use of these interventions warrant further study to better understand their efficacy, surgical indications, and potential complications [5–7]. Unfortunately, useful information on these aspects of shoulder arthroplasty is limited, partially due to methodological issues associated with the reported studies. For instance, a Cochrane systematic review of these surgeries for shoulder osteoarthritis was inconclusive, in part, because the primary studies comprising the review did not measure outcomes aligned with the research questions [8]. In fact, most outcomes important to the systematic reviewers were measured in only a single study. Another recent review of arthroscopy following shoulder arthroplasty noted significant heterogeneity in outcome reporting among primary studies which limited the reviewers’ ability to perform a quantitative synthesis of outcomes [9]. Standardization of outcomes for shoulder arthroplasty studies would help overcome limitations reported in previous systematic reviews and allow for more conclusive evaluations of efficacy.

Core outcome set (COS) methodology could address this problem using consensus approaches involving trialists, systematic reviewers, funders, patients, and other research stakeholders to derive a minimum set of outcomes for measurement across shoulder arthroplasty studies [10–12]. In conjunction with COS development, core outcome measurement sets establish the instruments that should be administered for outcome measurement [13]. For example, there are currently several shoulder measures available: the American Shoulder and Elbow Surgeons Society Standardized Shoulder Assessment Form (ASES), the Constant-Murley Shoulder Outcome Score, Disabilities of the Arm, Shoulder, and Hand Questionnaire (DASH), the QuickDASH, L’Insalata Shoulder Rating Questionnaire, Simple Shoulder Test (SST), the Oxford Shoulder Score (OSS), the Shoulder Disability Questionnaire (SDQ), and the Western Ontario Shoulder Instability Index (WOSI), among others [14,15]. Whether condition-specific symptoms should be limited to movement-related shoulder functions or more generally to include broader aspects of functioning (e.g., leisure activities or work) remains a source of debate [16] and the diversity of items and domains comprising such measures may impede meta-analytic investigations. A standardized recommendation for evaluation of shoulder function would improve the ability to synthesize evidence across studies. Given the impressive growth of TSA, HA, and RSA procedures, there is a need for continued evaluation of their efficacy and for determining whether an increased standardization of outcomes is necessary. Here, we conduct an analysis of shoulder arthroplasty intervention studies registered on
ClinicalTrials.gov to elucidate the diversity of methodologies and outcomes reported. The objective of this study is to provide an evidence-based foundation for the development of a COS for shoulder arthroplasty.

2 Methods

We conducted an analysis of studies catalogued in ClinicalTrials.gov to examine outcomes reported in registered orthopedic surgery clinical trials. This study did not meet the regulatory definition of human subject research as defined in 45 CFR 46.102(d) and (f) of the Department of Health and Human Services’ Code of Federal Regulations [17] and, therefore, was not subject to Institutional Review Board oversight. We consulted Li et al [18], the Cochrane Handbook for Systematic Reviews of Interventions [19], and the National Academies of Science, Engineering, and Medicine’s (formally the Institute of Medicine) Standards for Systematic Reviews [20] for best practices in data collection and management for systematic reviews as we developed our methodology. To adhere to best practices in reporting, we applied relevant PRISMA guidelines [21] (Checklist items 1–3, 5–11, 13, 16–18, 20, 23, 24, 26, 27) since our study involved the synthesis of multiple registered trials. We applied SAMPL guidelines [22] for reporting descriptive statistics. This study was registered with the Core Outcome Measurement in Effectiveness Trials (COMET) Initiative (http://www.comet-initiative.org/studies/details/812?result=true). Data from this study is publicly available on figshare (https://dx.doi.org/10.6084/m9.figshare.3464831.v2).

2.1 Eligibility criteria for considering studies for this review

Primary studies registered in ClinicalTrials.gov between 2005 and 2015 in which shoulder arthroplasty (including total shoulder arthroplasty, reverse shoulder arthroplasty, hemiarthroplasty, and glenoid resurfacing) was used as an intervention were eligible for this review. For this study, both open (not yet recruiting, recruiting) and closed (active, not recruiting; completed; terminated; suspended; withdrawn; enrolling by invitation) trials were eligible for inclusion. Randomized and non-randomized clinical trials as well as observational studies were included since these study designs may be registered on ClinicalTrials.gov [23]. We used the following definitions to classify study types. A clinical trial (National Institutes of Health definition) was defined as “a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.” An observational study was defined as “a biomedical or behavioral research study of human subjects designed to assess risk factors for disease development or progression, assess natural history of risk factors or disease, identify variations based on geographic or personal characteristics (such as race/ethnicity or gender), track temporal trends, or describe patterns of clinical care and treatment in absence of specific study-mandated interventions” [24].

2.2.1 Search strategy for identifying relevant studies

We consulted a research librarian to conduct a search for clinical trials registered on ClinicalTrials.gov that examined shoulder arthroplasty interventions reported in orthopedic surgery literature. ClinicalTrials.gov was searched in order to identify unpublished or ongoing trials. We used registered trials to minimize the possibility of selective outcome reporting bias and to better understand the outcomes reported in current orthopedic clinical trials. This search was narrowed for four common arthroplasty shoulder procedures: total shoulder arthroplasty (TSA), reverse shoulder arthroplasty (RSA), hemiarthroplasty (HA), and glenoid resurfacing; however, we did not impose a limiter for language or restrict the search by journal. The final
search string is as follows: Shoulder AND (Surg’ OR operat’ OR arthroplasty OR hemiarthroplasty OR (joint’ AND replace’)) OR debride OR debridement OR debrided OR (surface AND (replace OR replacement OR replaced)) OR resurface OR resurfaced OR resurfacing) | received from 01/01/2005 to 12/31/2016. The search was performed on June 30, 2017.

2.2.2 Study selection and data collection

Four authors (MTS, JTS, BMH, and GRD) equally divided the studies among one another and independently screened all of the studies for eligibility. To be eligible, a study must have reported the use of shoulder arthroplasty as an intervention. We included total, hemi-, and reverse arthroplasty as well as glenoid resurfacing; hence, arthroscopic studies were excluded from analysis. Studies must also have been registered on ClinicalTrials.gov between 2000 and 2016. We included both observational and interventional studies, as both commonly report primary and secondary outcomes in ClinicalTrials.gov. After the initial screening was completed, a second screening was performed by an author (BND) who was blinded from previous screening results. Discrepancies in screening were resolved by discussion between BND and the other authors. Final exclusions are outlined in the PRISMA flow diagram (Fig 1).

An abstraction manual was designed after consulting several sources [25–30] to ensure data abstraction was consistently and accurately performed by authors. Authors participated in a series of meetings to apply the abstraction manual to a subset of 15 studies as a pilot test before
launch. During these meetings, authors abstracted data elements by reviewing each study, discussing data elements, and reaching agreement on changes to the abstraction manual. Refinements were made based on pilot feedback and a final manual was produced. Data elements included:

- sponsor(s), title of the article;
- start date of trial (year);
- study status (not yet recruiting; recruiting; active, not recruiting; completed; terminated; suspended; withdrawn; enrolling by invitation);
- study type (interventional, observational, etc.);
- type of arthroplasty (TSA, RSA, HA, glenoid resurfacing, other);
- sample size;
- measured outcomes;
- outcome measurement device;
- specific metric of measurement (value at a time point, change from baseline, time to event, unclear);
- method of aggregation (mean, median, percent/proportion, absolute number, unclear);
- outcome classification (primary, secondary, other, unclear);
- whether the outcome was considered a side effect/harmful.

The registered studies meeting inclusion criteria were then equally divided for data abstraction among four authors (MTS, GRD, JTS, and BMH). Working in pairs, authors first abstracted data elements from articles in their set and then validated the abstracted data of their partner. Any discrepancies in data abstraction were settled by discussion between the pair, or when necessary, by adjudication with the blinded author (BND) to ensure the accuracy and integrity of this study.

2.3 Definition and classification of measured outcomes

We defined an outcome as the exact word-for-word terms (presented as either a primary or secondary outcome) in a trial for any clinical endpoint, or physiological, metabolic, or mortality event measured by clinicians or researchers [26]. Eleven outcome domains were determined based on the distribution of outcomes within this study and previously defined domains by Page et al [28]. Outcomes were classified under the following outcome domains: Adverse Events, Function/Disability, Global Assessment of Treatment Success, Health Related Quality of Life (HRQoL), Orthopedic Tests, Other, Pain, Radiologic Evaluation, Range of Motion (ROM), Strength, and Survival. Individual outcomes were distributed into each of these categories during the coding process. In order to decrease heterogeneity of reported outcomes, authors determined standardized terminology for each outcome.

2.4 Statistical analysis

Results were summarized using frequencies and percentages for binary outcomes, and medians and interquartile ranges (IRQs) for continuous outcomes. Locally weighted scatterplot smoothing (nonparametric regression method) was used to smooth the scatterplots of outcome domain use over time [28]. Our final scatterplot data is available on figshare (https://dx.
Descriptive statistics were used to summarize data and all analyses were conducted using STATA 13.1 (College Station, TX).

3 Results

A total of 114 clinical trials were identified on ClinicalTrials.gov. Forty-eight studies were excluded after failing to meet inclusion criteria (Fig 1). A final sample size of 66 trials underwent data abstraction and was included in the final data synthesis. Clinical trials included within this study started their research between 2000 and 2016, as summarized in Table 1.

3.1 Summary of shoulder arthroplasty trials characteristics

Nearly half of the studies were comprised of “Completed” (14/66, 21.2%) and “Recruiting” (18/66, 27.3%) studies. “Active, not recruiting” and “Unknown” trials each accounted for 10 and 9, respectively, (19/66, 28.8%) of the remaining trials (Table 1). Of the 66 studies, 37 were listed as interventional (37/66, 56.1%) and 29 were listed as observational (29/66, 43.9%). The most frequently reported shoulder arthroplastic procedure was TSA (37/66, 41.6%). RSA (24/66, 27%), HA (15/66, 16.9%), and glenoid resurfacing (11/66, 12.3%) were also commonly reported shoulder arthroplasties (Table 1).

3.2 Shoulder arthroplasty outcomes and domain categories

Following data abstraction, 383 shoulder arthroplasty outcomes were organized into 11 different outcome domains. The standardized outcomes, measurement devices and specific metrics were summarized and organized into domain categories, as displayed in Table 2.

Table 1. Characteristics of included studies (Updated to Reflect 2016 Data).

| Characteristics            | Number (%) of trials (n = 66) |
|----------------------------|-------------------------------|
| **Start Date of Trial**    |                               |
| 2000–2004                  | 6 (9.1)                       |
| 2005–2008                  | 13 (19.7)                     |
| 2009–2012                  | 20 (30.3)                     |
| 2013–2016                  | 27 (40.9)                     |
| **Phase of Trial**         |                               |
| Active, Not Recruiting     | 10 (15.2)                     |
| Completed                  | 14 (21.2)                     |
| Enrolling by Invitation    | 6 (9.1)                       |
| Not Yet Recruiting         | 3 (4.5)                       |
| Recruiting                 | 18 (27.3)                     |
| Suspended                  | 1 (1.5)                       |
| Terminated                 | 4 (6.1)                       |
| Unknown                    | 9 (13.6)                      |
| Withdrawn                  | 1 (1.5)                       |
| **Type of Trial**          |                               |
| Intervventional            | 37 (56.1)                     |
| Observational              | 29 (43.9)                     |
| **Procedure Frequency**    |                               |
| Hemiarthroplasty (HA)      | 15 (16.9)                     |
| Total Shoulder Arthroplasty (TSA) | 37 (41.6)             |
| Reverse Shoulder Arthroplasty (RSA) | 24 (27)                  |
| Glenoid Resurfacing        | 11 (12.3)                     |
| Other                      | 2 (2.2)                       |

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Table 2. Domain categories and reported outcomes, device, and metric within each domain (Updated to Reflect 2016 Data).

| Domains (n = 11)               | Outcomes (n = 383)                                                                 | Measurement Devices                                                                 | Specific Metric                  |
|--------------------------------|-----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------|
| **Adverse Events (n = 25)**    | Adverse events (7)                                                                | Frequency (19)                                                                        | Value at a time point (20)        |
|                                | Device associated adverse events (3)                                              | Unspecified (3)                                                                      | Unspecified (2)                  |
|                                | Biceps rupture (1)                                                                |                                                                                      |                                  |
|                                | Device migration (1)                                                              |                                                                                      |                                  |
|                                | Intraoperative bleeding (1)                                                       |                                                                                      |                                  |
|                                | Intraoperative neurovascular injury (1)                                            |                                                                                      |                                  |
|                                | Intraoperative prosthetic fracture (1)                                             |                                                                                      |                                  |
|                                | Lack of unanticipated device related serious adverse events (1)                   |                                                                                      |                                  |
|                                | Osteolysis (1)                                                                    |                                                                                      |                                  |
|                                | Postoperative bleeding (1)                                                        |                                                                                      |                                  |
|                                | Postoperative infection (1)                                                       |                                                                                      |                                  |
|                                | Postoperative instability (1)                                                     |                                                                                      |                                  |
|                                | Procedure associated adverse events (2)                                            |                                                                                      |                                  |
|                                | Revision complications (1)                                                        |                                                                                      |                                  |
| **Function/Disability (n = 16)**| Function (15)                                                                     | AS/ES (4)                                                                            | Value at a time point (13)        |
|                                | Function/disability (1)                                                           | SST (4)                                                                              | Change from baseline (3)          |
|                                |                                                                                   | Constant (3)                                                                          |                                  |
|                                |                                                                                   | SANE (2)                                                                              |                                  |
|                                |                                                                                   | Clinical outcome comparison (1)                                                      |                                  |
|                                |                                                                                   | Unspecified (1)                                                                       |                                  |
|                                |                                                                                   | VAS (1)                                                                               |                                  |
| **Global Assessment of Treatment Success (n = 60)** | Shoulder outcome score (56)                                                     | Constant (2)                                                                          | Value at a time point (42)        |
|                                | Impact of arm length difference on patient reported outcome (1)                   | AS/ES (19)                                                                            | Change from baseline (12)         |
|                                |                                                                                   | Oxford (5)                                                                            |                                  |
|                                |                                                                                   | PENN (3)                                                                              |                                  |
|                                |                                                                                   | DASH (3)                                                                              |                                  |
|                                |                                                                                   | QuickDASH (3)                                                                         |                                  |
|                                |                                                                                   | SSV (2)                                                                               |                                  |
|                                |                                                                                   | Modified Constant (1)                                                                |                                  |
|                                |                                                                                   | Nee's limited goals (1)                                                               |                                  |
|                                |                                                                                   | SANE (1)                                                                              |                                  |
|                                |                                                                                   | SPADI (1)                                                                             |                                  |
|                                |                                                                                   | UQLA (1)                                                                              |                                  |
|                                |                                                                                   |                                                                                      |                                  |
| **Health Related Quality of Life (n = 68)** | Quality of life (15)                                                             | EOSD (11)                                                                            | Value at a time point (39)        |
|                                | Multidimensional aspects of health (8)                                            | SF-36 (10)                                                                            | Change from baseline (20)         |
|                                | Patient satisfaction (9)                                                          | WOOS (8)                                                                              | Unspecified (1)                  |
|                                | Activities of daily living (4)                                                    | SF-12 (6)                                                                             |                                  |
|                                | Disease or joint specific measure (4)                                             | Unspecified (6)                                                                       |                                  |
|                                | General health component (2)                                                       | AS/ES (2)                                                                             |                                  |
|                                | Patient/objective data (2)                                                        | EOSD5L (2)                                                                            |                                  |
|                                | Patient/subjective data (2)                                                       | Patient assessment forms (2)                                                         |                                  |
|                                | Anxiety/depression (1)                                                            | VAS (2)                                                                               |                                  |
|                                | Mental component summary (1)                                                      | 1SD (2)                                                                               |                                  |
|                                | Mental health component (1)                                                       | ADLER (1)                                                                             |                                  |
|                                | Mobility (1)                                                                      | SPADI (1)                                                                             |                                  |
|                                | Personal dependency status (1)                                                    | Unspecified (1)                                                                       |                                  |
|                                | Physical component summary (1)                                                    | PENN (1)                                                                              |                                  |
|                                | Physical function (1)                                                             | 4-point rating (1)                                                                    |                                  |
|                                | Role emotional (1)                                                                | Constant (1)                                                                          |                                  |
|                                | Role physical (1)                                                                 | DASH (1)                                                                              |                                  |
|                                | Self-care (2)                                                                     | Quality of life survey (1)                                                            |                                  |
|                                | Social function (1)                                                               | SST (1)                                                                               |                                  |
|                                | Usual activities (1)                                                              |                                                                                      |                                  |
|                                | VAS (1)                                                                            |                                                                                      |                                  |
|                                | Vitality (1)                                                                      |                                                                                      |                                  |
|                                | Willingness to have surgery performed again (1)                                   |                                                                                      |                                  |
| **Orthopedic Tests (n = 7)**   | Test specific outcomes (4)                                                        | Abdominal compression test (2)                                                       | Change from baseline (5)          |
|                                | Integrity & function of subscapularis tendon (2)                                  | Lift off test (2)                                                                     | Value at a time point (2)         |
|                                | Internal rotation extension (1)                                                   | Hornblower’s test (1)                                                                 |                                  |
|                                |                                                                                   | Speed’s test (1)                                                                      |                                  |
|                                |                                                                                   | Yergason’s test (1)                                                                   |                                  |

(Continued)
| Domains (n = 11) | Outcomes (n = 383) | Measurement Devices | Specific Metric |
|-----------------|--------------------|---------------------|----------------|
| Other (n = 23)  | Cost association (1) | Unspecified (3) | Value at a time point (4) |
|                 | Health economics (1) | Health resource utilization instrument (1) | |
|                 | Recovery time (1) | | |
|                 | Surgical time (1) | | |
| Pain (n = 35)   | Pain (3) | VAS (10) | Value at a time point (21) |
|                 | Pain at rest (1) | ASSES (6) | |
|                 | Pain with active motion (1) | NRS (3) | |
|                 | Pain/discomfort (2) | | |
|                 | Pain/weakness (1) | Unspecified (3) | |
|                 | Preoperative pain (1) | SANE (2) | |
| Radiologic Evaluation (n = 79) | Acromiohumeral interval (1) | Radiograph (21) | Value at a time point (61) |
|                 | Actual versus optimal glenosphere position (1) | CT (12) | |
|                 | Actual versus predicted scapular notching (1) | Millimeters (2) | |
|                 | Bone density around the prosthesis (1) | Frequency (1) | |
|                 | Bony apposition (2) | Radiostereometric analysis (3) | |
|                 | Bony integration of the component (1) | Degrees (1) | |
|                 | Clinical outcome comparison (1) | | |
|                 | Component loosening (3) | Radiographic evaluation (3) | |
|                 | Component position (1) | Migration between cemented and press-fit RTSA humeral components (1) | |
|                 | Coracoid to glenohumeral joint distance (1) | Migration of resurfacing prosthesis (1) | |
|                 | Coracoid to tuberosity distance (1) | No evidence of device failure (1) | |
|                 | Correlation between bone density and prosthesis migration (1) | Postoperative clinical results (1) | |
|                 | Cumulative incidence of migration, radiolucency, osteolysis, and bone wear (1) | Qualitative documentation of surgical steps (1) | |
|                 | Decreased component loosening (2) | Radiographic failure (1) | |
|                 | Decreased radiolucent lines (2) | Radiolucent lines (5) | |
|                 | Determine if the use of autologous bone graft around the anchor-peg glenoid prosthesis correlate with bony apposition (1) | Scapular notching (1) | |
|                 | Determine if the use of autologous bone graft around the anchor-peg glenoid prosthesis correlate with decreased radiolucent lines and component loosening (1) | Subacromial space (3) | |
|                 | Determine if the use of autologous bone graft around the anchor-peg glenoid prosthesis correlate with functional outcomes (1) | Subsidence (5) | |
|                 | Difference in component migration between conventional and lateralized glenoid components (1) | Tuberosity thinning (3) | |
|                 | Evidence of movement or pending failure (1) | X-Rays (3) | |
|                 | Fixation to bone/early migration of the implants (1) | | |
|                 | Function (2) | | |
|                 | Glenoid component migration (1) | | |
|                 | Glenoid component position (3) | | |
|                 | Glenoid erosion (3) | | |
|                 | Glenoid status (2) | | |
|                 | Head to tuberosity distance (1) | | |
|                 | Humeral congruity (1) | | |
|                 | Humeral cortical thickness (1) | | |
|                 | Humeral stem position—valgus/varus (1) | | |
|                 | Humeral subluxation (1) | | |
|                 | Lateralization index (3) | | |
|                 | Location and placement of HRA device (1) | | |
|                 | Radiographic evaluation (3) | | |
|                 | Migration between cemented and press-fit RTSA humeral components (1) | | |
|                 | Migration of resurfacing prosthesis (1) | | |
|                 | No evidence of device failure (1) | | |
|                 | Postoperative clinical results (1) | | |
|                 | Qualitative documentation of surgical steps (1) | | |
|                 | Radiographic failure (1) | | |
|                 | Radiolucent lines (5) | | |
|                 | Scapular notching (1) | | |
|                 | Subacromial space (3) | | |
|                 | Subsidence (5) | | |
|                 | Tuberosity thinning (3) | | |
|                 | X-Rays (3) | | |
| Domains (n = 11)          | Outcomes (n = 383)                          | Measurement Devices | Specific Metric                  |
|--------------------------|--------------------------------------------|---------------------|----------------------------------|
| **Range of Motion**      | Range of motion (11)                       | Constant (10)       | Change from baseline (21)        |
| (n = 38)                 | External rotation (4)                      | Unspecified (17)    | Value at a time point (13)       |
|                          | Internal rotation (3)                      | Goniometer (4)      |                                  |
|                          | Active external rotation (2)               | Range of motion (1) |                                  |
|                          | Flexion (2)                                | ASES (1)            |                                  |
|                          | Passive external rotation (2)              | Degrees (1)         |                                  |
|                          | Active abduction (1)                       |                     |                                  |
|                          | Passive flexion (1)                        |                     |                                  |
|                          | Active internal rotation (1)               |                     |                                  |
|                          | Active range of motion (1)                 |                     |                                  |
|                          | Passive abduction (1)                      |                     |                                  |
|                          | Passive flexion (1)                        |                     |                                  |
|                          | Passive internal rotation (1)              |                     |                                  |
|                          | Passive range of motion (1)                |                     |                                  |
|                          | Postoperative clinical results (1)         |                     |                                  |
|                          | Scaption (1)                               |                     |                                  |
| **Strength**             | External rotation strength (2)             | Pounds (5)          | Value at a time point (10)       |
| (n = 16)                 | Flexion strength (2)                       | Lafayette manual muscle testing system (4) |                |
|                          | Internal rotation strength (2)             | Iso-force machine (2)|                                  |
|                          | Strength (2)                               | Unspecified (1)     | Change from baseline (2)         |
|                          | External abduction strength (1)            |                     |                                  |
|                          | Scapula abduction strength (2)             |                     |                                  |
|                          | Thumb down abduction strength (1)          |                     |                                  |
| **Survival**             | Implant survival (1)                       | Frequency (8)        | Time to event (11)               |
| (n = 16)                 | Revision/reoperation (3)                   | Kaplan-Meier (5)    | Value at a time point (4)        |
|                          | Device success rate (1)                    | Unspecified (5)      | Unspecified (1)                  |
|                          | Time to first revision (1)                 |                     |                                  |
The Radiologic Evaluation domain contained the greatest number of outcomes (n = 79) followed by the HRQoL (n = 68) and Global Assessment of Treatment Success (n = 60) domains (Table 2). In terms of outcome reporting, the Radiologic Evaluation domain contained a large number of unique outcomes that were measured in a few studies. The Global Assessment of Treatment Success domain contained the most commonly reported outcome, shoulder outcome score (n = 58). Pain (n = 33), quality of life (n = 15), function (n = 15), ROM (n = 11) and implant survival (n = 11) were also frequently reported outcomes (Table 3). Across all domains, 61 outcomes had an unspecified measurement device. The most common measurement devices were the Constant-Murley Shoulder Outcome Score (n = 38), American Shoulder and Elbow Surgeons (ASES) Shoulder Score (n = 33), and frequency counts (such as number of adverse events or revisions) (n = 30) (Table 2).

There was a mean of six outcomes reported per study, with a range between one and thirty-seven outcomes reported per study. In each trial registry, the outcomes received a classification of primary, secondary, other, or unspecified. Of the 383 reported outcomes, 68.7% (263/383) were classified as secondary outcomes and the remaining were predominantly primary outcomes (120/383, 31.3%).

3.3 Frequency of outcome domains over time

The frequency of reported outcomes over time is shown in Fig 2. Solid lines are smoothed values calculated from the nonparametric regression locally weighted scatterplot smoothing method (LOWESS). Visual inspection of the smoothed scatterplots indicates the survival outcome domain showed a trend of an overall increase from 2000 to 2016 while the pain outcome domain showed an increase following a significant decrease in reporting prior to 2005. The orthopedic tests and strength domains remained stable over time while global assessment of treatment success domain maintained a stable decline in outcome reporting over time (Fig 2).

4 Discussion

Results from our study suggest the need for greater standardization of outcomes as well as the instruments used to measure them. Interestingly, concurrent evaluations to ours by Page et al. [31–32] have affirmed the need for greater standardization of outcomes and measurement for shoulder disorders. Our findings are complimentary and confirmatory even though we used different search methodologies and applied different inclusion criteria. We limited our search to registered trials to minimize selective outcome reporting, whereas Page et al. reviewed published trials that served as primary studies in Cochrane reviews or were indexed in PubMed. Furthermore, while we examined outcomes reported across studies applying specific interventions (i.e., arthroplastic procedures), Page et al. looked more broadly at shoulder disorders. Despite these differences, we observed similar inconsistencies in trial outcomes. The lack of consistency observed in these studies indicates that developing a core outcome set for shoulder arthroplasty trials would be worthwhile. Such standardization would allow for more effective study to study comparisons in systematic reviews, while at the same time consider important outcomes that may be underrepresented otherwise.

While six outcomes, on average, were measured across trials, there were trials with as many as 37 outcomes measured in a single trial. Core outcome sets are developed to refine outcomes to those most meaningful and important across investigations and could help limit the number of outcomes being measured. Large numbers of outcomes in trials could result in increased occurrences of selective outcome reporting bias [33] or p-hacking [34], both of which may adversely affect our understanding of the true nature of clinical trial results.
### Table 3. Outcomes reported by frequency of measurements (Updated to Reflect 2016 Data).

#### Outcomes reported in >5 studies

| Outcomes reported in >5 studies                     | Function                  | Implant Survival | Multidimensional aspects of health |
|-----------------------------------------------------|---------------------------|------------------|------------------------------------|
| Adverse events                                      |                           |                  |                                    |
| Pain                                                | Patient satisfaction     | Range of motion  | Shoulder outcome score             |
| Quality of life                                      |                           |                  |                                    |

#### Outcomes reported in 2–5 studies

| Active external rotation | Activities of daily living | Bony apposition | Component loosening |
|--------------------------|-----------------------------|-----------------|---------------------|
| Decreased component loosening | Decreased radiolucent lines | Device associated adverse events | Disease or joint specific measure |
| External rotation        | External rotation strength  | Flexion         | Flexion strength    |
| General health component | Glenoid component position | Glenoid erosion | Glenoid status      |
| Integrity & function of subscapular tendon          | Internal rotation          | Internal rotation strength | Lateralization index |
| Passive external rotation | Patient objective data     | Patient subjective data | Postoperative clinical results |
| Radiographic evaluation | Radiolucent lines          | Revision/reoperation | Scapula abduction strength |
| Strength               | Subacromial space          | Subsidence      | Test specific outcomes |
| Tuberosity thinning     | X-Rays                     |                 |                      |

#### Outcomes reported only once

| Acromiohumeral interval | Active abduction            | Active flexion | Active internal rotation |
|------------------------|-----------------------------|----------------|--------------------------|
| Active range of motion | Actual versus optimal glenosphere position | Actual versus predicted scapular notching | Anxiety/depression |
| Biceps rupture         | Bone density around the prosthesis | Bony integration of the component | Clinical outcome comparison |
| Component position     | Coracoid to glenohumeral joint distance | Coracoid to tuberosity distance | Correlation between bone density and prosthesis migration |
| Cost association       | Cumulative incidence of migration, radioluency, osteolysis, and bone wear | Determine if the use of autologous bone graft around the anchor-peg glenoid prosthesis correlate with decreased radiolucent lines and component loosening | Determine if the use of autologous bone graft around the anchor-peg glenoid prosthesis correlate with functional outcomes |
| Determine if the use of autologous bone graft around the anchor-peg glenoid prosthesis correlate with bony apposition | Device migration | Device success rate | Difference in component migration between conventional and lateralized glenoid components |
| Effectiveness          | Evidence of movement or pending failure | External abduction strength | Fixation to bone/early migration of the implants |
| Function/disability    | Glenoid component migration | Head to tuberosity distance | Health economics |
| Humeral congruity      | Humeral cortical thickness  | Humeral stem position-valgus/varus | Humeral subluxation |
| Impact of arm length difference on patient reported outcome | Internal rotation extension | Intraoperative bleeding | Intraoperative neurovascular injury |
| Intraoperative prosthetic fracture | Lack of unanticipated device related serious adverse events | Location and placement of HRA device | Mental component summary |
| Mental health component | Migration between cemented and press-fit RTSA humeral components | Migration of resurfacing prosthesis | Mobility |
| No evidence of device failure | Osteolysis | Pain at rest | Pain with active motion |
| Pain/discomfort        | Pain/weakness              | Passive abduction | Passive flexion |
| Passive internal rotation | Passive range of motion | Personal dependency status | Physical component summary |
| Physical function      | Postoperative bleeding     | Postoperative infection | Postoperative instability |
| Preoperative pain      | Procedure associated adverse events | Qualitative documentation of surgical steps | Radiographic failures |
| Recovery time          | Revision complications     | Role emotional  | Role physical           |
| Scaption               | Scapular notching          | Self-care       | Social function         |

(Continued)
We found a wide variety of shoulder instruments used across trials. For global assessment of treatment success, the Constant-Murley Score and ASES were used more frequently than other instruments. A systematic review of psychometric properties for the Constant-Murley Score reported the need for greater standardization for performing the score and greater caution during score interpretation [35]. Other issues, such as weighting the subscales, are ongoing matters of investigation with this scale. For most shoulder instruments, psychometric studies have focused on traditional validity and reliability estimates. Additional research is needed to determine important outcomes such as the minimal clinically important difference [35,36].

We noted several temporal trends in outcomes in this study. For example, our results suggest that HRQoL outcomes decreased over time. This finding is contrary to recent calls to include patient-centered outcomes in clinical research [37–41]. As early as 1990s, researchers recognized the importance of including patient-centered outcomes in orthopedic surgery research, rather than reliance on revision rates or clinical judgments to evaluate post-operative improvement [42]. Xu et al described HRQoL outcomes as a “necessity to fully understand the

Table 3. (Continued)

| Surgical time | Thumb down abduction strength | Time to first revision | Usual activities |
|---------------|-------------------------------|------------------------|-----------------|
| Visual analog scale | Vitality                      | Willingness to have surgery performed again | |

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Fig 2. Smoothed scatterplots of outcome domain use over time. The frequency of reported outcomes over time are shown in these nonparametric regression locally weighted scatterplot smoothing method (LOWESS).

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effects” of orthopedic interventions [43]. Furthermore, given recent indications of the prevalence of clinical depression in patients undergoing elective TSA, improved understanding of important quality of life variables is clearly warranted [44].

5 Limitations

Our study has the following limitations. We limited our sample to outcomes reported on ClinicalTrials.gov based on the recommendation of Clark and Williamson [45]. We chose this approach to include the most current outcomes, while simultaneously limiting selective outcome reporting bias. Although ClinicalTrials.gov is a United States based trial registry platform, there are currently 201 countries utilizing the registry and accounting for nearly 50% of registered studies [46]. Challenges also exist with registry-listed outcomes, which include the potential for vague and incomplete reporting. These challenges have been noted by the WHO and ClinicalTrials.gov, and actions are being taken to improve the accurate reporting of trial outcomes. We also did not search other trial registries, as Moja et al found that ClinicalTrials.gov contained enough data to adequately describe the ongoing research and was most valuable of all registries to finding ongoing clinical trials [47]. Furthermore, we wanted to avoid translating registrations that were written in other languages. We also did not search databases of published works, like MEDLINE or Embase, since published studies have been known to limit outcome reporting to only those which were found to be statistically significant [48–50]; therefore, the published literature may not contain all outcomes originally intended for measurement [51].

6 Conclusion

In summary, this study found a lack of standardization regarding outcomes and measurement devices. This lack of standardization limits systematic reviews to outcomes reported and measured consistently across studies. Important outcomes may be omitted from a subset of studies, limiting data synthesis. Our study provides a summary of outcomes most frequently reported and co-occurring outcomes as a foundation for a follow up study to begin developing a core outcome set for shoulder arthroplasty studies.

Supporting information

S1 File. PRISMA checklist.

(DOC)

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References
1. Killian ML, Cavinato L, Galatz LM, Thomopoulos S. Recent advances in shoulder research. Arthritis Res & Ther. 2012; 14. https://doi.org/10.1186/ar3846 PMID: 22709417
2. Day JS, Lau E, Ong KL, Williams GR, Ramsey ML, Kurtz SM. Prevalence and projections of total shoulder and elbow arthroplasty in the United States to 2015. J Shoulder Elbow Surg. 2010; 19:1115–1120. https://doi.org/10.1016/j.jse.2010.02.009 PMID: 20554454
3. Izquierdo R, Voloshin I, Edwards S, Freehill M, Stanwood W, Wiater JM, et al. Treatment of glenohumeral osteoarthritis. J Am Acad Orthop Surg. 2010; 18:375–382. https://doi.org/10.5435/00124635-201006000-00010 PMID: 20511443
4. Wiater JM, Fabing MH. Shoulder arthroplasty: prosthetic options and indications. J Am Acad Orthop Surg. 2009; 17:415–425. https://doi.org/10.5435/00124635-200907000-00002 PMID: 19871297
5. Bohsali KI, Wirth MA, Rockwood CA. Complications of total shoulder arthroplasty. J Bone Joint Surg. Am. 2006; 88:2279–2292. https://doi.org/10.2106/JBJS.F.00125 PMID: 17015609
6. Cheung EV, Diaz R, Athwal GS, Sanchez-Sotelo J, Sperling JW. Shoulder Arthroplasty: Key Steps to Improve Outcomes and Minimize Complications. Instr Course Lect. 2015; 65:109–126.
7. Cvjetanovich GL, Frank RM, Chalmers PN, Verma NN, Nicholson GP, Romeo AA. Surgical Management of Proximal Humeral Fractures: The Emerging Role of Reverse Total Shoulder Arthroplasty. Orthopedics. 2016; 39:e465–e473. https://doi.org/10.3928/01477447-20160324-02 PMID: 27045483
8. Singh JA, Sperling J, Buchbinder R, Mcmaken K. Surgery for shoulder osteoarthritis. Cochrane Database Syst Rev. 2010;(10). https://doi.org/10.1002/14651858.CD008089.pub2 PMID: 20927773
9. Horner NS, de Sa D, Heaven S, Simunovic N, Bedi A, Athwal GS, et al. Indications and outcomes of arthroscopy after shoulder arthroplasty. J Shoulder Elbow Surg. 2016; 25:510–518. https://doi.org/10.1016/j.jse.2015.09.013 PMID: 26652703
10. Clarke M, Williamson PR. Core outcome sets and systematic reviews. Syst Rev. 2016; 5. https://doi.org/10.1186/s13643-016-0188-6 PMID: 26792080
11. Harman NL, Bruce IA, Kirkham JJ, Tierney S, Callery P, O’Brien K, et al. The Importance of Integration of Stakeholder Views in Core Outcome Set Development: Otitis Media with Effusion in Children with Cleft Palate. PloS one. 2015; 10. https://doi.org/10.1371/journal.pone.0129514 PMID: 26115172
12. Tunis SR, Clarke M, Gorst SL, Gargon E, Blazeby JM, Altman DG, et al. Improving the relevance and consistency of outcomes in comparative effectiveness research. J Comp Eff Res. 2016; 5:193–205. https://doi.org/10.2217/cer-2015-0007 PMID: 26930385
13. Boers M, Kirwan JR, Tugwell P, Beaton D, Bingham III CO, Conaghan PG, et al. The OMERACT Handbook. OMERACT. 2014. Available at http://www.omeract.org/pdf/OMERACT_Handbook.pdf. Accessed June 21, 2016.
14. Angst F, Schwzyer HK, Aeschlimann A, Simmen BR, Goldhahn J. Measures of adult shoulder function: Disabilities of the Arm, Shoulder, and Hand Questionnaire (DASH) and its short version (QuickDASH), Shoulder Pain and Disability Index (SPADI), American Shoulder and Elbow Surgeons (ASES) Society standardized shoulder assessment form, Constant (Murley) Score (CS), Simple Shoulder Test (SST), Oxford Shoulder Score (OSS), Shoulder Disability Questionnaire (SDQ), and Western Ontario Shoulder Instability Index (WOSI). Arthritis Care & Res. 2011; 63 Suppl 11:S174–S188. https://doi.org/10.1002/acr.20630 PMID: 22588743
15. Wright RW, Baumgarten KM. Shoulder outcomes measures. J Am Acad Orthop Surg. 2010; 18:436–444. https://doi.org/10.5435/00124635-201007000-00006 PMID: 20595136
16. Roe Y, Soberg HL, Bautz-Holter E, Ostensjo S. A systematic review of measures of shoulder pain and functioning using the international classification of functioning, disability and health (ICF). BMC Musculoskelet Disord. 2013; 14. https://doi.org/10.1186/1471-2474-14-73 PMID: 23445557
17. 45 CFR 46 | HHS.gov. Available at http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/. Published June 21, 2016. Accessed June 21, 2016.
18. Li T, Vedula SS, Hadar N, Parkin C, Lau J, Dickersin K. Innovations in data collection, management, and archiving for systematic reviews. *Ann Intern Med.* 0; 162:287–294. https://doi.org/10.1016/j.aml.2015.06.006 PMID: 26092288

19. Cochrane Handbook for Systematic Reviews of Interventions. Available at http://handbook.cochrane.org/. Published November 19, 2014. Accessed June 21, 2016.

20. Standards for Systematic Reviews: Health and Medicine Division. Available at http://www.nationalacademies.org/hmd/Reports/2011/Finding-What-Works-in-Health-Care-Standards-for-Systematic-Reviews/Standards.aspx. Accessed June 21, 2016.

21. PRISMA 2009 Checklist. Available at http://www.prisma-statement.org/documents/PRISMA2009checklist.pdf. Accessed June 22, 2016.

22. Lang TA, Altman DG. Basic statistical reporting for articles published in biomedical journals: The “Statistical Analyses and Methods in the Published Literature” or The SAMPL Guidelines. In: Smart P, Maison-Neuve H, Polderman A (eds). *Science Editors’ Handbook*, European Association of Science Editors, 2013. Available at http://www.equator-network.org/wp-content/uploads/2013/07/SAMPL-Guidelines-6-27-13.pdf. Accessed June 21, 2016.

23. Williams RJ, Tse T, Harlan WR, Zarlin DA. Registration of observational studies: is it time? *CMAJ*. 2010; 182:1638–1642. https://doi.org/10.1503/cmaj.092252 PMID: 20643833

24. Glossary, CRG, NHLBI, NIH. Available at http://www.nhlbi.nih.gov/research/funding/research-support/crg/application/observational-interventional.htm. Published June 29, 2016. Accessed June 29, 2016.

25. Benstoem C, Moza A, Autschbach R, Stoppe C, Goetzennich A. Evaluating outcomes used in cardiothoracic surgery interventional research: a systematic review of reviews to develop a core outcome set. *PloS one*. 2015; 10. https://doi.org/10.1371/journal.pone.0122204 PMID: 25830921

26. Hopkins JC, Howes N, Chalmers K, Savovic J, Whale K, Coulman KD, et al. Outcome reporting in bariatric surgery: an in-depth analysis to inform the development of a core outcome set, the BARIACT Study. *Obes Rev*. 2015; 16:88–106. https://doi.org/10.1111/obr.12240 PMID: 25442513

27. McNair AGK, Whistance RN, Forsythe RO, Rees J, Jones JE, Pullyblank AM, et al. Synthesis and summary of patient-reported outcome measures to inform the development of a core outcome set in colorectal cancer surgery. *Colon Rectal Dis*. 2015; 17:O217–O229. https://doi.org/10.1111/rect.13021 PMID: 26058878

28. Page MJ, McKenzie JE, Green SE, Beaton DE, Jain NB, Lenza M, et al. Core domain and outcome measurement sets for shoulder pain trials are needed: systematic review of physical therapy trials. *J Clin Epidemiol.* 2015; 68:1270–1281. https://doi.org/10.1016/j.jclinepi.2015.06.006 PMID: 26092288

29. Saldanha IJ, Dickersin K, Wang X, Li T. Innovations in data collection, management, and archiving for systematic reviews. *PloS one*. 2014; 9. https://doi.org/10.1371/journal.pone.0109400 PMID: 25329377

30. Whitehead L, Perkins GD, Clarey A, Haywood KL. A systematic review of the outcomes reported in cardiac arrest clinical trials: the need for a core outcome set. *Resuscitation*. 2015; 88:150–157. https://doi.org/10.1016/j.resuscitation.2014.11.013 PMID: 25497393

31. Buchbinder R, Page MJ, Huang H, Verhagen AP, Beaton D, Kopkow C, et al. A Preliminary Core Domain Set for Clinical Trials of Shoulder Disorders: A Report from the OMERACT 2016 Shoulder Core Outcome Set Special Interest Group. *J Rheumatol*. 2017; https://doi.org/10.3899/jrheum.161123 PMID: 28089972

32. Page MJ, Huang H, Verhagen AP, Gagnier JJ, Buchbinder R. Outcome reporting in randomized trials for shoulder disorders: Literature review to inform the development of a core outcome set. *Arthritis Care Res*. 2017; https://doi.org/10.1002/acr.23254 PMID: 28388821

33. Rongen JJ, Hannink G. Comparison of Registered and Published Primary Outcomes in Randomized Controlled Trials of Orthopaedic Surgical Interventions. *J Bone Joint Surg Am*. 2016; 98:403–409. https://doi.org/10.2106/JBJS.15.00400 PMID: 26935463

34. Head ML, Holman L, Lanfear R, Kahn AT, Jennions MD. The extent and consequences of p-hacking in science. *PLoS Biol*. 2010; 13. https://doi.org/10.1371/journal.pbio.1002106 PMID: 25768323

35. Roy JS, MacDermid JC, Woodhouse LJ. A systematic review of the psychometric properties of the Constant-Murley score. *J Shoulder Elbow Surg*. 2010; 19:157–164. https://doi.org/10.1016/j.jse.2009.04.008 PMID: 19559690

36. Roy JS, MacDermid JC, Woodhouse LJ. Measuring shoulder function: a systematic review of four questionnaires. *Arthritis Rheumat*. 2009; 61:623–632. https://doi.org/10.1002/art.24326 PMID: 19405008

37. Chau DB, Ciullo SS, Watson-Smith D, Chun TH, Kurkchubasche AG, Luks FI. Patient-centered outcomes research in appendicitis in children: Bridging the knowledge gap. *J Pediatr Surg*. 2016; 51:117–121. https://doi.org/10.1016/j.jpedsurg.2015.10.029 PMID: 26545589
38. Kanzaria HK, McCabe AM, Meisel ZM, LeBlanc A, Schaffer JT, Bellolio MF, et al. Advancing Patient-centered Outcomes in Emergency Diagnostic Imaging: A Research Agenda. *Acad Emerg Med*. 2015;22:1435–1446. https://doi.org/10.1111/acem.12832 PMID: 26574729

39. Mancuso CA, Duculan R, Cammissa FP, Sama AA, Hughes AP, Lebl DR, et al. Proportion of Expectations Fulfilled: A New Method to Report Patient-centered Outcomes of Spine Surgery. *Spine*. 2016;41:963–970. https://doi.org/10.1097/BRS.0000000000001378 PMID: 26679871

40. Rising KL, Carr BG, Hess EP, Meisel ZF, Ranney ML, Vogel JA. Patient-centered Outcomes Research in Emergency Care: Opportunities, Challenges, and Future Directions. *Acad Emerg Med*. 2016;23:497–502. https://doi.org/10.1111/ace.m.12944 PMID: 26919027

41. Zygmont ME, Lam DL, Nowitzki KM, Burton KR, Lenchik L, McArthur TA, et al. Opportunities for Patient-centered Outcomes Research in Radiology. *Acad Radiol*. 2016;23:8–17. https://doi.org/10.1016/j.acra.2015.08.027 PMID: 26683507

42. Beaton DE, Bombardier C, Katz JN, Wright JG, Wells G, Boers M, et al. Looking for important change/differences in studies of responsiveness. OMERACT MCID Working Group. Outcome Measures in Rheumatology. Minimal Clinically Important Difference. *J Rheumatol*. 2001;28:400–405. PMID: 11246687

43. Xu M, Garbuz DS, Kuramoto L, Sobolev B. Classifying health-related quality of life outcomes of total hip arthroplasty. *BMC Musculoskelet Disord*. 2005;6. https://doi.org/10.1186/1471-2474-6-48 PMID: 16144550

44. Mollon B, Mahure SA, Ding DY, Zuckerman JD, Kwon YW. The influence of a history of clinical depression on peri-operative outcomes in elective total shoulder arthroplasty: a ten-year national analysis. *Bone Joint J*. 2016;98-B:816–824. https://doi.org/10.1302/0301-620X.98B6.37208 PMID: 27235526

45. Clarke M, Williamson P: Core outcome sets and trial registries. *Trials*. 2015;16:216. https://doi.org/10.1186/s13063-015-0738-6 PMID: 25971905

46. Trends, Charts, and Maps. ClinicalTrials.gov. Available at https://clinicaltrials.gov/ct2/resources/trends. Accessed on October 11, 2017.

47. Moja LP, Moschetti I, Nurthai M, et al. Compliance of clinical trial registries with the World Health Organization minimum data set: a survey. *Trials* [Electronic Resource] 2009;10:56.

48. Nissen T, Wayant C, Wahltstrom A, Sinnett P, Fugate C, Herrington J, Vassar M. Methodological quality, completeness of reporting and use of systematic reviews as evidence in clinical practice guidelines for paediatric overweight and obesity. *Clin Obes* 2017;2017;7(1):34–45. https://doi.org/10.1111/cob.12174 PMID: 28112500

49. Howard B, Scott JT, Blubaugh M, Roepke B, Scheckel C, Vassar M. Systematic review: Outcome reporting bias is a problem in high impact factor neurology journals. *PLoS One* 2017;12(7):e0180986. https://doi.org/10.1371/journal.pone.0180986 PMID: 28727834

50. Wayant C, Scheckel C, Hicks C, Nissen T, Leduc L, Som M, Vassar M. Evidence of selective reporting bias in hematology journals: A systematic review. *PLoS One* 2017;12(6):e0178379. https://doi.org/10.1371/journal.pone.0178379 PMID: 28570573

51. Fleming PS, Koletsi D, Dwan K, Pandis N. Outcome discrepancies and selective reporting: impacting the leading journals? *PLoS ONE*. 2015;10(6):e0127495. https://doi.org/10.1371/journal.pone.0127495 PMID: 25996928; PubMed Central PMCID: PMC4440809.