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Towards Consensus on the Reporting of Core Outcome Domains in Total Joint Replacement Clinical Trials: The Derivation of the Preliminary Core Outcome Domain Set

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Abstract

Background: There is no consensus on how to report total joint replacement (TJR) trials. To our knowledge, core outcome domains for TJR clinical trials have not been defined. Our objective was to develop data-driven, consensus-based, preliminary recommendations for core outcome domains for TJR clinical trials.

Method: We surveyed two groups of experts/stakeholders, who rated potential core outcome domains (mapped to Outcome Measures in Rheumatology Trials (OMERACT) filter 2.0 framework) for their relevance to TJR clinical trials during the 2014 American Academy of Orthopaedic Surgeons [AAOS] and Outcome Research Interest Group of the Orthopaedic Research Society (ORS) annual meeting and the 2014 OMERACT meeting. Ratings were on a 1-9 scale, 1-3 indicating domain of limited importance, 4-6 being important domain, and 7-9 being critically important domain.

Results: Seventeen participants at the AAOS/ORS Outcomes Research Interest Group and 19 at OMERACT meeting completed the survey. At the two meetings, 73% and 36% were arthroplasty researcher/surgeons, 0% and 10% were patients and 58% and 31% were above 54 years, respectively. The following domains were rated as core outcome domains by both groups, with a median score of 7 and above (median score from AAOS/ORS *vs.* OMERACT): Joint pain (9 vs. 9), functional ability (8 vs. 9), joint-specific quality of life (8 vs. 7), patient satisfaction (7 vs. 8), revision surgery (8 vs. 7), adverse events (9 vs. 8), death (9 vs. 7.5), serious adverse events (8.5 vs. 8), reoperation (8 vs. 8), and cost (7 vs. 7).

Conclusion: Stakeholders achieved consensus on preliminary core outcome domain set for TJR clinical trials. This set will be further vetted with multi-stakeholder input to achieve a fully endorsed TJR core outcome domain set.

Keywords: Total joint replacement; Arthroplasty; Outcome measures; Domains; Harmonization; Consensus

Abbreviations: TJR: Total Joint Replacement; AAOS: Academy of Orthopaedic Surgeons; ORS: Orthopaedic Research Society; OMERACT: Outcomes in Rheumatology Clinical Trials; AEs: Adverse Events

Introduction

In 2010 (the most recent year with data available nationally), 719,000 total knee replacements (TKRs) and 332,000 total hip replacements (THRs) were performed in the United States [1,2]. Total Joint Replacement (TJR) utilization is increasing worldwide [3-9]. Heterogeneity in outcomes [10] and use of outcomes that are not validated [11] in TJR trials are a significant barrier to the translation of advances in TJR to clinical practice.

Despite these challenges, leaders in the field recognize the importance of having a core set of standardized outcome measures for TJR clinical trials. Outcome Measures in Rheumatology Trials (OMERACT) has developed a framework based on the World health Organization's (WHO) WHO's International Classification of Functioning, Disability, and Health (ICF) conceptual model. It proposes four core areas to assess the impact of disease, namely Death, Life Impact, and Pathophysiological Manifestations and one recommended, but optional area, Resource Use/Economic Impact and within each area to select one or more domains applicable to every condition of interest [12]. The need for core outcome domain sets is recognized well by the leaders in clinical trial conduct, and has been the focus of many organizations, such as the OMERACT [13] and the COMET initiative [14]. The objective of this study was to perform a survey of important stakeholders to develop preliminary recommendations for core outcome domains to be reported in TJR clinical trials.

Methods

We performed surveys in two groups of experts/participants. Each group was provided with background information regarding the current gaps in the published arthroplasty clinical trials literature related to inconsistent reporting of the outcome measures and the challenges in harmonization of outcome measures. The 20-minute PowerPoint presentation included review of results of a systematic review of joint replacement clinical trials that showed that >20 different outcome measures were used in the hip trials, and >14 in knee trials. There was an extensive variation across trials in the general construct being measured [11]. We examined each of these outcomes from the systematic review and identified all relevant outcome domains for consideration for TJR clinical trial outcomes. These surveys of participant opinions from expert surgeons/clinicians were annonymized.

	AAOS/ORS Outcomes Research Interest group meeting	**OMERACT meeting**
	N (%)[2]	N (%)[2]
# survey participants	N=17	N=19
% female[1]	7 (58%)	14 (73%)
Age category[1] (in years)		
18-24	0	0
25-34	1 (8%)	2 (10%)
35-44	3 (25%)	6 (31%)
45-54	1 (8%)	5 (26%)
55-64	5 (42%)	6 (31%)
65-74	3 (16%)	0
≥ 75	0	0
Missing	5	0
Background[1]		
Arthroplasty surgeon or researcher	11 (73%)	7 (36%)
Orthopaedic surgeon, not focused on arthroplasty	2 (13%)	0%
Patient	0	2 (10%)
Other	2 (13%)	10 (54%)[3]
Missing	2	0
Policy maker	0	0
Time spent planning/conducting arthroplasty trials[1]		
0-10%	5 (55%)	8 (80%)
11-20%	2 (22%)	1 (10%)
21-30%	1 (11%)	0
31-50%	1 (11%)	1 (10%)
>50%	0	0
Not applicable	6	9

[1]Missing values for AAOS/ORS and OMERACT cohorts: sex: 5 vs. none; age, 5 vs. none; background, 2 vs. none;

[1]Time spent planning/conducting arthroplasty trials was only applicable for a subgroup of respondents who were involved with arthroplasty clinical trials, 11 from AAOS survey and 10 from the OMERACT survey.

[2]N (%) – percent of those that responded to each question

[3]Other category included 4 clinicians, 2 occupational/physical therapists and 4 methodologists

Table 1: Participant characteristics.

Participants at each meeting (the Outcome Special Interest Group at the 2014 American Academy of Orthopaedic Surgeons [AAOS] Annual Meeting and the Outcome Research Interest Group of the Orthopaedic Research Society (ORS) 2014 Annual Meeting), and the 2014 Outcomes in Rheumatology Clinical trials [OMERACT]) were provided with a short questionnaire, that asked participants to rank outcome domains as potential core set outcome domains for arthroplasty on a 1 to 9 scale, indicating 1-3 as domain of limited importance, 4-6 being important, but not critical, and 7-9 being critical. Participants were asked to specify their background, gender, age category, and if they were orthopaedic surgeons, the years in practice and percent time spent planning or conducting arthroplasty clinical trials.

The AAOS Outcome Special Interest group had the power-point presentation followed by a Q/A session, followed by completion of the survey. The OMERACT group was given the same power-point presentation highlighting the gaps in TJR trial reporting and completed the same survey. Results of both the AAOS and OMERACT participants was presented to the OMERACT group, followed by 1 hour discussion of the results of these surveys and further feedback. Due to achievement of consensus among the OMERACT survey participants for survey responses regarding core domain set for TJR clinical trials during this face-to-face discussion, further cycles of Delphi survey were not needed. Proportions were calculated for characteristics of survey respondents. We calculated median scores and interquartile range for the ratings of each domain.

Results

A total of 17 participants at the 2014 AAOS/ORS Outcome Special Interest Group meeting and 19 participants at OMERACT completed the questionnaire. Of these, 58% and 73% were female, 73% and 36% were arthroplasty researcher/surgeons, 0% and 10% were patients and 58% and 31% were over 54 years of age, respectively (Table 1).

There was remarkable consistency in rating of the core outcome domains to be included in every TJR clinical trial by these two diverse groups of stakeholders. Joint pain, functional ability, joint-specific quality of life, patient satisfaction, revision surgery, adverse events (total and specific), and death were rated as critical core outcome domains by both groups, with a median score of 7 and above, by both groups (Table 2). Generic quality of life was rated important, but not critical by the AAOS/ORS Outcome Special Interest group, and rated critical by the OMERACT group. Both the AAOS/ORS Outcome Special Interest Group and the OMERACT group rated patient expectation as important, but not critical. Additional domains to be considered for reporting in TJR clinical trials that received a median

score of 7 or above by both groups were serious adverse events, reoperation and cost (Table 2). The groups rated rest of the domains with median scores ranging 5 to 7 (Table 2).

	AAOS/ORS Outcomes Research Interest group Median (IQR)	OMERACT Median (IQR)	Both combined Median (IQR)
Main (Core) Domains to be reported in every TJR clinical trial			
Joint Pain	9 (8,9)	9 (9,9)	9 (8,9)
Function or functional ability (ability to function in society, work; work productivity, employability; disability; work disability)	8 (8,9)	9 (8,9)	9 (7,9)
Generic Quality of life (including fatigue, sleep, mood, stress, anxiety, depression)	6 (4,9)	7 (5.75,8.25)	7 (5,8)
Joint-specific Quality of life	8 (7,9)	7 (5,7.25)	7 (6,8)
Patient Satisfaction (satisfaction with the outcome, satisfaction with the procedure)	7 (5,8)	8 (7,9)	7.5 (5.75,9)
Patient expectation of surgical outcome	5 (4,8)	5 (4,7)	5 (4,7)
Revision surgery	8 (6,9)	7 (7,9)	8 (6,9)
Adverse events*	9 (8,9)	8 (7,9)	8 (7,9)
Death	9 (8,9)	7.5 (5,9)	8 (6,9)
Additional domains for consideration			
Serious Adverse events (e.g. skin and deep infections)	8.5 (7,9)	8 (8,9)	8 (7,9)
Cardiac Adverse events (e.g. Myocardial infarction, unstable angina, worsening of congestive heart failure)	7.5 (5.75,8)	6 (5.5,7.5)	6 (6,8)
Pulmonary Adverse events	7 (5.75,8)	6 (5.5,7)	7 (6,8)
(e.g. Pneumonia, Pulmonary Embolism)			
Reoperation (for any reason, not only for the removal of the implant components)	8 5.5,9)	8 (7,8)	8 (6.25,8)
Cost	7 (4,8)	7 (6,7)	7 (6,8)
Health care utilization (e.g. length of hospital stay, Emergency room visits)	5 (3,7.25)	7 (6,7)	6 (5,7)
Readmission (e.g. 90-day readmission)	6.5 (5,8.75)	7 (6,7)	7 (6,9)
*The OMERACT group specified that adverse events should include both the total number of adverse events as well reporting of specific adverse events of importance, such as local wound complications etc. and cardiac/pulmonary adverse events.			

Table 2: Preliminary core outcome domains for TJR clinical trials.

In the comments section, one participant suggested that serious adverse events (SAEs), cardiac adverse events (AEs), pulmonary AEs, reoperation and cost all fit in the core outcome domains. Another participant proposed return to work, work comp and temporary/permanent disability as core outcome domains.

Discussion

This study included multi-stakeholders and provides a preliminary consensus regarding which core areas/domains should be included in the reporting of TJR clinical trials. We surveyed two groups, one with a predominance of arthroplasty surgeons and researchers and the other with a predominance of clinical researchers, methodologists and patients (but also including orthopaedic surgeons). The study provides a platform to start building consensus and set international standards in TJR clinical trial reporting by having a multi-stakeholder involvement and collaborative consensus building. A few observations deserve further discussion.

The two groups selected the same core outcome domains to be critical for reporting in every TJR clinical trial, independent of each other. Both groups selected seven domains as critical, namely, joint pain, functional ability, joint-specific quality of life, patient satisfaction, revision surgery, adverse events, and death. The OMERACT group selected generic QOL as critical and the AAOS/ORS Outcome Special Interest Group rated it as important, but not critical. This preliminary consensus within two groups and between two independent groups provides support to using this preliminary core set of domains as potential starting point for a wider consensus building for TJR clinical trial reporting. The groups also proposed additional domains for consideration including, serious adverse events, reoperation and cost,

in addition to the core domains. It is extremely reassuring that the core outcome domains proposed by the group are entirely consistent with the OMERACT filter 2.0. That recommends inclusion of at least one domain in three core areas in developing outcomes in any condition, namely pathophysiological manifestations (pain, functional limitation, revision surgery), life impact (joint pain, functional ability, joint-specific quality of life, patient satisfaction) and death, as well as adverse events. Since trialists are obligated to report adverse events and death during clinical trial, their inclusion in preliminary core domain set does not add extra burden for reporting.

Considering the additional area of cost proposed by the two groups, the optional core area of resource utilization is also included. In the past, focus had been on local complications, implant survivorship and cumulative revision rate in TJR trials. This perspective has evolved to include patient reported measures and quality of life measurement, in addition to these important complications.

One of the reasons that pulmonary and cardiac AEs were not rated very high by the OMERACT group was that they commented that they consider these to be included in the core area of AEs (total and specific), already rated as critical by them. This indicated that both groups rated AEs to be a critical domain, i.e., to be reported in every TJR clinical trial.

Our current work lays the foundation for the next steps in this consensus process to define core outcomes for TJR clinical trials. To our knowledge, there are no published studies by any other group regarding development of a core domain for TJR clinical trials; therefore, we are unable to compare our findings to any other study. Harmonization of core outcomes is needed in these trials as well as in risk adjustment models and alternative payment projects such as the Comprehensive Care for Joint Replacement (CJR) model, which is being implemented by Medicare to provide a bundled payment for TJR rather than each episode of care for complications etc. [15]. Since our preliminary core outcome domains fit the OMERACT filter 2.0, we will follow this framework to further develop a harmonized set of TJR trial outcomes. The next steps in the process, which will take at least 2-4 years to complete, are summarized as follows: (1) endorsement and refining of the preliminary core outcome domains by a broader, multi-stakeholder group, using Delphi method; (2) Once the core set of domains are finalized, we will review existing candidate outcome measures and assess whether they meet the principles of truth, discrimination and feasibility; (3) If the existing measure/s are valid, we plan to perform a Delphi with multi-stakeholders for consensus; and (4) then this will be proposed as TJR core measurement set. If there were an absence of validated measures for core outcome domains, then measures would need to be validated or developed for domains that are missing validated measures; this could take >5 years since various measurement properties of a new measure would need to be tested and its validity established.

Our study has several limitations. We have performed surveys with two groups that provide a wide representation of stakeholders. It is possible that in our next step to obtain a broader endorsement, the preliminary findings from this study might change. However, endorsement of the same core outcome domains by two independent groups might indicate that this might be more generalizable; however this remains to be seen. We chose OMERACT framework for our initiative, since it's based on WHO's ICF framework; other frameworks exist, and may work just as well. The preliminary core domain set developed as a result of this process is only applicable to TJR clinical trials. Observational studies or registries are not a current focus of this initiative.

In conclusion, in this study, experts and stakeholders identified a preliminary set of core outcome domains for TJR clinical trials. This core set of domains for TJR clinical trials needs further endorsement by a broader group of stakeholders, particularly, patients and surgeons. Our next steps are to identify key stakeholder groups through discussions from other (collaborating) organizations. By using a consensus-based data-driven process, we aim to develop the TJR clinical trial core outcome domain set. After completing this step, our objective is to identify validated outcome measures for each included domain, which will lead to the development of a core outcome measurement set for TJR clinical trials, in the near future.

Declarations

Ethical approval and Consent to participate: These surveys of participant opinions were annonymized, no protected health information (PHI) was collected and participants were attendees of scientific meetings. Therefore, no approval was needed from the Institutional Review Board.

Consent for Publication

All authors have reviewed this manuscript and provide consent for publication. "All authors have disclosed potential conflicts of interest, have read the journal's policy on conflicts of interest and have read the journal's authorship agreement."

Availability of Supporting Data

Not applicable

Competing Interests

JAS has received research grants from Takeda and Savient and consultant fees from Savient, Takeda, Regeneron, Merz, Bioiberica, Crealta 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. SY has no conflicts to declare. Neither author has any non-financial conflict. MD has no relevant interests to declare.

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Author Contributions

JAS: Study conception and design, development of study protocol, conduct of statistical analyses, writing the first draft of the manuscript,

critical revisions, approval of the final manuscript version and submission of the manuscript. MD: Review of the protocol and analyses and provision of feedback, critical revisions and approval of the final manuscript version.

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