AAOS
American Academy of Orthopaedic Surgeons

AAOS / Committee on Devices, Biologics, and Technology

Technology Overview Methodology

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Overview

The AAOS understands the importance of a consistent evidence-based approach to providing high quality Technology Overviews (TO), and the Academy goes to great lengths to ensure the integrity of evidence analyses. The AAOS addresses bias beginning with the selection of work group members. Applicants with financial conflicts of interest (COI) related to the TO topic cannot participate if the conflict occurred within one year of the start date of TO development or if an immediate family member has, or has had, a relevant financial conflict. Additionally, all TO work group members sign an attestation form agreeing to remain free of relevant financial conflicts for one year following publication.

Technology Overviews are prepared by physician development groups (clinical experts) with assistance from the AAOS Clinical Quality and Value (CQV) Department (methodologists) at the AAOS. As the physician experts, the TO work group defines the scope of the work by creating PICO Questions (i.e. population, intervention, comparison, and outcome) that direct the literature search. When necessary, these clinical experts also provide content help, search terms and additional clarification for the AAOS medical librarian. The medical librarian creates and executes the search(es). The supporting group of methodologists (AAOS CQV Department) review all abstracts, recall pertinent full-text articles for review and evaluate the quality of studies meeting the inclusion criteria. They also abstract, analyze, interpret, and summarize the relevant data for each PICO question and prepare the initial draft for the final work group meeting. Upon completion of the systematic reviews, physician development groups participate in a report finalization meeting. To complete their charges, the physician experts and methodologists evaluate and integrate all material to develop the final report. The final report is written first by the methodologist, edited and expanded upon by the project's chairs, and then presented, edited as necessary, and voted on by the development group. The draft report receives final review by the methodologists to ensure that it is substantively consistent with the published data. The draft is then completed and submitted for a review period and submitted to a musculoskeletal journal for publication.

After the review period, the TO draft may be edited in response to the review submissions. Thereafter, the draft TO is sequentially approved by the AAOS Committee on Devices, Biologics, and Technology, AAOS Council on Research and Quality, and the AAOS Board of Directors. All AAOS TO are reviewed and updated or retired every five years.

The methodology for developing and publishing technology overviews very closely mirrors the AAOS clinical practice guideline (CPG) methodology. The largest difference methodologically between the two is the final output. CPGs result in recommendations which should be clinically actionable. Technology Overviews summarize the published evidence as it relates to pre-defined standardized fields.

Workgroup Composition

Technology Overview development workgroups are chaired by members of the Committee on Devices, Biologics, and Technology who do not have relevant financial conflicts of interest to the topic addressed. The remainder of the development workgroup is to be filled out by volunteers and nominees from relevant specialty societies who also do not have relevant financial conflicts of interest.

Selecting Scope

- Nominate topic (biologic treatment modality and affected population) – Open to all via electronic survey.
- Select a topic – The AAOS Committee on Devices, Biologics, and Technology (DBT) prioritizes the nominated topics and selects which topics should move forward as Technology Overviews. Topics which address areas for biologic treatment modalities where regulatory guidance may be interpreted as unclear will be given priority in the topic selection process.

The project chairs work group begins their work on CPGs by constructing a set of PICO questions. These questions specify the patient population of interest (P), the intervention of interest (I), the comparisons of interest (C), and the patient-oriented outcomes of interest (O). They function as questions for the systematic review, not as conclusions. Once established, these *a priori* PICO questions cannot be modified.

Systematic Literature Review

Following the selection of topic, scope, PICO question(s), and creation of development groups, the AAOS medical librarian designs and executes a literature search of peer-reviewed journals.

Articles considered for inclusion are published prior to the start date of the search in a minimum of three electronic databases; PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials. The medical librarian conducts the search using key terms determined from the a priori workgroup topic selections.

Dedicated clinical review analysts review and include only primary literature. The primary literature search is supplemented with a manual search of the bibliographies of secondary literature sources such as systematic reviews. Recalled articles are evaluated for possible inclusion based on the study selection criteria and are summarized for the workgroup who assist with reconciling possible errors and omissions.

A study PRISMA Flow diagram is provided in the appendix of each document that details the numbers of identified abstracts, recalled and selected studies, and excluded studies that were evaluated in the technology overview. The search strategies used to identify the abstracts are also included in the appendix of the final overview.

Standard Exclusion Criteria

- Article must be a full article report of a clinical study (studies using registry data can be included if it is published in a peer-reviewed journal and meets all other inclusion criteria/quality standards).
- Non-comparative case series, descriptive statistics, meeting abstracts, meta-analyses, systematic reviews, historical articles, editorials, letters, and commentaries are ***excluded***. However, the bibliographies of systematic reviews/meta-analyses will be manually searched for any relevant articles that may have been missed by the initial search criteria if the title and/or abstract addresses a target population, condition, and comparison.
- Confounded studies (i.e. studies that give patients the treatment of interest AND another treatment without appropriate sub-analysis or statistical adjustment) are ***excluded***.
- Controlled trials in which patients were not stochastically assigned to groups AND in which there was either a difference in patient characteristics or outcomes at baseline AND where the authors did not statistically adjust for these differences when analyzing the results are ***excluded***.
- All studies of "Very Low" quality of evidence (e.g. Level V) are ***excluded***.
- Study must appear in a peer-reviewed publication
- For any included study that uses "paper-and-pencil" outcome measures (e.g. Composite measures, SF-36, etc.), only those outcome measures that have been validated will be included
- For any given follow-up time point in any included study, there must be ≥ 50% patient follow-up (if the follow-up is >50% but <80%, the study quality will be downgraded by one Level)
- Study must be of humans
- Study must be published in English
- Study results must be quantitatively presented
- Study must not be an in vitro study
- Study must not be a biomechanical study
- Study must not have been performed on cadavers

Customized Inclusion Criteria

- Study must be specific to population identified in PICO question
- Study must be published in or after the year **2000**
- Study should have **10 or more patients** per group
- Consider all follow-up times

Best Evidence Synthesis

Technology Overviews include only the best available evidence for any given patient-oriented outcome addressing the population and treatment comparison of interest (as defined by the PICO question). Accordingly, we first include the highest quality evidence for any given outcome if it was available. In the absence of two or more occurrences of an outcome at this quality, we consider outcomes of the next lowest quality until at least two or more occurrences of an outcome has been acquired. For example, if there were two 'moderate' quality occurrences of an outcome that addressed a target comparison, we do not include 'low' quality occurrences of this outcome. A summary of the evidence that met the inclusion criteria but was not best available evidence is created for each project and can be viewed within each document's appendix.

Study Quality Evaluation

The quality forms used to assess the quality of literature considered for inclusion in the SR are based on a variety of validated appraisal forms dependent on the study design. The AAOS quality appraisal form for randomized, observational, prognostic, and diagnostic studies are based on the GRADE, ROBINS-I, QUIPS, and QUADAS-2 forms respectively. The details of these appraisal forms are described below.

Randomized Study Appraisal Form

Resources used to develop the Randomized Quality Appraisal System:

- 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 www.handbook.cochrane.org. The following domains are evaluated to determine the study quality of randomized study designs.
- Guyatt, G. H., Oxman, A. D., Sultan, S., et al. (2011). GRADE guidelines: 9. Rating up the quality of evidence. Journal of Clinical Epidemiology, 64(12), 1311–1316.

Randomized Study Quality Appraisal Domains

- Random Sequence Generation
- Allocation Concealment
- Blinding of Participants and Personnel
- Incomplete Outcome Data
- Selective Reporting
- Other Bias

Randomized Study Design Quality Key

High Quality Study	<2 Flaw
Moderate Quality Study	≥2 and <4 Flaws
Low Quality Study	≥4 and <6 Flaws
Very Low Quality Study	≥6 Flaws

Observational Study Appraisal Form

Resources used to develop the Observational Intervention Study Quality Appraisal System:

- Sterne JAC, Higgins JPT, Elbers RG, Reeves BC and the Development group for ROBINS-I. Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I): detailed guidance, updated 12 October 2016. Available from http://www.riskofbias.info [accessed july 2018

- Guyatt GH, Oxman AD, Vist G, et al. GRADE guidelines: 4. Rating the quality of evidence–study limitations (risk of bias). J Clin Epidemiol 2011;64:407–15.

- Guyatt, G. H., Oxman, A. D., Sultan, S, et al. (2011). GRADE guidelines: 9. Rating up the quality of evidence. Journal of Clinical Epidemiology, 64(12), 1311–1316.

Observational Study Design Quality Appraisal Domains

The following questions are used to evaluate the study quality of observational study designs. Note that all non-randomized intervention studies begin the appraisal process at "low quality" due to design flaws inherent in observational studies. They can only be upgraded to moderate quality in rare cases if they meet one of the criteria for upgrading listed below.

- Does the strategy for recruiting participants into the study differ across groups?
    - Enrolled new users of a treatment rather than current users of a treatment
    - Patients were not excluded for outcomes that occurred after the start of the study.

- Is treatment status measured/recorded accurately?
    - measured at the same time treatment started and did not rely on patient recall.

- Did the authors fail to take important confounding variables into account in the design and/or analysis (e.g., through matching, stratification, interaction terms, multivariate analysis, or other statistical adjustment such as instrumental variables)?

- Is there a high risk that outcomes were measured inaccurately?
    - Measured the same way in all patients
    - Blinded outcome evaluation or outcome was objective and couldn't be influenced by lack of blinding

- Are there low rates of missing outcome, treatment status, and confounder variable data OR were the rates and/or reasons for missing data similar between groups?

- Were results for all outcomes, statistical analyses and patient populations specified in the methods section, also reported in the results section?
    - No selective reporting of outcomes
    - Results from all statistical models described in methods section are reported
    - Study was not a subgroup analysis of a previously published study
    - No conflict of interest

Observational Study Design Quality Key

Low Quality Study	< 3 flaws
Very Low Quality Study	≥3 flaws

Statistical Methods

Analysis of Intervention/Prevention Data

When possible, AAOS staff recalculate the results reported in individual studies and compiles them to answer the research question. The results of all statistical analysis by the AAOS CQV are conducted using STATA 12.1 and SAS 7.1. STATA is used to determine the magnitude, direction, and/or 95% confidence intervals of the treatment effect. For data reported as means (and associated measures of dispersion) the mean difference between groups and the 95% confidence interval is calculated and a two-tailed t-test of independent groups is used to determine statistical significance. When published studies report measures of dispersion other than the standard deviation the value is estimated to facilitate calculation of the treatment effect. In studies that report standard errors or confidence intervals, the standard deviation is back-calculated. In some circumstances statistical testing is conducted by the authors and measures of dispersion is not reported. In the absence of measures of dispersion, the results of the statistical analyses conducted by the authors (i.e. the p-value) are considered as evidence. For proportions, we report both the proportion and percentage of patients that experienced an outcome. The variance of the arcsine difference is used to determine statistical significance. P-values < 0.05 are considered statistically significant.

When the data are available, meta-analyses using the random effects method of DerSimonian and Laird are performed. A minimum of three studies are required for an outcome to be considered for meta-analysis. Heterogeneity is assessed with the I-squared statistic. Meta-analyses with I-squared values less than 50% are considered as evidence. Those with I-squared larger than 50% are not considered as evidence for inclusion though the individual study results are still considered. All meta-analyses are performed using STATA 12.1. The arcsine difference is used in meta-analysis of proportions. In order to overcome the difficulty of interpreting the magnitude of the arcsine difference, a summary odds ratio is calculated based on random effects meta-analysis of proportions and the number needed to treat (or harm) is calculated. The standardized mean difference is used for meta- analysis of means, and magnitude is interpreted using Cohen's definitions of small, medium, and large effect.

Final Report Formatting

The final report is written first by the methodologist, edited and expanded upon by the project's chairs, and then presented, edited as necessary, and voted on by the development group. The draft report receives final review by the methodologists to ensure that it is substantively consistent with the published data.

The final TO report consists of standardized fields describing the treatment of interest for the identified population:

- Introduction
- Summary of findings – describes the evidence and implications of evidence
- Benefits & Harms
- Important/Priority Outcomes
- Cost Effectiveness/Resource Utilization
- Acceptability
- Feasibility
- Conflicts of Interest
- Future Research

In addition to these standardized domains, Technology Overviews also include a PRISMA Flow diagram, summary of findings tables, and quality appraisal domain tables.