Arthroscopy Journal Systematic Review/Meta-Analysis Template

- GENERAL
  - Word count: 4,500 (excluding title page, blind title page, references, figure legends)
    - Abstract word count: 300
  - Figure count: 7 (15 total figure parts)
  - Table count: 4
  - Any new systematic review or meta-analysis should ensure that the new proposed manuscript has not already been done in the recent past (within five years) – if so, why is a new one needed? New evidence that will change conclusion is a requirement.
  - See Harris JD, et al Arthroscopy 2017 Aug;33(8):1594-1602 for more information on the pearls and pitfalls of meta-analyses and systematic reviews.

- TITLE
  - Concise, precise
  - Should be attention-getting, controversial
  - Should say “…..: A Systematic Review” or “…..: A Meta-Analysis” or “…..: A Systematic Review and Meta-Analysis” in the title
  - Watch abbreviations – spell out, ensure clarity
  - No industry names

- ABSTRACT
  - Should be able to “stand-alone” – any author/reviewer/editor should be able to read the abstract and obtain ALL the relevant information about study design, conduct, findings, conclusions
  - Abstract plays three roles (Ibrahim AM, Dimick JB; Writing for Impact: How to prepare a journal article; 2017):
    - When writing
      - Improves your research question, manuscript writing
    - Once submitted
      - Convinces editors it’s worthy of 1) peer review, 2) publishing
      - Half of manuscripts at high-impact journals are rejected based on abstract alone
    - After publication
      - Getting the rest of the article read
      - Readers start at the abstract and decide if rest of article worth reading
  - Abstract PEARLS:
    - Far too many authors choose a title and abstract just before submission, with little thought put into either. Unfortunately, these are the first (and frequently, the only) parts of the paper that will be read
- **PURPOSE**
  - Should verbatim match the purpose in the manuscript body’s Introduction.
  - No background, no introduction, no hypothesis
  - Should be specific, precise
  - Should be an “answerable question” (yes, no, discrete number, better, worse, etc.)
  - Should include (paraphrased): “...to perform a systematic review to determine....”
    Or “...to perform a meta-analysis to determine....”

- **METHODS**
  - Should use PRISMA guidelines (Preferred Reporting Items for Systematic reviews and Meta-Analyses) – http://www.prisma-statement.org/
  - Should register via PROSPERO (international prospective registry of systematic reviews) - https://www.crd.york.ac.uk/PROSPERO/
  - Should report specific inclusion and exclusion criteria
  - Should report the databases used (two or more)
  - Should utilize methodological quality and bias assessment tool (CLEAR-NPT, Coleman, Modified Coleman, CONSORT, Pedro, Cochrane, Delphi, Detsky, Downs and Black, Jadad, Level of evidence, MINORS, Newcastle-Ottawa, QUADAS, Quality Appraisal Tool, STARD, Strobe, AMSTAR, R-AMSTAR, etc.)
  - Should utilize a recommendation tool (GRADE, SORT)
  - Assess heterogeneity for MA
  - No commercial / proprietary names (unless exceptional reason)
  - Statistical analysis, including brief meta-analysis methods (including if computerized review manager used)

- **RESULTS**
  - Should report a brief summary of studies analyzed
    - Number of studies (and methodological quality score[s])
    - Report heterogeneity
    - Number of subjects (sex distribution, age)
    - Number of interventions/surgeries (side distribution R/L; dominant/non-dominant)
  - Directly answer the primary purpose(s)
  - Should utilize specific p-values (e.g. p=0.03, p=0.43, etc.), not < or > (only exception p<0.001)
  - If individual-level (e.g. subjects, patients) data able to be pooled, a comparison to measures of clinical relevance (e.g. MCID [minimal clinically important difference], PASS [patient acceptable symptom state], SCB [substantial clinical benefit]) should be reported

- **CONCLUSIONS**
  - Should verbatim match the conclusions in the manuscript body’s conclusions
  - Narrow, specific, supported by the data/results/findings
  - Only report significant findings in a MA

- **LEVEL OF EVIDENCE**
  - Equates to the lowest level of evidence of included studies (e.g. if a systematic review as 10 studies and nine are level I, but one is level IV, then the systematic review is level IV).
  - Meta-analyses should only be performed with level I (preferred) or II evidence studies with relatively homogeneous participants, interventions, groups, and outcomes
**CLINICAL RELEVANCE**
- One to two sentences
- For non-clinical studies (e.g. biomechanical, animal model)
- For clinical studies that do not fit study type (i.e. therapeutic, diagnostic, prognostic, economic)

**INTRODUCTION**
- Concise summary of literature with appropriate references
- Should give the author/reviewer/editor context and a reason to care about the topic, why it is important
- Should create a knowledge gap, making it clear to the author/reviewer/editor what is known and unknown
- Should state how the current investigation will address the knowledge gap with a specific purpose(s) and hypothesis(es)
  - **Purpose**
    - Second to last sentence.
    - Should verbatim match the purpose in the abstract
    - Should be as specific as possible and address the primary outcome measure
  - **Hypothesis**
    - Last sentence
    - Specific, matches the purpose (should either be supported or rejected in the conclusion)
    - Must be tested by the Methods

**METHODS**
- Should be able to “stand alone” – telling the author/reviewer/editor exactly and transparently everything you did.
- PRISMA guidelines should be followed for every systematic review and/or meta-analysis
  - A PRISMA checklist should also be provided (shows page number of all 27 items)
  - A PRISMA flowchart should be generated (Figure) that shows application of exclusion criteria to eligible studies
- PROSPERO registration should be performed. Reviews that have progressed beyond point of completing data extraction at time of registration are not eligible for inclusion in PROSPERO. Stages of registration include (in order of completion):
  - Preliminary searches
  - Piloting of study selection process
  - Formal screening of search results against eligibility criteria
  - Data extraction
  - Risk of bias (quality) assessment
  - Data analysis
- Clear, specific inclusion and exclusion criteria
  - Should follow PICOS (participants, interventions, comparators, outcomes, study design) in order to optimize inclusion and exclusion criteria
  - If analyze therapeutic studies, should retain high quality studies (randomized, prospective, greater than 80% follow-up, greater than two years follow-up, comparative [versus gold standard intervention(s)])
    - If level I and II and homogeneous participants and interventions, then meta-analysis can be performed.
    - Do not perform meta-analysis on level III and IV data*
* in some cases, a meta-analysis of level III and IV may be warranted (examining rare outcomes or interventions that don’t lend themselves to randomization). Consult Cochrane Handbook of Systematic Reviews for further guidance on inclusion of non-randomized studies.

- If analyze diagnostic studies, should retain high quality studies (consistently applied reference gold standard comparison)
- If analyze prognostic studies, should retain high quality studies (inception cohort studies)
- If analyze economic studies, should retain high quality studies (computerized simulations – Monte Carlo, Markov – derived from level I studies)
- See CEBM (Center for Evidence-Based Medicine) new Level of evidence classifications - https://www.cebm.net/2016/05/cebm-levels-of-evidence/

- Should account for duplicate study populations in different studies
  - Choose: higher level of evidence, greater number of subjects, clearer description of methods and results, longer duration follow-up

- Should use two or more databases
  - If use MEDLINE, Embase, and Cochrane Central Register of Controlled Trials will generate a recall rate of over 97% in identification of all relevant studies in orthopedic surgery meta-analyses
  - MEDLINE, Embase, Cochrane, Scopus, PEDro, SportDiscus, CINAHL, Web of Science, Science Direct, and Clinical Key are just a few common ones used in arthroscopic and related surgery
  - Exact search algorithm strategy should be provided (transparency)

- Should use two or more reviewers in study identification, screening, eligibility, and inclusion (PRISMA flowchart)

- Should utilize at least one appropriate methodological quality score or recommendation score:
  - EQUATOR Network (Enhancing the QUAlity and Transparency Of health Research) – “umbrella” organization for guidelines, peer-reviewed articles, funding resources, and other entities collaborating to improve research quality
  - AGREE – Appraisal of Guidelines REsearch & Evaluation for clinical practice guidelines
  - ARRIVE – Animal Research: Reporting of In-Vivo Experiments
  - CARE – CAse REport guidelines for completeness, transparency, and data analysis in case reports
  - CHEERS – Consolidated Health Economic Evaluation Reporting Standards
  - CLEAR-NPT – CheckList to Evaluate A Report of a Non-Pharmacologic Trial
  - Cochrane Quality Assessment Tool – for randomized trials
  - Coleman/Modified Coleman – for randomized and non-randomized orthopedic trials
  - CONSORT – CONsolidated Standards of Reporting Trials for parallel group randomized controlled trials
  - COREQ – CONsolidated criteria for REporting Qualitative research – 32 item checklist for interviews and focus groups
  - Delphi - 8-item quality assessment tool for randomized and non-randomized trials
  - Detsky – 14-item quality assessment tool for randomized and non-randomized trials
  - Downs and Black - 27-item quality assessment tool for randomized and non-randomized trials
- GRADE – Grading of Recommendations, Assessment, Development, and Evaluation
- Jadad – simple three question (randomization, blinding, withdrawals) scale (not recommended)
- Level of evidence – I-V based on Center for Evidence-Based Medicine (CEBM)
- MECIR – Methodological Expectations of Cochrane Intervention Reviews
- MINORS – Methodological Index for NON-Randomized Studies
- Newcastle-Ottawa – quality assessment of non-randomized studies to be used in systematic reviews
- PRISMA – Preferred Reporting Items for Systematic reviews and Meta-Analyses
- QUADAS – QUality Assessment of Diagnostic Accuracy Studies
- Quality Appraisal Tool – percentile quality rating for non-randomized trials
- R-AMSTAR/AMSTAR – Revised Assessment of Multiple Systematic Reviews
- SORT – Strength Of Recommendation Taxonomy
- SPIRIT – Standard Protocol Items: Recommendations for Interventional Trials
- SQUIRE – Standards for QUality Improvement Reporting Excellence
- SRQR – Standards of Reporting Qualitative Research
- STARD – STAndards for Reporting Diagnostic accuracy studies
- STROBE - STrengthening the Reporting of OBservational studies in Epidemiology

  o Should include an assessment of risk of bias
    - Cochrane’s Risk of Bias tool for randomized studies.
    - ROBINS-I tool (Risk of Bias in Non-randomized Studies- of Interventions)
  o Should use two independent raters and include a description of how disagreements were resolved for both methodological quality and risk of bias.
  o Reliability statistics (kappa, ICC, etc.) should be calculated to quantify the degree of agreement between the raters.
  o Should assess bias qualitatively
    - Selection, detection, performance, transfer, non-responder, publication, study design
  o If a meta-analysis is performed the rationale for pooling data should be described.
  o Should address statistical analysis completely with all relevant details – if meta-analysis, then statistician should be involved; if systematic review, then best-evidence synthesis should be performed.
    - Should include comparison of statistically significant findings to that of clinical importance/relevance: MCID, PASS, SCB – it is critical to ensure that these concepts are used for “within-individual” change, not “group level”, “population level” changes observed with means of groups. See Harris JD, et al Arthroscopy 2017 Jun;33(6):1102-12 for a complete description of concept.
  o If meta-analysis, should appropriately describe methods used: fixed-effect versus random-effects
    - Fixed-effect: based on the assumption that single common (“fixed”) effect underlies each study included. Under this assumption, all studies are estimating the same common effect. The only reason the included studies have different results is due to random error (chance, sampling variation).
      - Requires included studies to be homogeneous both clinically and methodologically
      - Larger, less variable studies receive more weight than smaller, more variable studies
      - Interpretation: The summary estimate represents best estimate of effect
- Random-effects: allows for differences in treatment effect from study to study. Recognizes that both random error and differences between the study are responsible for why the included studies have different results.
  - When there are clinical and methodological differences among the included studies, only accounting for random error (fixed effect analysis) is not sufficient. Random effects incorporates these differences into the summary estimate.
  - Interpretation: The summary estimate represents an average of different effects. Important distinction from a fixed effect analysis where a single common effect is assumed across all studies. The utility of a random effects summary estimate depends on how well the differences between studies are identified and explored (see below).
- Heterogeneity should be assessed statistically with the I^2 statistic as well as clinically through evaluation of the studies (statistical heterogeneity may be absent despite a clinically heterogeneous group of studies).
- Heterogeneity should be explored. Statistical approaches include sub-group analyses or meta-regression
  - Especially important with random effects analysis as the summary estimate represents an average of different effects. Identifying contributors to heterogeneity helps understand what clinical and methodological factors may be responsible for the different effects and how those effects change when studies are sub grouped or further explored in regression.
- Prediction intervals should be reported for a meta-analysis using random effects.
  - Prediction intervals incorporate both random error and heterogeneity to provide a range of possible effects.
- Should generate forest plot to graphically display whether individual (and weighted mean) studies favor treatment or control groups
- Should generate funnel plot – a scatterplot that demonstrates systematic heterogeneity as a means to graphically illustrate publication bias

- RESULTS
  - Should be able to “stand alone” – telling the author/reviewer/editor exactly and transparently everything you found – in essence, match the Methods section.
  - Should completely describe all relevant demographics:
    - Study – number of studies, quality scores, geography, conflict of interest
    - Participants – number of subjects, age, gender, side, body part, length of follow-up
    - Interventions – non-surgical, surgical, rehabilitation
    - Outcomes – subjective patient-reported, objective clinician-measured, complications
  - Should directly answer the primary (and secondary/tertiary) outcome(s)
  - Avoid redundancy between text and tables/figures
  - If subjective qualitative analysis (best-evidence synthesis) performed, is the interpretation unbiased?
- DISCUSSION
  - First paragraph should briefly summarize the principal findings of the study and whether hypothesis(es) were confirmed or rejected.
  - Should not just re-state the results.
Should compare and contrast results of the current systematic review or meta-analysis with that of any other similar (or same) systematic reviews or meta-analyses.

Should discuss statistical significance versus clinical relevance for statistically significant results.

LIMITATIONS

- Should be final paragraph of Discussion
- All types of bias should be addressed and discussed

CONCLUSIONS

- Should verbatim match that of the Conclusions section in the Abstract.
- Specific, narrow, based only on actual results/findings/data/outcomes, without speculation, overstatement, or opinion

REFERENCES

- Should be up-to-date, most within the past five years
- Follow PubMed journal abbreviations
- Should be numbered consecutively in the order in which they appear in the text

FIGURES, TABLES

- Excellent way to efficiently summarize results
- Legends must define all abbreviations
- Should be able to “stand-alone”, so that the author/reviewer/editor can understand everything relevant to the figure/table with a single take-home educational message
- Should always mention patient position, viewing perspective (portal), side, imaging orientation