Answering Reviewers: Should Antibiotics Be Administered Before Arthroscopic Knee Surgery? A Systematic Review of the Literature

Reviewer #1: Well, antibiotics use for arthorscopy surgery is in controversy. The evidence was scarcely explored in past. Compared with the exprience we held before, this manuscript seems to provide us more interesting information.

Thank you for taking the time to review our manuscript.

Reviewer #2: The authors aim to address an important topic, and do this to a decent standard. However I feel the following points require addressing prior to being able to recommend the paper for publication: 1) The authors validly comment that: 'Being able to identify procedures and patient groups that do not require antibiotic prophylaxis offers the potential to reduce hospital costs, reduce the risk of allergic reaction to medication, and slow the development of drug resistant organisms.' And so, the authors should be cautious with the conclusions they draw (i.e. This is the first study demonstrating that prophylactic antibiotics are effective in preventing septic arthritis following simple knee arthroscopy), particularly when the sub-group analysis which 'excluded studies that involved bony procedures' found no significant difference in infection rates between the 'antibiotic vs no-antibiotic' groups. I feel the authors should better define the cohorts they have used for the 'arthroscopic procedures that do not involve the implantation of a graft'. Also when describing the results in the abstract, they should provide a balanced perspective, taking into account the heterogeneity of the procedures, and the negative results for arthroscopy which 'excluded studies that involved bony procedures'. Otherwise, the authors are unfairly advocating routine antibiotic use in all knee arthroscopy procedures.

We have added a comment in the abstract about the heterogeneity of procedures and the results of the analysis excluding bony procedures. Regarding the comment about better defining our cohorts, we are limited by the retrospective nature of our study and the fact that we are analyzing data that others have published. Aside from listing the procedures performed in each study that was included (if available), we do not feel these groups can be better defined other than by the fact that consist of patients undergoing arthroscopic knee procedures with no graft implantation during surgery.

2) The authors states in the abstract that: 'There is strong evidence to suggest that antibiotics should be used prophylactically for arthroscopic surgeries involving graft implantation, particularly ACL reconstruction.' However, within the review, they do not compare 'antibiotics vs no-antibiotics' for arthroscopic surgeries involving graft implantation. Thus this phrase should be removed or revised, where it is used throughout the text.

The phrase has been revised to say “Our literature search demonstrates that there is little to no debate that antibiotics should be used prophylactically for arthroscopic surgeries involving graft implantation, given we were unable to find any studies in which antibiotics were not used. However, our findings regarding the addition of graft soaking indicate that further steps can be taken to reduce the rate of infection.”

3) The p value for the meta-analysis of the 'antibiotic vs no-antibiotic' groups in arthroscopies 'not undergoing graft procedures, is p=0.05 in the abstract and the results text, but is p=0.04 in Table 2. Please correct accordingly.

Corrected

4) The authors have not used a scoring system (e.g. Coleman Methodology Score) to assess the quality of the included studies. This can provide very useful information for the reader. The authors should strongly consider including this.

To our knowledge, the Coleman methodology score has not been used in the context of septic arthritis. Furthermore, we are not assessing outcomes in our study, only one specific type of complication. We feel that statistical analysis of study heterogeneity is sufficient to describe the quality of studies included in our analysis.

5) Inclusion of the Review Articles and Survey results in Table 1 is slightly novel, though can be justified given the information provided.

We agree that the information in Table 1 is simplified. However, we feel that this allows key information regarding numerous studies to be presented in a concise and efficient manner.

Reviewer #3: This interesting review summarizes evidence for the protective usefulness of antiobiotics administered prior to knee arthroscopy. Results show show statistically significant but very small differences in post-surgical infection rates. More than 1000 patients have to be treated to prevent one infection. The question of clinical relevance of this small should be discussed by the author(s) in more detail. Thereby, author(s) should discuss the potential benefit and the risk of antibiotica use with more numbers (number of knee arthroscopy per year, costs of antibiotic prophylaxe, expected number of allergic reactions to antibiotics, expected number of persons who become resistant to antibiotics, etc.).

This would certainly be good information to know. Despite our findings, we do not believe that the debate of whether antibiotics should be used in arthroscopy is settled. Increasing antibiotic use would certainly not be without consequences. For this reason, we mention in our article that further study is warranted to determine if certain patient populations do not need antibiotics prior to arthroscopy. The cost of antibiotics and rates of antibiotic resistance are variable from region to region, and thus we feel that these topics are too broad to discuss in this article.

In the abstract and in conclusion as well as in core tips author(s) should not state that antibiotic prophylaxis is effective without stating a lack of efficiency, clinical meaningsfulness, and potential harm from side-effects that outweight the small benefits.

A comment about this has been added to manuscript.

Author(s) do report effectiveness of antibiotic prophylaxis via soaked graft. The discussion should compare the tremendous difference in effect size and should add other effect sizes for antibiotic prophylaxis for other types of orthopedic surgery so that readers who are not that familiar with risk estimates have a better frame of reference for the usefulness of antibiotic prophylaxis in knee arthroscopy .

We feel that the NNT (57) that is discussed adequately demonstrates the effectiveness of this treatment. Furthermore, we do not feel it would be appropriate to compare effect size to other orthopaedic surgeries given arthroscopy is substantially less invasive (and therefore introduces the questions of whether antibiotic prophylaxis is needed at all). To compare effect sizes between arthroscopic and non-arthroscopic procedures could mislead the reader into over-estimating the effectiveness of graft soaking and underestimate the impact of IV prophylaxis in combination with good sterile technique in the operating room.

The key issue is to decide which patients would benefit from antibiotic prophylaxis in knee arthroscopy more than others. Another issue might be under what circumstances in knee arthroscopy antibiotic prophylaxis in knee arthroscopy is especially effective (e.g., ambulatory care versus hospital surgery, etc.). Author(s) should try to analyse such person-related and situation-related moderators of effect size. Author(s) should try to analyse potential differences with respect to (a) the kind of antibiotic agent that was administered, (b) the time when the antibiotic agent was administered before surgery, and (c) the dose of antibiotic agent. The author(s) state that evidence merely depends on a large single study and author(s) of that study are more hesitating to state effectiveness than the current author(s). In my view it could be a good idea to invite the author(s) of that single study to make a small comment to the present study that is published, too. Author(s) should add a flow diagramm illustrating the search and decision process on primary studies. Information on inclusion and exclusion criteria should be extended.

A PRISMA diagram has been added. We will consider reaching out to Wyatt et al for comments regarding our study. Unfortunately, we do not have access to the remaining information requested (time antibiotic agent was administered, dose, etc.).

Minor point : Line 35 : «exensively »

Corrected

Reviewer #4: Dear colleages, First of all, I has been a pleasure to review your manuscript about

the antibiotics administration and knee surgery. I think this is an interesting study for clinicians who are involved in this field. The research question is very common in clinical practice setting. It is well written and well structured, making it easy to read and follow. Technically is well developed. Statistical analysis is adequate and correct for available data. In order to improve the quality of the manuscript, I would like to make some observations and suggestions after reading the manuscript: - Please, ensure that references format are in line with the WJO editorial rules. In the manuscript there are a mix of formats!

Corrected

- It would be appropriate to provide a graph that reflects the flow for the selection of studies (repeated, excluded, etc.). - Please, provide fulfilled PRISMA checklist for systematic review studies.

PRISMA diagram has been added

- Your obtained NNT is very high, how can this impact on clinical practice? Discuss more in depth this issue.

Intro and conclusion has been modified per reviewer #3's comments to clarify that the clinical significance of our findings is unclear given the high NNT.

- Line 254, change "do", for "to"…

corrected