Author's response to reviews

Title: Evaluation of symptomatic slow-acting drugs in osteoarthritis using the GRADE system

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Author's response to reviews:

Dear Editor,

Thank you very much for the care taken in reviewing our manuscript. We have taken into account all comments and we hope to have improved our manuscript.

Sorry for the delay for re-submitting this manuscript but we have had to organize a small meeting with all authors.

Do not hesitate to contact me if you need more information.

Very best regards

Olivier Bruyere

Response to reviewer/editorial board:

Reviewer 1: The clarity and the quality of the manuscript has increased after revision. However, the importance of Glucosamin sulfate is still somewhat overestimated, given the effect sizes the authors themselves report in the paper. Literature evidence is still overweighed within the manuscript to my opinion. The reader will not get an impression about the individual author's rating strong or weak. A table giving the individual ratings for the respective compounds anonymously would allow the reader to have information about experts’ opinion.

Authors: We agree that, mainly because of the heterogeneity showed in some meta-analysis, the quality evidence for glucosamine sulfate should be reduced from “High” to “Moderate”. Regarding the second point, the GRADE recommendation is reached by consensus and not by individual rating. It has been added in the text.

Editorial Board:
1. Glucosamine and chondroitin are listed as having moderate to strong evidence of efficacy. This highly controversial statement is not supported by the data presented in the paper. Both agents have strong evidence of heterogeneity ie the results differ by more than chance alone. The reasons for this are not clear. The conclusions need to be much more circumspect and the presence and significance of heterogeneity needs to be discussed so that the reader is clear what the implications of this are.

Authors: We agree that because of the heterogeneity, glucosamine sulfate should be reduced from High to Moderate. However, we would suggest to avoid to decrease the quality evidence for chondroitin, based only on heterogeneity because with other treatment (i.e. Avocado/soybean unsaponifiables, risedronate), no meta-analysis are available and, consequently, no heterogeneity could be calculated. The consequence of heterogeneity for the recommendation has been discussed in the text.

2. The disclosures are not sufficient. Please be specific about which relevant companies each author has worked for and also include a statement about how personal papers were approached. I accept that the authors had editorial independence for this paper but the reader still needs sufficient information to make an informed decision.

Authors: We agree that it is an important point. We have provided the information.

3. In addition, the site specificity of results needs to be considered more prominently eg glucosamine appears ineffective for hip OA.

Authors: This is also an important point and the information has been added in the discussion.