Author's response to reviews

Title: Does Alendronate Reduce the Risk of Fracture in Men? A Meta-analysis Incorporating Prior Knowledge of Anti-Fracture Efficacy in Women

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To the Editor of BioMed Central Musculoskeletal Disorders,

Thank you for recently sharing with us the additional comments of Dr. Huson. We would again like to thank the editor and the statistical reviewer, Dr. Huson, for reviewing our revised manuscript, titled, “Does Alendronate Reduce the Risk of Fracture in Men? A Meta-analysis Incorporating Prior Knowledge of Anti-Fracture Efficacy in Women” (MS 1079418594774445). We have responded to the questions and comments of Dr. Huson in the following pages. We have incorporated the suggested changes in the enclosed revised manuscript, which we would like to resubmit at this time. If you have any questions or concerns about the manuscript, please contact Dr. Adachi or A. Sawka

Sincerely,

A.M. Sawka, MD and J.D. Adachi, MD
Responses to the Comments of Dr. Huson:

General Comments: We appreciate that the Reviewer has indicated that the statistical aspects of the manuscript are generally acceptable.

General Comments and Comment #4: The Reviewer has suggested a summary table of odds ratios of treatment effects of included studies should be added. In fact, the odds ratios of treatment effects individual included studies are tabulated within revised Figure 2 so we have chosen not to repeat this information in a second table.

1) In our last response letter from April/2005, we have already responded to the Reviewer’s questioning of justification of the Bayesian approach (on page 4) as the other reviewers had requested such justification and an explanation of Bayesian statistical methodology. As per the suggestion of the Reviewer, we have deleted Figure 1.

2) The Reviewer has suggested that the phrase “how likely are the data given the calculated odds ratio” or “calculated parameter” be substituted with the phrase, “how likely are the data given the null hypothesis” (page 5 [continued paragraph from page 4] and page 12). We have made the substitutions suggested.

3) The Reviewer has indicated that it is common to use an inverse-gamma prior distribution for heterogeneity (variance) in this type of analysis. In fact, the gamma distribution of the precision (1/variance) that was used in this analysis is mathematically equivalent to an inverse-gamma distribution of the variance so we have not changed the manuscript. The Reviewer has suggested that it may be appropriate to include a brief comment on the need to discard early iterations in Gibbs sampling. The reason for discarding early iterations is that sampling needs to be performed after convergence has been achieved and we have added this statement to the sentence in question (page 8, 2nd paragraph, 4th sentence).

4) The Reviewer has commented on the limitation of the paucity of trials included in the review and we have also highlighted this limitation in the first sentence of the Discussion. However, this review highlights the need for more studies of osteoporosis therapies in both genders (as indicated in the final statement of the Discussion).