

Correspondence

Reply

To the Editor:

We appreciate the invaluable comments submitted by Tam et al¹ in response to our article.² They raise some important points on the methodologic principles of the meta-analysis.

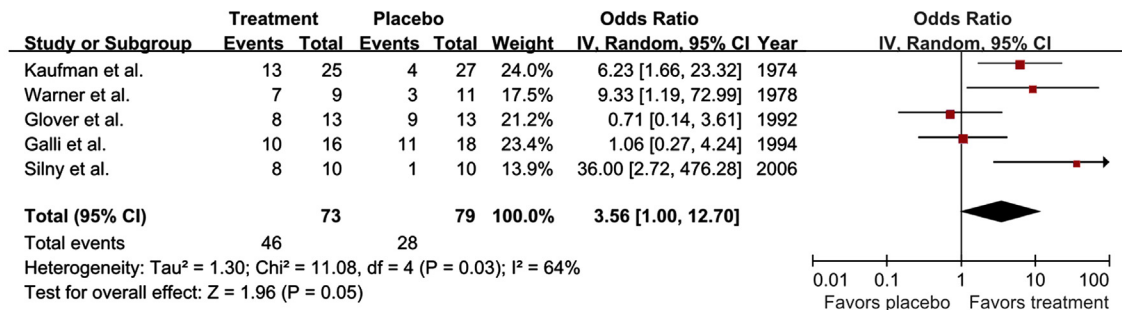
We agree completely that an *a priori* protocol is essential for a systematic review and meta-analysis to restrict the likelihood of biased *post hoc* decisions.³ We are also aware that “outcome-level” assessments are preferred and that the protocol must be prepared for the selection of a single primary outcome for an overall meta-analysis.³ However, in our critical appraisal of this topic, we endeavored to integrate all available evidence with appropriate mathematic methods to delineate the efficacy of the treatment modality with only limited information. We created an *a priori* protocol to include all published randomized controlled trials. The primary outcome of interest was dichotomized in terms of treatment success, which was defined as “the proportion of patients whose condition improved,” and we also included continuous outcomes measured by using any scoring system to estimate “the percentage reduction from baseline.” We planned to use the formula suggested by Chinn⁴ that the standardized mean difference can be re-expressed as the log odds ratio (OR) by multiplying by $\pi/\sqrt{3}$ to convert the continuous outcome to a dichotomous one in our protocol to combine all published data until the present.

We agree with the concern related by Tam et al¹ that this data manipulation could lead to an exaggeration of any treatment benefit. Therefore we conducted a new subgroup analysis of 5 studies that originally presented dichotomous variables and still calculated a marginally significant result (OR, 3.56; 95% CI, 1.00-12.70; $P = .05$; Fig 1, A). The inherent heterogeneity of atopic dermatitis clinical trials still remains problematic, and we hope that the results of *post hoc* sensitivity analyses (each study sequentially excluded) could be helpful at least in part.²

We would like to correct one entry error, as pointed out by Tam et al,¹ which had been committed in the process of dropout restoration for an intention-to-treat analysis. We substituted 25 treatment/27 placebo subjects for 26 treatment/26 placebo subjects, respectively, in the study by Kaufman and Roth,⁵ and present a corrected meta-analysis here (OR, 5.45; 95% CI, 1.63-18.19; $P = .006$; Fig 1, B). However, we encountered no error in the study by Glover and Atherton,⁶ and we confirmed that the dropouts were properly added in our result.

In conclusion, Tam et al¹ are quite correct in their advice on interpreting the results of the systematic review and on the importance of an *a priori* and rigorous approach accounting for different outcome categories in undertaking systematic reviews. We would like to express our gratitude for their comments once again. Despite some limitations, we maintain that our findings could provide a perspective on allergen-specific immunotherapy for atopic dermatitis and that systematic reviews with different

A A subgroup analysis of 5 studies of dichotomous data



B Overall meta-analysis of 8 studies

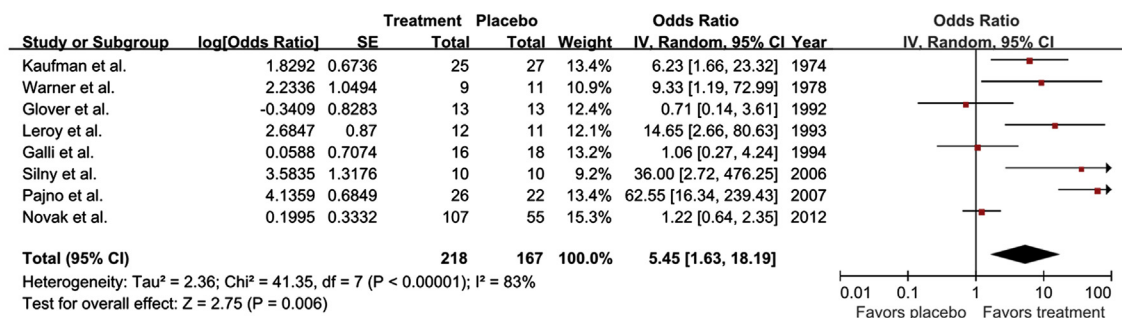


FIG 1. Corrected forest plots. A subgroup analysis of 5 studies of dichotomous data (A) and a meta-analysis of 8 studies for the overall efficacy of allergen-specific immunotherapy for atopic dermatitis (B) are shown.

protocols and additional well-designed clinical trials are still needed.

Jung Min Bae, MD^{a,b,c,*}
Yoon Young Choi, MD^{d,*}
Chang Ook Park, MD^{b,c,*}
Kwang Hoon Lee, MD, PhD^{b,c,e}

From ^athe Department of Dermatology, College of Medicine, The Catholic University of Korea; ^bthe Department of Dermatology, Severance Hospital, Yonsei University College of Medicine; ^cCutaneous Biology Research Institute, Yonsei University College of Medicine; ^dthe Department of Surgery, Severance Hospital, Yonsei University College of Medicine; and ^eBrain Korea 21 Project for Medical Science, Yonsei University College of Medicine, Seoul, Korea. E-mail: kwanglee@yuhs.ac.

*These authors contributed equally to this work.

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