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In response to ‘Differences in the prevalence of positive penicillin allergy test results in children and adults’

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To Howard Miller, Editor in Chief:

In the letter to the editor 'Differences in the prevalence of positive penicillin allergy test results in children and adults', the authors presented results of their meta-analyses generated from the data we collected by systematic review. Their results differed from ours. Specifically, their results and our meta-analysis respectively showed pooled estimates of 8.12% (95% CI; 1.76%–18.29%) versus 1.98% (95% CI; 1.35%–2.60%) in the pediatric group, and 6.84% (95% CI; 4.85%–9.12%) versus 7.78% (95% CI; 6.53%–9.04%) in the adult group.

The authors raised some concerns regarding the difference from our findings that we address in the following sections.

The authors performed statistical analyses using the R software, whereas we used Stata (version 12.0). We used the *metan* function to perform the meta-analysis with the data presented in the original paper. As the weight placed on each study may vary based on the software and statistical analysis function used, we expect the results may also differ. The *metan* function specifically uses inverse-variance weighting, both to calculate the pooled effect, and to generate the squares in the forest plot. The relative weights are calculated from the confidence intervals, as to reflect the relative sizes of the studies. We have attached below the results of the meta-analyses, separated by age group, and the associated forest plots. The results are consistent with the estimates previously published.

Further, the estimate of true penicillin allergy in children we obtained in the original paper is consistent with two large subsequent pediatric studies by Exius et al. [1]

and Mill et al. [2] based on drug challenge. These studies reveal that the prevalence of true amoxicillin allergy in children is 2.2% and 2.1% respectively.

In conclusion, we believe that our initial meta-analysis was valid. Further, the findings of our research are well supported by the current literature.

Reference

1. Exius, R., Gabrielli, S., Abrams, E., O'Keefe, A., Protudjer, J., Lavine, E., Pitt, T., Atkinson, A., Eiwegger, T., McCusker, C. and Ben-Shoshan, M., 2021. Establishing Amoxicillin Allergy in Children Through Direct Graded Oral Challenge (GOC): Evaluating Risk Factors for Positive Challenges, Safety, and Risk of Cross-Reactivity to Cephalosporines. *The Journal of Allergy and Clinical Immunology: In Practice*,.
2. Mill, C., Primeau, M., Medoff, E., Lejtenyi, C., O'Keefe, A., Netchiporouk, E., Dery, A. and Ben-Shoshan, M., 2016. Assessing the Diagnostic Properties of a Graded Oral Provocation Challenge for the Diagnosis of Immediate and Nonimmediate Reactions to Amoxicillin in Children. *JAMA Pediatrics*, 170(6), p.e160033.

Table 1. Prevalence of immediate penicillin allergy for studies including children only

Study	ES	[95% Confidence Interval]	% Weight
1 (Zambonino)	0.894	[0.235-1.553]	89.15%
2 (Caubet)	14.773	[7.359-22.186]	8.51%
3 (Fox)	10.283	[8.149-12.417]	1.64%
4 (Ahmed)	12.139	[7.272-17.005]	0.71%
I-V Pooled ES	1.975	[1.352-2.597]	100%

Figure 1. Forest plot of meta-analysis results for studies including children only

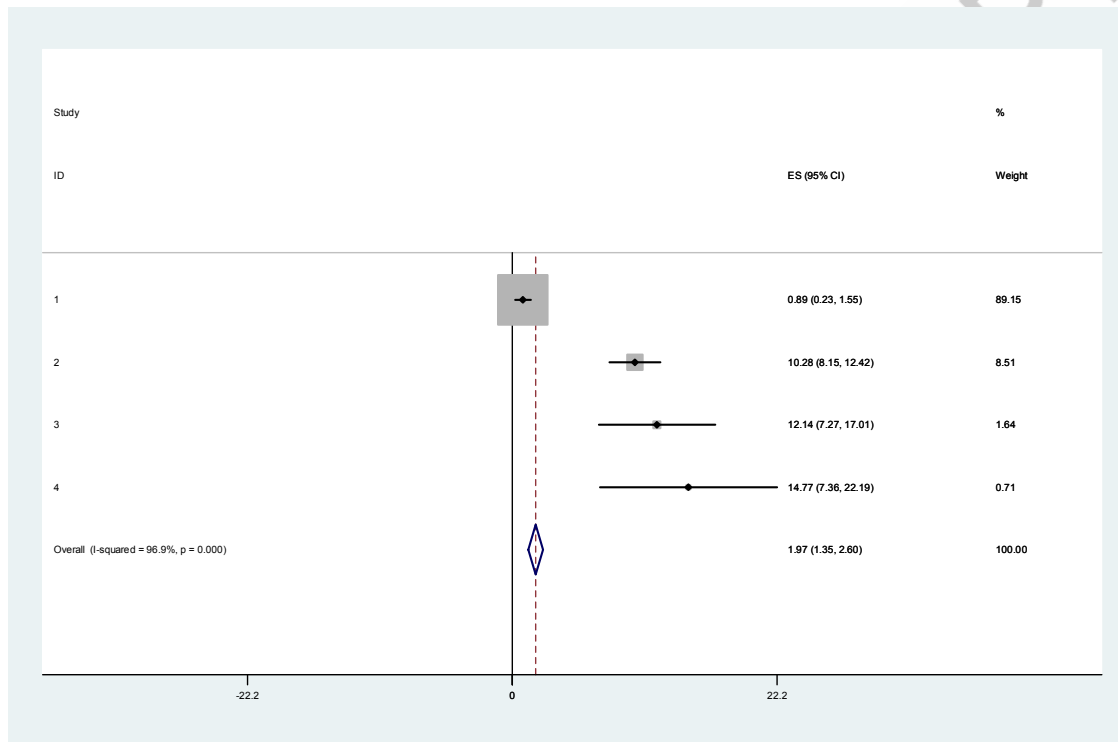


Table 2. Prevalence of immediate penicillin allergy for studies including adults only

Study	ES	[95% Confidence Interval]	% Weight
1 (Romano)	17.000	[13.126-20.874]	10.50%
2 (Park)	2.817	[-1.032-6.666]	10.64%
3 (Macy)	4.000	[0.864-7.136]	16.03%
4 (Kopac)	7.042	[4.613-9.472]	26.70%
5 (Hjortlund, 2013)	7.018	[4.310-9.725]	21.50%
6 (Hjortlund, 2012)	11.389	[8.107-14.671]	14.63%
I-V Pooled ES	7.782	[6.526-9.037]	100%

Figure 2. Forest plot of meta-analysis results for studies including adults only

