

Correspondence

Childhood asthma exacerbations and ADRB2 polymorphism: Caution is needed

To the Editor:

Turner et al¹ are cautious in discussing their meta-analysis of a possible interactive effect on the risk of exacerbation between treatment given to children with asthma and allele count at position 16 (rs1042713) in the β_2 -adrenoceptor gene (ADRB2), where exacerbation was defined somewhat differently in different

studies but was most commonly limited to occurrence in the previous 6 months. However, their analysis can be criticized as not mounting a direct attack on the interaction but instead making inferences indirectly by comparing statistical significance, a practice that cannot be recommended.²

A possible formal analysis of the interaction would be to do a meta-analysis of the meta-analyses. If it is the case that allele-score exacerbation association is independent of the treatment given, then the weighted average over treatments would be a suitable estimate of this overall association and the traditional test

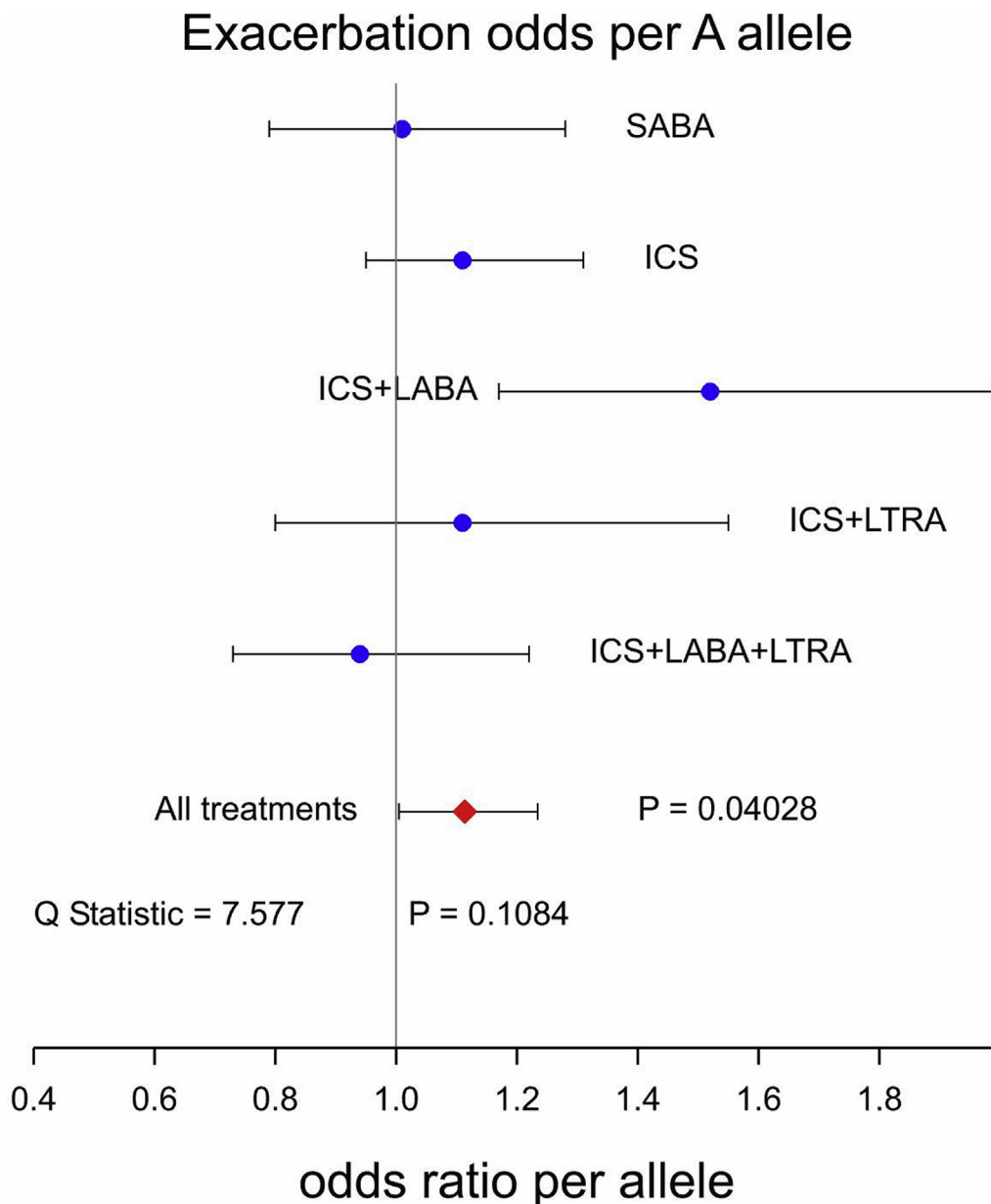


FIG 1. Fixed effects meta-analysis of meta-analyses by Turner et al of association between allele score and exacerbation. ICS, Inhaled corticosteroid; LABA, long-acting beta-agonist; LTRA, leukotriene receptor agonist; SABA, short-acting beta-agonist.

of heterogeneity would be a means of examining the hypothesis of no interaction.

Using the confidence intervals that Turner et al helpfully provide in their Table II, taking the results for all cohorts combined (column 7), and log transforming, it is possible to recover the standard errors on the log-odds scale for each of the 5 meta-analyses they conducted. These, together with the point estimate of the log-scale, can provide the raw inputs to a further meta-analysis: combining across treatments. The result of such a fixed effects meta-analysis is shown in Fig 1.

The Q statistic is 7.6 on 4 degrees of freedom ($P = .11$). This is an excess of heterogeneity but the P value is modest and the result is not formally significant. As a check on this analysis, one can note that the P value for the overall allele trend effect is .040 compared with the value of .035 that the authors themselves found by proceeding in a different order: averaging across treatments within cohorts first and then averaging cohorts (see their Table E2). The difference is plausibly due to the effects of rounding. Both the 2 values are, of course, conventionally significant but

very modest. One possible inference may be that children, after all, are not so different from adults.³

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