

Author Response 2

Reviewer #1:

Comment 1:

“I have one remaining concern, I read through the QUADAS-2 and the Reitsma et al Bivariate Model papers, and there’s no real accounting for the quality of the predictive methods used in each of the included (5) studies. I still think its likely these papers didn’t replicate in independent populations, and it's also likely the models were trained on the same data they were tested upon. I then verified that the Rodrigo-Munez et al Allergy 2019 paper does indeed have these flaws. I suggest the authors include some kind of limitation stating that the methodologies employed do not assess the quality of the model generation in the included studies or their generalizability.”

Answer: Thanks for your good suggestions. The QUADAS-2, revised based on the QUADAS, is a common tool used to evaluate the quality of studies included in diagnostic analysis (Whiting P, et al., 2003, and Whiting, P, et al., 2011) from 4 domains (patient selection, index test, reference standard, and flow of patients). As you pointed out, we applied QUADAS-2 for quality assessment of included studies instead of the Bivariate Model. Besides, limited to the data included, we were not able to verify the results in an independent cohort in our study. Thus, we have added the limitation in the Discussion part as follows: “Finally, though the Bivariate Model is widely used in diagnostic meta-analysis (Hegedus, E. J.. et al., 2012) (Reiman MP. et al., 2015) (Fuccio L. et al., 2013) (Xiao G. et al., 2017), we were not able to verify the results in an independent data set due to the limitations of the included data”.