Author's response to reviews

Title: Kawasaki disease and subsequent risk of allergic diseases: a population-based matched cohort study

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Author's response to reviews:

Response to reviewer 1 comments:

Q1. Clarify whether the index year for the ambulatory visits for the control group matched for the year of hospitalization for their KD case. Therefore, state that controls were also chosen from 1997 to 2005 and, as KD patients, followed up to 2010 (if necessary). No new controls were picked up after 2005.

Response 1: We now state that controls were also chosen from 1997 to 2005 according to your suggestion (page 5, line 4).

Q2. Clearly list the confounders. Are they the same presented in Table 1? Were age and gender included in the model even though cases and controls were initially matched for these two variables? What the reason? For model adjustment?

Response 2: Yes, the confounders mentioned in text are the same as those presented in Table 1. Age and gender were included in the model because they are potential confounders and therefore should be adjusted for in the statistical model.

Q3. Before stating that "The mechanism by which KD may increase the risk of future development of allergic disease remain unclear" there should be some discussion on how the results do not preclude a common path to both diseases, even if allergy was developed after KD. To further bring more light into the issue, one would have to follow a cohort of newborns, for instance, and explore the different groups (controls without disease, allergic patients that future developed KD, KD patients that future developed allergies).
Response 3: We mention this point in the discussion section (page 8, 3rd paragraph).

Q4. I do not think I agree with the way the second and the third limitations are described. The fact that some correlation between KD and allergy has previously been shown present us with the (theoretical) possibility that doctors are more inclined to find allergic diseases in patients who had KD. So, not only misclassification of allergic diseases might not be non-differential but also combined to the fact that KD patients were seen more often by doctors, could make this population more susceptible to have allergies diagnosed. Particularly light cases. It is a limitation of the study that cannot be overcome with the data presented.

Response 4: We agree with your comments. We mention this point in the discussion section according to your suggestion (page 10, lines 2-9).

Q5. First paragraph-- These cross-sectional data suggest that patients with KD tended to develop allergic diseases is imprecise. Cross-sectional data do not allow to cause-effect inference. Use correlation or a similar term.

Response 5: We have now re-written the sentence (page 3, 2nd paragraph, line 6).

Q6. Second paragraph- Exclude "a country with the third highest... . It has already been stated in the previous paragraph.

Response 6: We now exclude the sentence according to your suggestion.

Discussion and conclusion

Q7. Fifth paragraph- However, the confounding effect of medical attention.." should be excluded as it is a measured factor and therefore it is not related to the previous statement.

Response: We now exclude the sentence according to your suggestion.

Table 2

Q8. b instead of "matching variable" describe them.

Response: We now use age and gender to replace matching variables according to your suggestion (Table 2).

Abstract-Background

Q9. Among the (exclude) Kawasaki..."
Response: We now exclude "the" according to your suggestion.

Q10. "involvement of CAL" switch to "presence of CAL"
Response: We now use presence to replace "involvement" according to your suggestion.

Q11. "proxy to measure of (exclude) children's SES"
Response 11: We now exclude "of" according to your suggestion.

Q12. "Table 1 presents .. study subjects (include) and controls"
Response 12: We now include "and controls" according to your suggestion (page 7, line 4).

Q13. "allergic diseases compared with (include) the general population.
Response 13: We now include "the" according to your suggestion.

Q14. "children's enrollee" (instead of enrolee)
Response 14: We now use enrollee to replace enrolee. Thank you for your careful review.

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Response to reviewer 2 comments:

Q1. Authors could discuss deeply the relation between asthma/allergy and Th1 inflammatory diseases (including data from other Th1 diseases).
Response 1: Thank you for your comments. The relation between asthma/allergy and Th1 inflammatory diseases (including other Th1 diseases) contains a lot of information which requires discussion. It will make the manuscript too lengthy if we discuss this point. The aim of this study was to investigate the risk of allergic diseases among children after KD in Taiwan. We feel that our discussion is informative and sufficient to explain our study findings. We believe that not to discuss the relation between asthma/allergy and Th1 inflammatory diseases would not have affected the validity and the important finding of this study.

Q2. The absence of data from family history of allergic diseases is the main limitation.
Response 2: We agree with your opinion and mention this point in the discussion section (page 10, lines 9-12).
Q3. Monthly income is shown in table 1 without unit information (American dollars ?).

Response 3: No, the unit of monthly income is National Taiwan dollars (NT$). We now show the unit in Table 1 (Table 1).