

Correspondence

Reply

To the Editor:

In our article on childhood asthma remission from the Childhood Asthma Management Program (CAMP) cohort,¹ we identified predictors of both asthma remission and persistence into adulthood. The predicted probability of asthma remission was the highest (82.6%) in subjects with a baseline FEV₁ to forced vital capacity (FEV₁/FVC) ratio of greater than or equal to 85%, provocative concentration causing a 20% fall in FEV₁ (PC₂₀) of greater than or equal to 1 mg/mL, and serum eosinophil count of less than 500 cells/ μ L. A key question left unanswered in our study was whether our results were generalizable to more severe asthma, given that CAMP included only those with mild-to-moderate persistent childhood asthma.

Carpaij et al evaluated our prognostic model in a combined cohort of 251 children with asthma from The Netherlands.²⁻⁴ Notably, the baseline characteristics describe children with significantly lower lung function (FEV₁ as a percent of predicted was in the mid 70% to low 80% range, whereas those in CAMP were in the low 90% range), suggesting a greater level of severity at baseline for the combined Dutch cohort. Further supporting this increased level of baseline severity is the report that their combined cohort demonstrated an overall remission rate of only 10.0% versus 26.1% in CAMP. Despite this, the Dutch children with asthma who met our prognostic remission criteria had a 40.0% (8 of 20) probability of asthma remission, greater than 5-fold higher than did those without the criteria (7.4%; 17 of 231). Overall, this validates our prediction model for remission across a range of childhood asthma severity. Conversely, we also identified a subgroup of children much more likely to have persistence of asthma into adulthood. Children with a baseline FEV₁/FVC ratio of less than 80% had a less than 10% probability of asthma remission. Similarly, Carpaij et al found the probability of remission to be 5.6% (10 of 181) in this subgroup of those with asthma. We wonder if treatments to improve baseline FEV₁/FVC in pediatric asthmatic patients would increase their probability of outgrowing the disease.

Clinical measurements are surrogate measures for biologic processes that in turn are influenced by genetics, epigenetics, and

the environment. Therefore, to truly understand the biology and the factors influencing asthma remission, further studies in these fields are required. Indeed, the Dutch group has described genetic variants associated with remission across multiple cohorts, while we have previously noted microRNAs predictive of resolution of airways hyperresponsiveness in CAMP.^{5,6} We anticipate that by combining clinical and multiomic data using systems biology, we will be able to further elucidate the mechanisms governing asthma remission and persistence. This will enable us to create personalized and more accurate prediction models for asthma remission and may eventually lead to novel therapeutic approaches for the secondary prevention of asthma.

Alberta L. Wang, MD, MS^{a,b}

Kelan G. Tantisira, MD, MPH^{a,c}

From ^athe Channing Division of Network Medicine, ^bthe Division of Rheumatology, Immunology and Allergy, and ^cthe Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Mass. E-mail: rekgt@channing.harvard.edu.

This study was supported by the National Institutes of Health (grant nos. T32 AI007306, R01 HL127332, R01 HL129935, and U01 HL65899).

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Wang AL, Datta S, Weiss ST, Tantisira KG. Remission of persistent childhood asthma: early predictors of adult outcomes. *J Allergy Clin Immunol* 2018 <https://doi.org/10.1016/j.jaci.2018.09.038> [Epub ahead of print].
2. Carpaij OA, Vonk JM, Nawjin MC, Kerstjens HAM, Koppelman GH, Van den Berge M. Applying the CAMP trial asthma remission prediction model to the Dutch asthma remission studies. *J Allergy Clin Immunol* 2019;143:XXX-XXX.
3. Carpaij OA, Nieuwenhuis MAE, Koppelman GH, van den Berge M, Postma DS, Vonk JM. Childhood factors associated with complete and clinical asthma remission at 25 and 49 years. *Eur Respir J* 2017;49:1601974.
4. Vonk JM, Postma DS, Boezen HM, Grol MH, Schouten JP, Koeter GH, et al. Childhood factors associated with asthma remission after 30 year follow up. *Thorax* 2004; 59:925-9.
5. Vonk JM, Nieuwenhuis MAE, Dijk FN, Boudier A, Siroux V, Bouzigon E, et al. Novel genes and insights in complete asthma remission: a genome-wide association study on clinical and complete asthma remission. *Clin Exp Allergy* 2018;48: 1286-96.
6. McGeachie MJ, Davis JS, Kho AT, Dahlin A, Sordillo JE, Sun M, et al. Asthma remission: predicting future airways responsiveness using a miRNA network. *J Allergy Clin Immunol* 2017;140:598-600.e8.

<https://doi.org/10.1016/j.jaci.2019.01.041>