

Asthma breathomics – promising biomarkers in need of validation

Dear Editor,

I read with interest the engaging review by Neerincx et al ¹ – Breathomics from exhaled volatile organic compounds (VOCs) in pediatric asthma. The results are encouraging, suggesting good predictive accuracy for VOC profiles in asthma diagnosis. However, the authors report on only those studies which they were aware of and limit their scope to the last 10 years. Given that the first study of an exhaled VOC in asthma may well have been Olopade et al in 1997 ² we wanted to ascertain whether the review had indeed captured all the relevant literature.

We conducted a systematic search using the following key words and MeSH terms - metabolomics, breathomics, exhaled breath, breath test, volatile organic compound and asthma. Searches were conducted in PubMed, Medline Ovid and Embase, with no date limits.

Example search string (used in PubMed):

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((("Breath Tests"[Mesh] OR "Exhalation"[Mesh] OR "exhaled"[All Fields] OR breath[All Fields]) AND ("Asthma"[Mesh] OR "asthma"[All Fields] OR "asthmatic"[All Fields]) AND ("Volatile Organic Compounds"[Mesh] OR "Volatile Organic Compound"[All Fields])) OR ((("asthma"[MeSH Terms] OR "asthma"[All Fields] OR "asthmatic"[All Fields]) AND (Breathomic*[All Fields] OR ("metabolomics"[MeSH Terms] AND ("exhalation"[MeSH Terms] OR "exhalation"[All Fields] OR "exhaled"[All Fields] OR breath[All Fields] OR "breath tests"[MeSH Terms])))))
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The search process is summarised in the Prisma diagram below. We identified seventeen references to pediatric asthma breathomic studies. Six were abstracts, of which three were not published in full elsewhere ³⁻⁵; two presented identical data - early findings from a study by the review authors which is yet to be published ^{6,7}; and one has since been published in full ⁸. The list of full studies identified by our search is similar but not identical to that of Neerincx et al. They included two papers ^{9,10} examining pre-school wheeze (not asthma), while we identified a paper published more than 10 years ago ¹¹; this was a longitudinal study of asthmatic children living in a high pollution area (n=26). This study reported largely non-significant results, with the

exception of exhaled benzene which exhibited a moderate positive association with bothersome / severe asthma symptoms. The study was limited by the small number of breath samples obtained on symptom-free days (n=6).

An absence of significant findings is of course one reason why abstracts might not progress to full publication. While there are good reasons for excluding abstracts from a review – including the inability to assess the quality of studies and risk of bias – this does have the potential to give an unbalanced viewpoint; one which emphasises positive associations and downplays null findings. Of the abstracts not subsequently published in full - Gahleitner et al ⁴ did not report any results; while Brinkman et al ³ report a cluster analysis which identified groups that differed significantly in clinical parameters. Wang et al ⁵ found a correlation with night waking but not with asthma control; whereas Vijverberg et al ^{6,7} reported an area under the curve of between 0.71 and 0.97 for the identification of disease control.

It would seem then that the review by Neerincx et al succeeded in capturing the majority of relevant literature; the additionally identified study adds little to their findings. The abstracts identified by our search present results largely relating to the ability of VOCs to differentiate between states of disease control, the results of which were conflicting. Overall we found little to either challenge or expand the findings of their review; the future of pediatric beathomics now lies in the ability to validate these findings in prospective cohort studies.

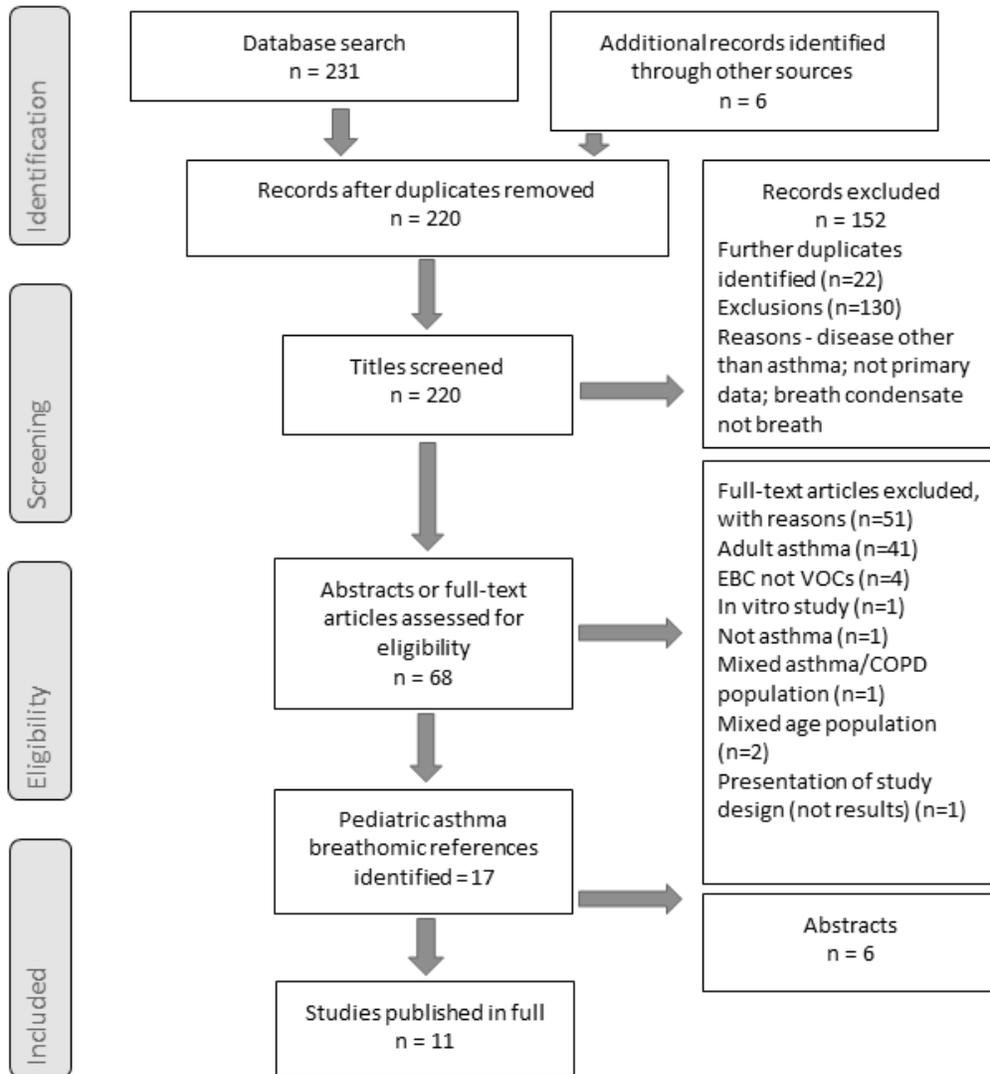
Authors: Adam M Peel¹, Prof. Andrew M Wilson¹, Prof. Yoon K Loke¹

¹Norwich Medical School, University of East Anglia, Norwich Research Park, Norwich, NR4 7TJ,
UK

Correspondance: Adam Peel¹ a.peel@uea.ac.uk

Key words: Asthma, metabolomics, breath tests

Fig. 1 – PRISMA Diagram



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