Exploring exhaled breath volatile organic compounds in occupational asthma: A pilot cross-sectional study

Hilde Heiro[1], Tonje Trulssen Hildre[1], Amy Craster[2], Liam Grimmett[2], Matteo Tardelli[2] and Bato Hammarström[1]

[1]Oslo University Hospital, Division of Medicine, Department of Pulmonary Medicine, Environmental and Occupational Medicine, Oslo, Norway. [2]Owlstone Medical Ltd. Cambridge, United Kingdom.

Introduction and Aims

Occupational asthma (OA), affecting 16% of adult-onset asthma cases, can be divided into allergic asthma (AA) and irritant-induced asthma (IIA).

IIA can be further subdivided based on degree of exposure and latency of asthma. While biomarkers for asthma are widely studied, few studies have focused on breath volatile organic compounds (VOCs) in OA.

This study aims to identify specific VOCs in exhaled breath that could serve as biomarkers to distinguish OA from healthy controls (HC) and differentiate between IIA subtypes. Understanding these metabolic changes could lead to improved diagnosis and treatment strategies.

Methods

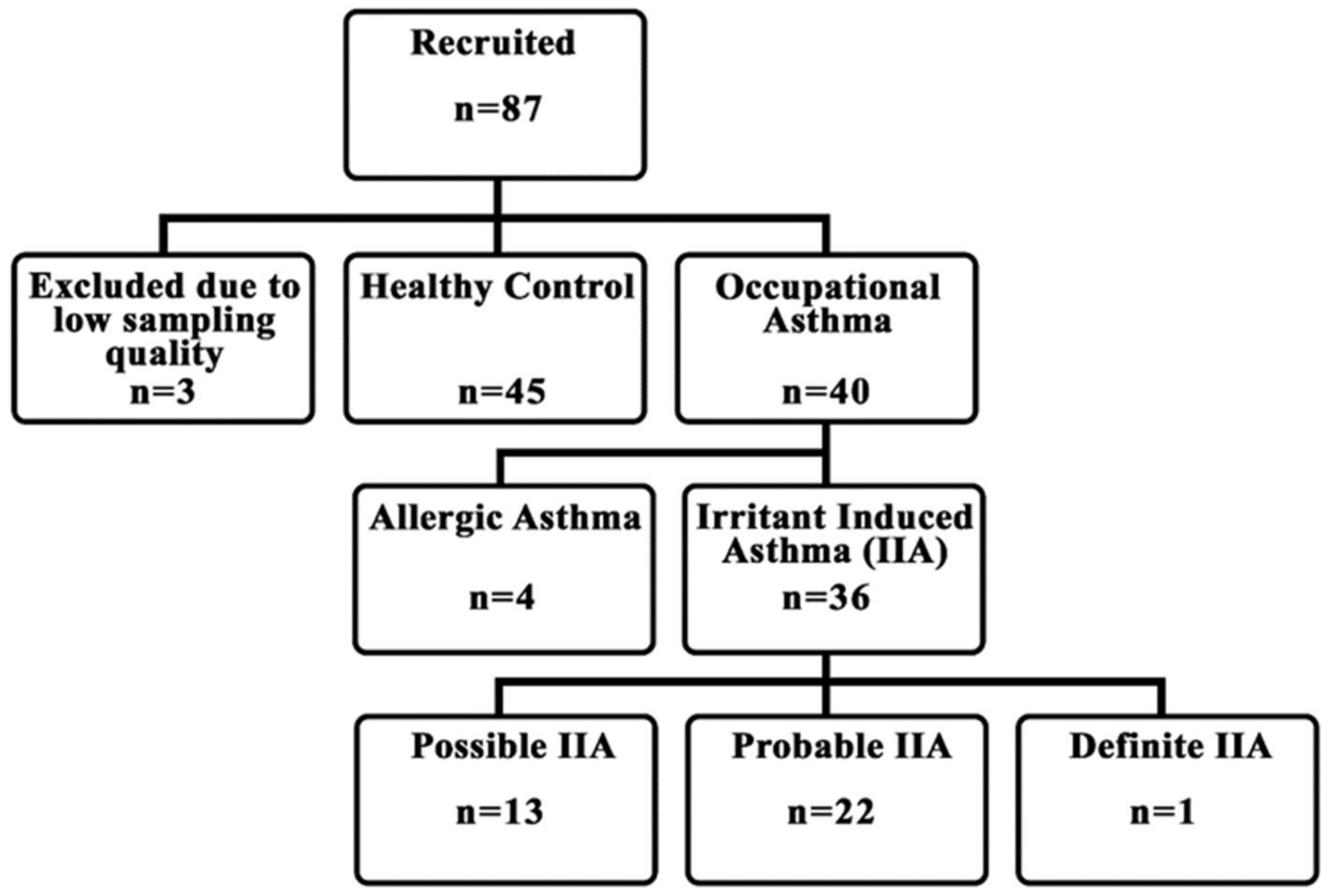


Figure 1. Overview of the study design

This cross-sectional study involved 40 OA patients and 45 respiratory-healthy healthcare workers (HC) (**Figure 1**). Breath samples were collected using the ReCIVA® Breath Sampler, and VOCs were analyzed using thermal desorption-gas chromatography mass spectrometry (TD-GC-MS). Statistical methods, including principal component analysis and multivariate regression models, were employed to compare VOC profiles between OA and HC. Differences between possible and probable IIA subtypes were also explored, accounting for BMI, sex, time since last exposure, and medication as confounders.

Results

A total of 536 distinct VOCs were identified in the breath samples and 76 were classified as Tier 1 (**Figure 2**). Significant differences in VOC profiles were found between OA and HC, particularly for compounds such as 1-hexadecanol, 2,3-butanediol, phenol, xylene (**Figure 3**). These VOCs are linked to biological pathways involving reduced nicotinamide adenine dinucleotide (NADH) and the production of reactive oxygen species (ROS), which are associated with airway inflammation and asthma development (**Figure 4**). Multivariate models based on 76 significant VOCs demonstrated high classification performance, with a ROC-AUC of 0.94 for distinguishing OA from HC. Key VOCs, such as 1-hexadecanol and acetone, were associated with occupational exposures, including low molecular weight chemicals, acids, and alkalis (**Figure 5**).

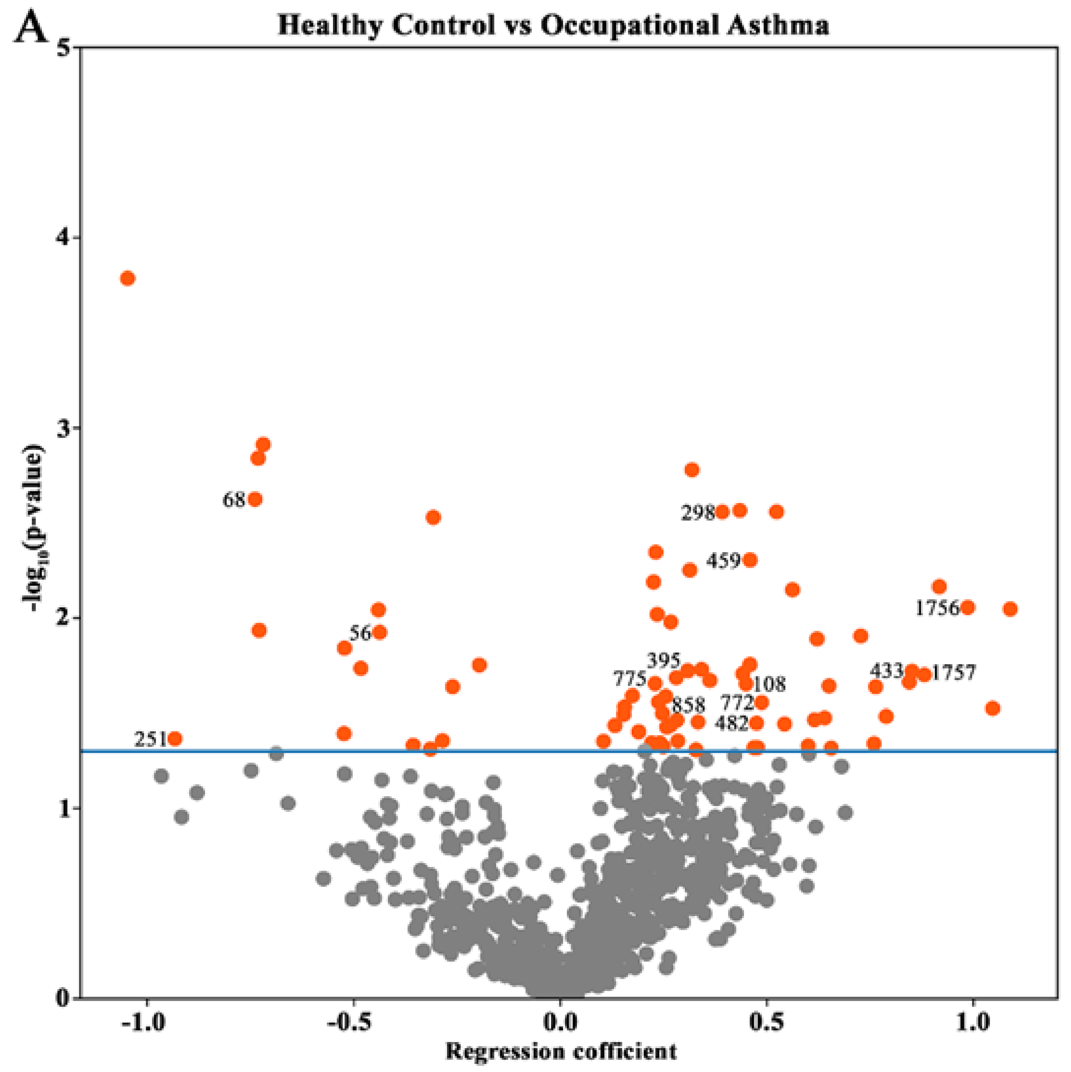


Figure 2. Volcano Plot of significant VOCs in Occupational Asthma

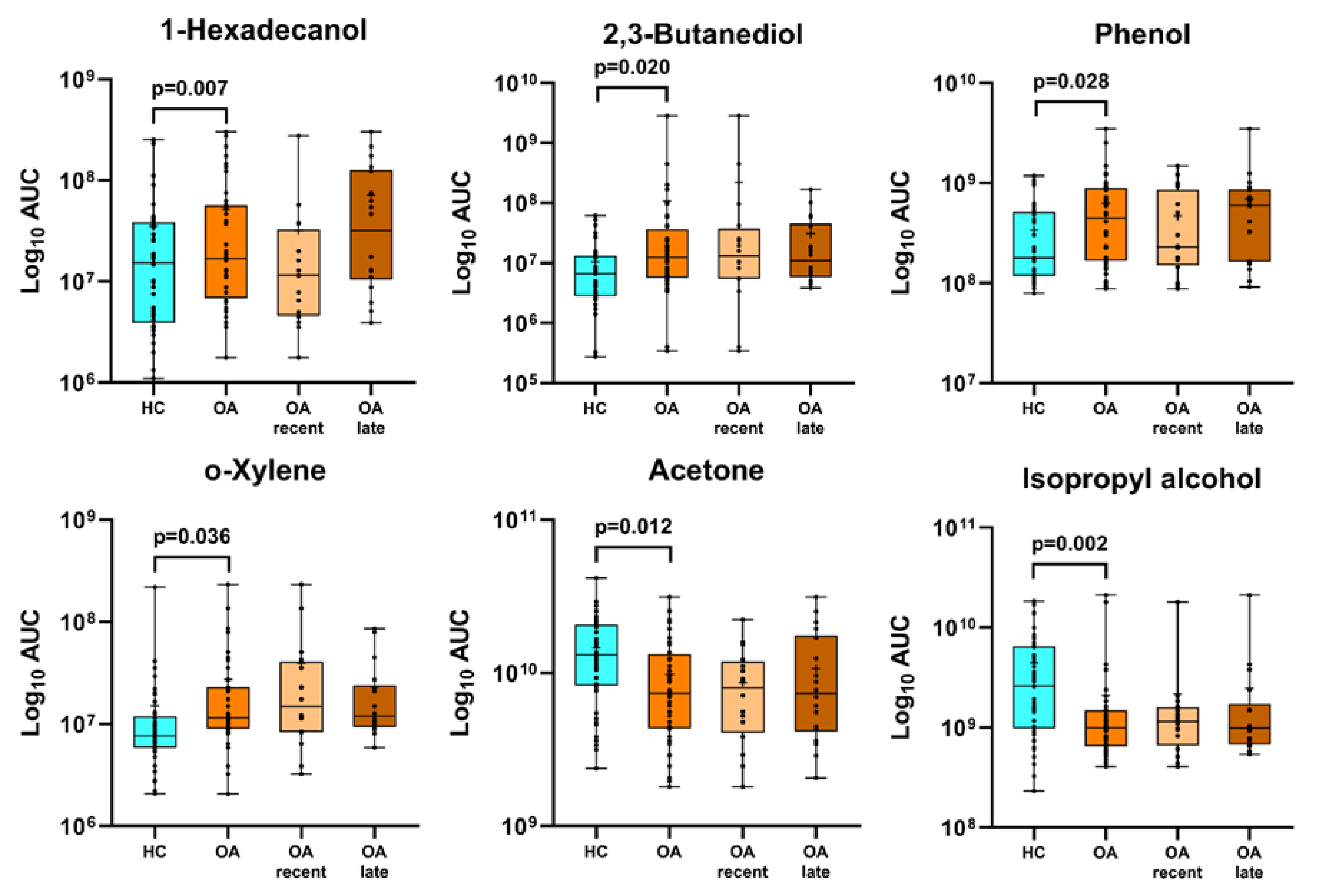


Figure 3. Significant tier 1 exhaled breath VOCs in occupational asthma

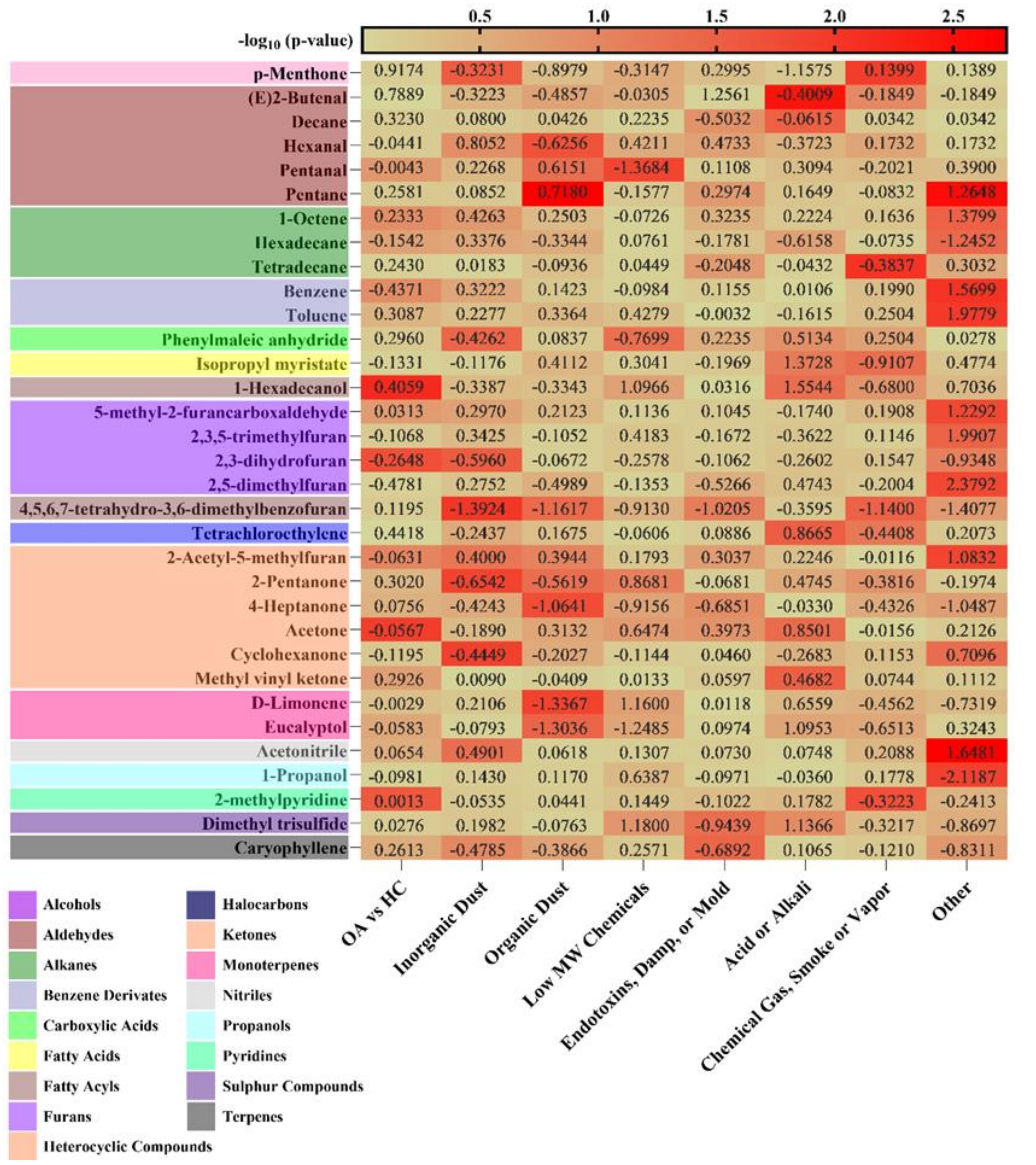
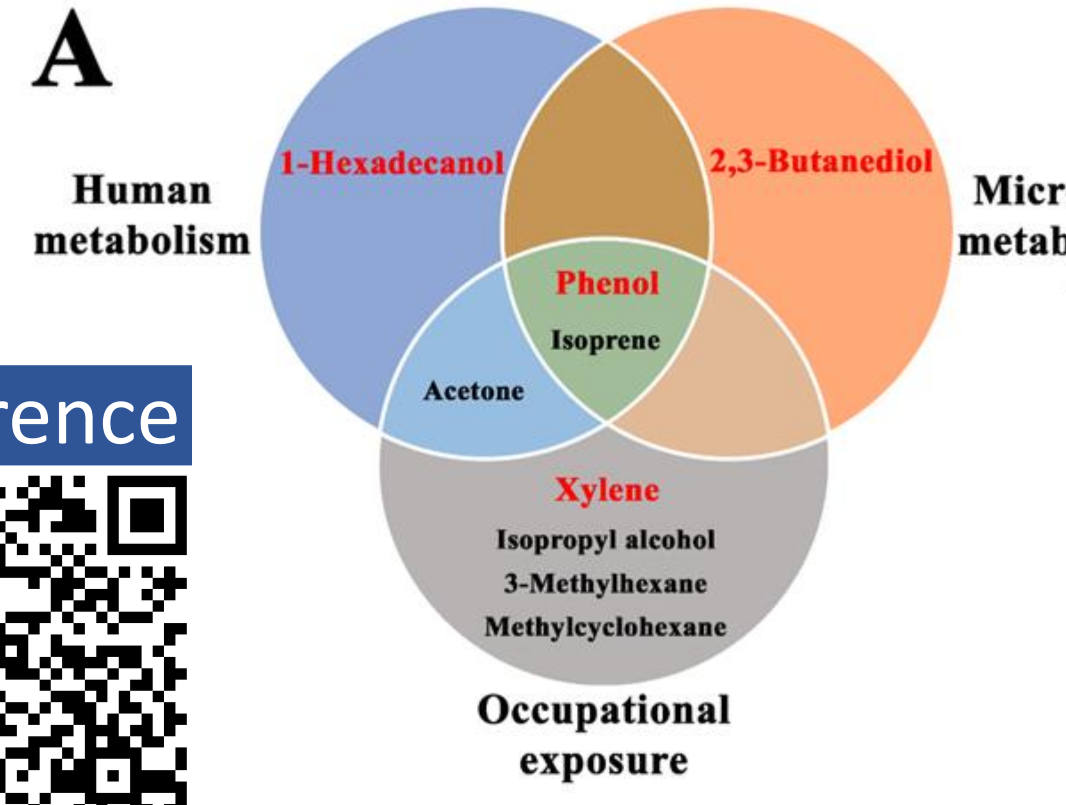


Figure 5. Exhaled breath VOCs associated with occupational exposures



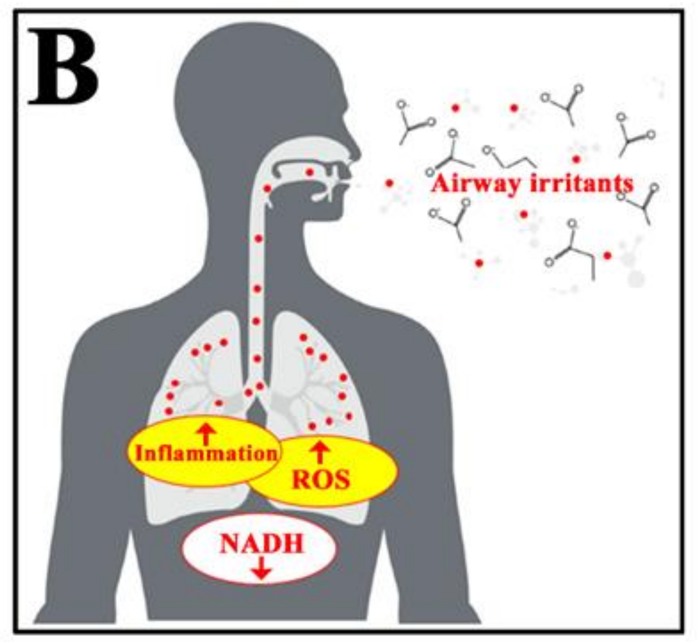


Figure 4. Exhaled breath VOCs associated with occupational asthma

Reference

https://iopscience.iop.org/article/10.1088/1752-7163/ad7b6a

Conclusions

This study provides preliminary evidence that exhaled breath VOCs may serve as biomarkers for OA and its subtypes, with 1-hexadecanol, 2,3-butanediol, phenol, and xylene showing particular promise. The findings suggest a connection between these VOCs and NADH-related ROS production, contributing to airway injury and inflammation in OA. These VOCs could provide a non-invasive method for diagnosing OA and differentiating between AA and IIA subtypes. Further research is required to validate these biomarkers and their potential role in clinical practice, which could enhance diagnostic accuracy and optimize treatment strategies for patients with OA.