



¹Oslo University Hospital, Division of Medicine, Department of Pulmonary Medicine, Oslo, Norway. ²Owlstone 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.

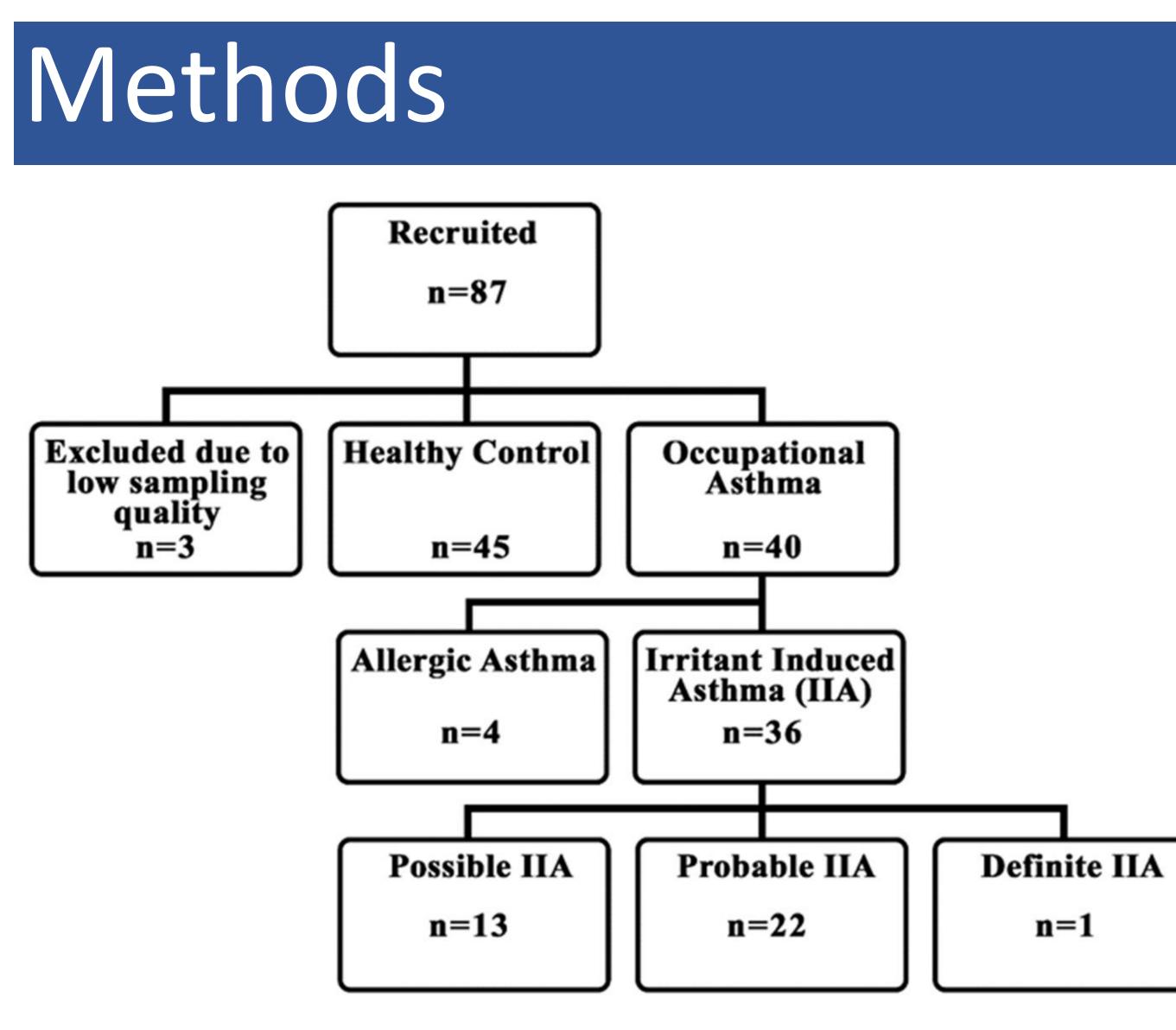


Figure 1. Overview of the study design

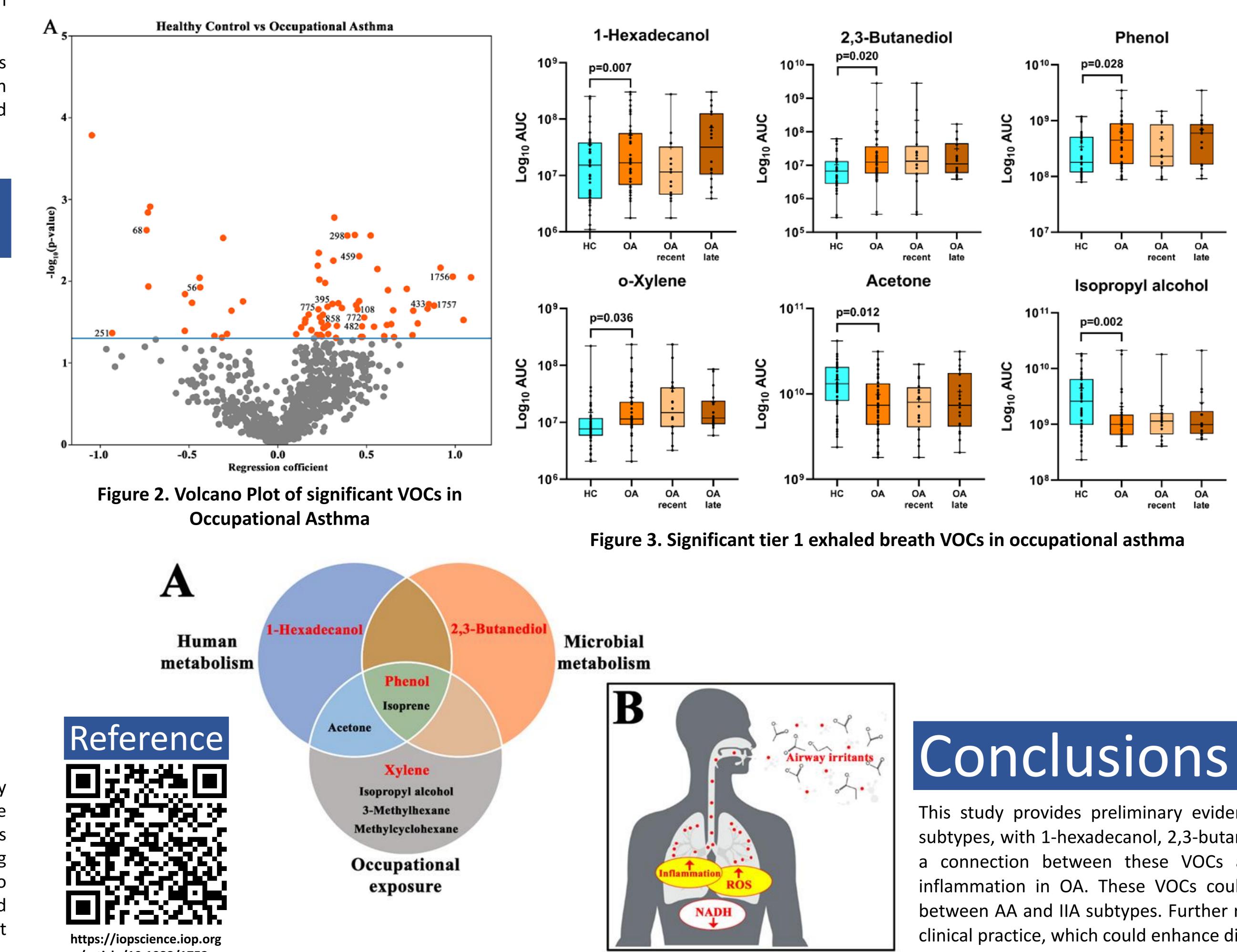
This cross-sectional study involved 40 OA patients and 45 respiratory-healthy healthcare workers (HC) (Figure 1). Breath samples were collected using the ReCIVA[®] Breath Sampler, and VOCs were analyzed using thermal desorption-gas chromatography mass spectrometry (TD-GC-MS). Statistical methods, including 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.

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

Hilde Heiro¹, Tonje Trulssen Hildre¹, Amy Craster², Liam Grimmett², Matteo Tardelli² and Bato Hammarström¹

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 1hexadecanol, 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).



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Figure 4. Exhaled breath VOCs associated with occupational asthma

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.



		0.5	1.0		1.5	2.0		2.5
-log ₁₀ (p-value)								
p-Menthone-	0.9174	-0.3231	-0.8979	-0.3147	0.2995	-1.1575	0.1399	0.1389
(E)2-Butenal	0.7889	-0.3223	-0.4857	-0.0305	1.2561	-0.4009	-0.1849	-0.1849
Decane	0.3230	0.0800	0.0426	0.2235	-0.5032	-0.0615	0.0342	0.0342
Hexanal	-0.0441	0.8052	-0.6256	0.4211	0.4733	-0.3723	0.1732	0.1732
Pentanal	-0.0043	0.2268	0.6151	-1.3684	0.1108	0.3094	-0.2021	0.3900
Pentane	0.2581	0.0852	0.7180	-0.1577	0.2974	0.1649	-0.0832	1.2648
1-Octene	0.2333	0.4263	0.2503	-0.0726	0.3235	0.2224	0.1636	1.3799
Hexadecane	-0.1542	0.3376	-0.3344	0.0761	-0.1781	-0.6158	-0.0735	-1.2452
Tetradecane	0.2430	0.0183	-0.0936	0.0449	-0.2048	-0.0432	-0.3837	0.3032
Benzene	and the second	0.3222	0.1423	-0.0984	0.1155	0.0106	0.1990	1.5699
Toluene	0.3087	0.2277	0.3364	0.4279	-0.0032	-0.1615	0.2504	1.9779
Phenylmaleic anhydride	A CONTRACTOR OF A CONTRACTOR O	-0.4262	0.0837	-0.7699	0.2235	0.5134	0.2504	0.0278
Isopropyl myristate		-0.1176	0.4112	0.3041	-0.1969	1.3728	-0.9107	0.4774
1-Hexadecanol	THE REPORT OF TH	-0.3387	-0.3343	1.0966	0.0316	1.5544	-0.6800	0.7036
5-methyl-2-furancarboxaldehyde	0.0313	0.2970	0.2123	0.1136	0.1045	-0.1740	0.1908	1.2292
2,3,5-trimethylfuran	-0.1068	0.3425	-0.1052	0.4183	-0.1672	-0.3622	0.1146	1.9907
2,3-dihydrofuran		-0.5960	-0.0672	-0.2578	-0.1062	-0.2602	0.1547	-0.9348
2,5-dimethylfuran	-0.4781	0.2752	-0.4989	-0.1353	-0.5266	0.4743	-0.2004	2.3792
4,5,6,7-tetrahydro-3,6-dimethylbenzofuran	0.1195	-1.3924	-1.1617	-0.9130	-1.0205	-0.3595	-1.1400	-1.4077
Tetrachloroethylene	0.4418	-0.2437	0.1675	-0.0606	0.0886	0.8665	-0.4408	0.2073
2-Acetyl-5-methylfuran	A REAL PROPERTY AND A REAL	0.4000	0.3944	0.1793	0.3037	0.2246	-0.0116	1.0832
2-Pentanone	Contraction of a	-0.6542	-0.5619	0.8681	-0.0681	0.4745	-0.3816	-0.1974
4-Heptanone	STATUTE OF THE OWNER WATER OF THE O	-0.4243	-1.0641	-0.9156	-0.6851	-0.0330	-0.4326	-1.0487
	-0.0567	-0.1890	0.3132	0.6474	0.3973	0.8501	-0.0156	0.2126
Cyclohexanone	and an and a second second	-0.4449	-0.2027	-0.1144	0.0460	-0.2683	0.1153	0.7096
Methyl vinyl ketone	and a second second second	0.0090	-0.0409	0.0133	0.0597	0.4682	0.0744	0.1112
D-Limonene-	North Contractor	0.2106	-1.3367	1.1600	0.0118	0.6559	-0.4562	-0.7319
Eucalyptol		-0.0793	-1.3036	-1.2485	0.0974	1.0953	-0.6513	0.3243
Acetonitrile	and the second second	0.4901	0.0618	0.1307	0.0730	0.0748	0.2088	1.6481
1-Propanol-	-0.0981	0.1430	0.1170	0.6387	-0.0971	-0.0360	0.1778	-2.1187
2-methylpyridine	AT STATISTICS OF A DESCRIPTION OF A DESCRIPANTA DESCRIPTION OF A DESCRIPTION OF A DESCRIPTION OF A DESCRIPTI	-0.0535	0.0441	0.1449	-0.1022	0.1782	-0.3223	-0.2413
Dimethyl trisulfide Caryophyllene	0.0276	0.1982	-0.0763	1.1800	-0.9439	1.1366	-0.3217	-0.8697
Caryophynene		-0.4785	-0.3866	0.2571	-0.6892	0.1065	-0.1210	-0.8311
	x	1St	sic Dust	als	NA	ila	of	net
Alcohols Halocarbons	151	"CDr	. Pr	micr	410	Alle	725	Other
Aldehydes Ketones O	AVSHC	ant op	at O		o	e e	•	
Alkanes Monoterpenes	THOLY	anic Dust Orea	1 mm	Danny	Act	Smok		
Benzene Derivates Nitriles			10	AIRS		635		
Carboxylic Acids Propanols			Endot	osins, Damp.	or Mold Acido			
Fatty Acids Pyridines			v		Chet			
Fatty Acyls Sulphur Compound	ls				- -			
Furans Terpenes								
Heterocyclic Compounds								

Figure 5. Exhaled breath VOCs associated with occupational exposures