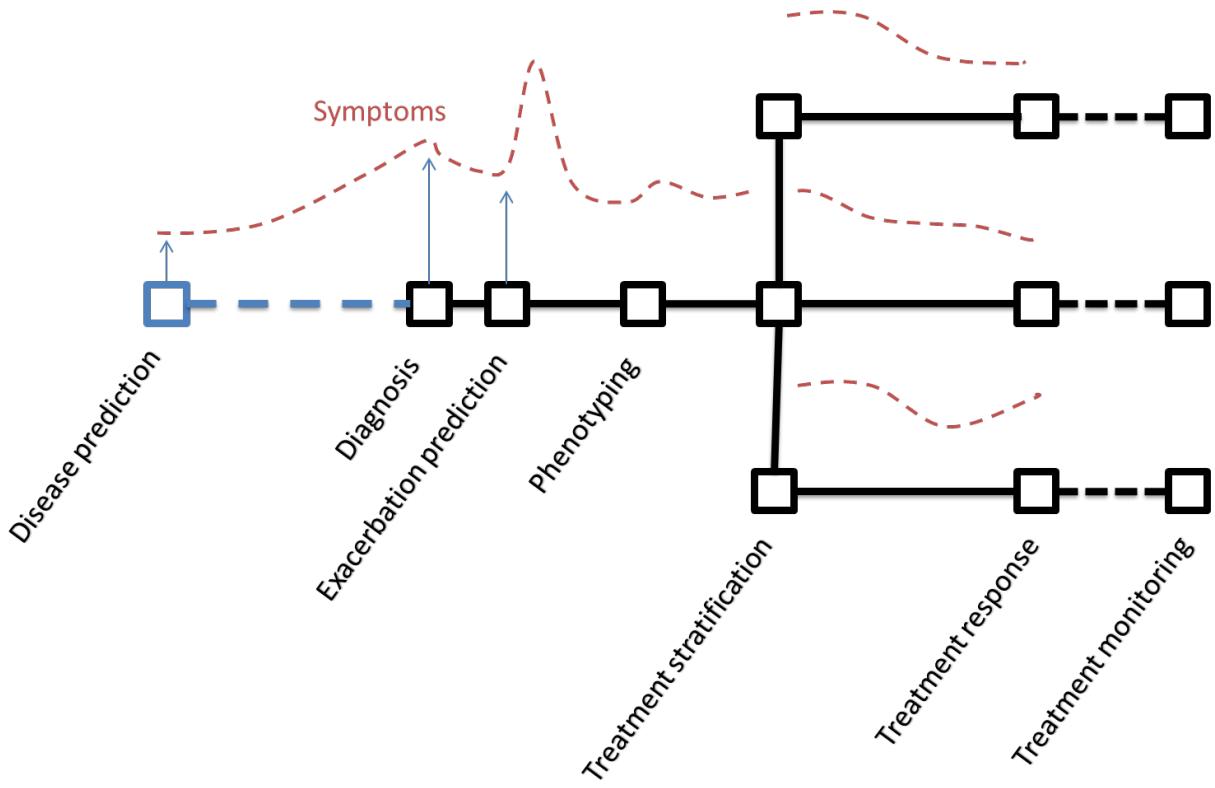




Future Clinical Applications of Breath Analysis: Asthma

Stephen J Fowler
Senior Clinical Lecturer
& Consultant Respiratory Physician



Potential clinical targets for a breath test (in asthma)

(Adapted from)

Current perspectives

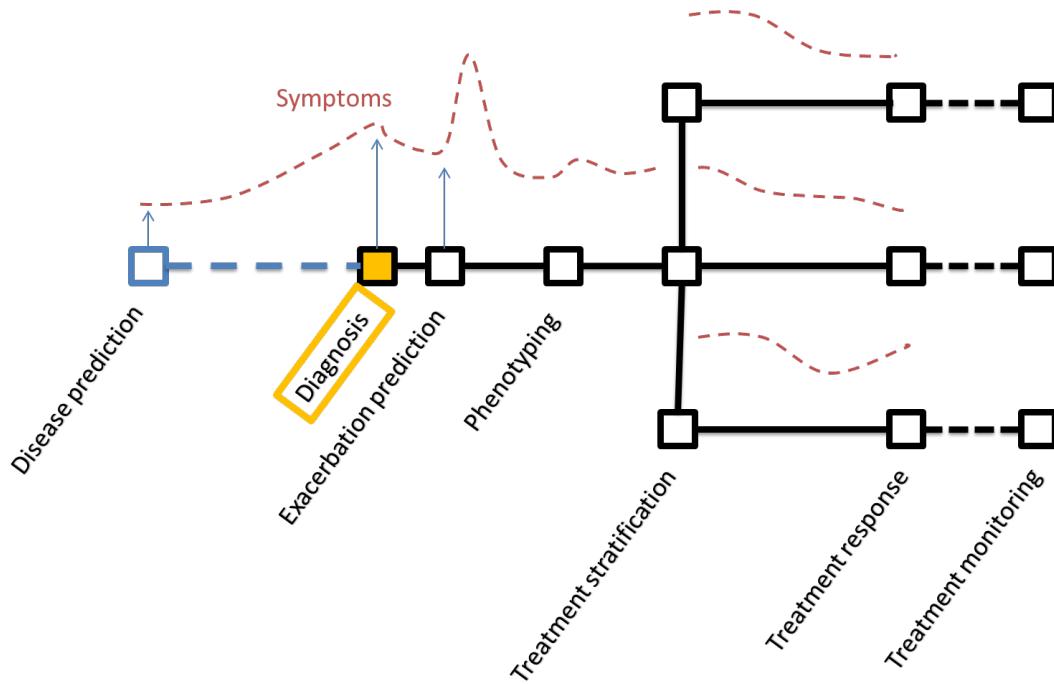
(J Allergy Clin Immunol 2016;138:970-6.)

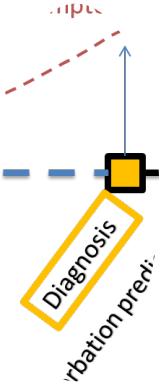
Breathomics in the setting of asthma and chronic obstructive pulmonary disease



CrossMark

Potential uses: Diagnosis



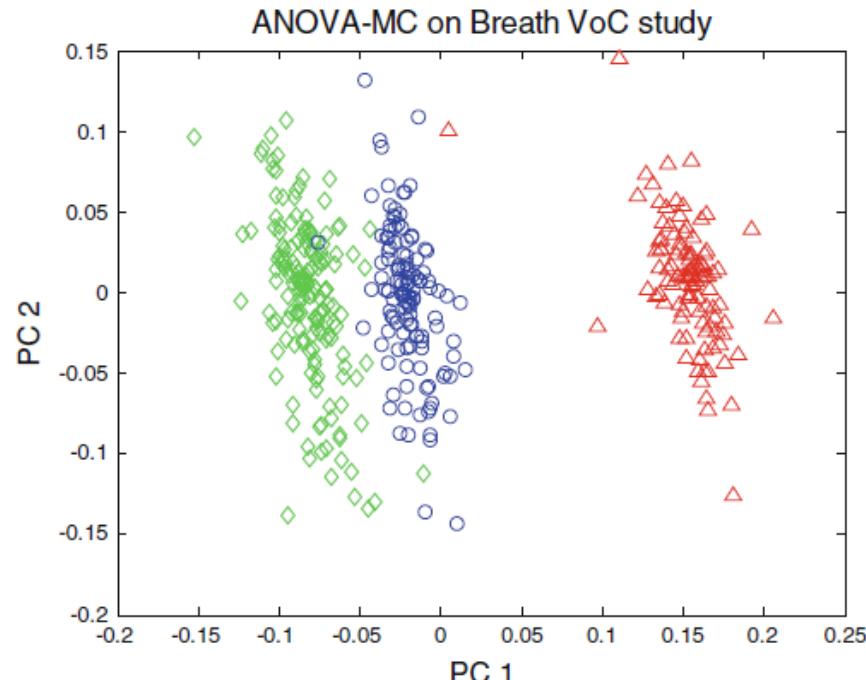


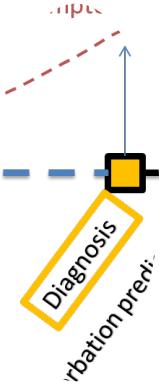
“Diagnosis”:

Asthma
vs.
COPD
vs.
Healthy

Chemometrics models for overcoming high between subject variability: applications in clinical metabolic profiling studies

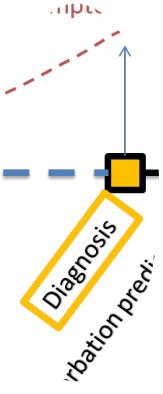
Yun Xu · Stephen J. Fowler · Ardeshir Bayat ·
Royston Goodacre





Common limitations of VOC “diagnostic” studies

- Patients with established disease
- Imbalanced control groups
- Treatment effects



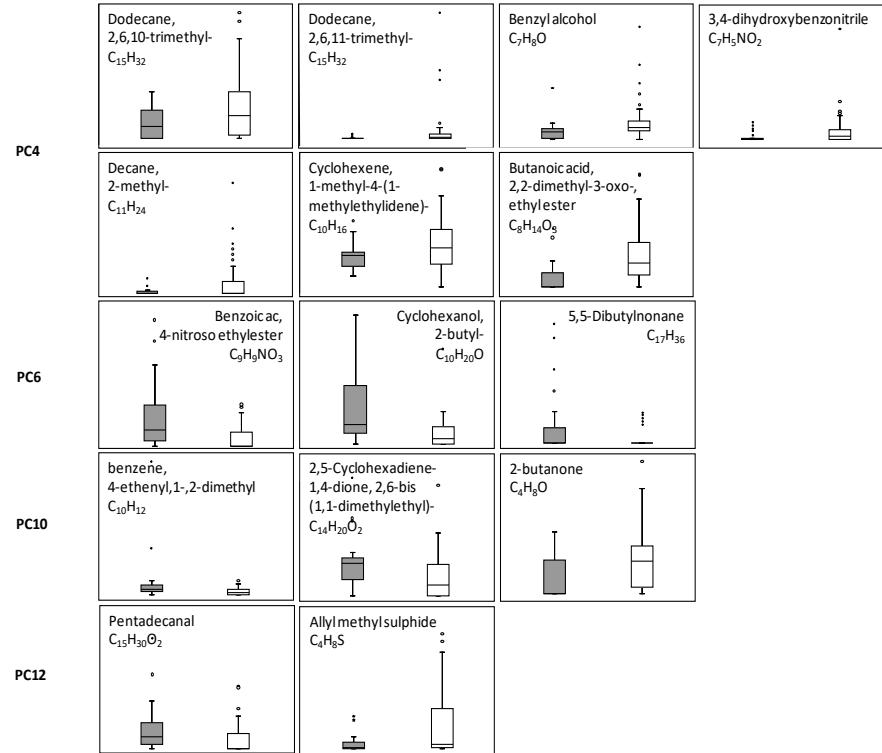
.....is a biological diagnostic for asthma (or COPD) realistic?

Definitions:

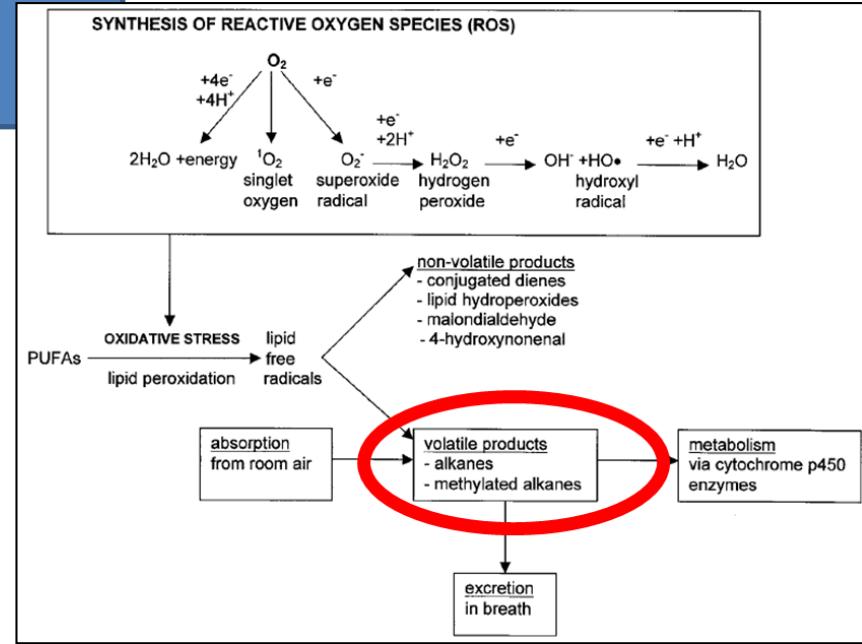
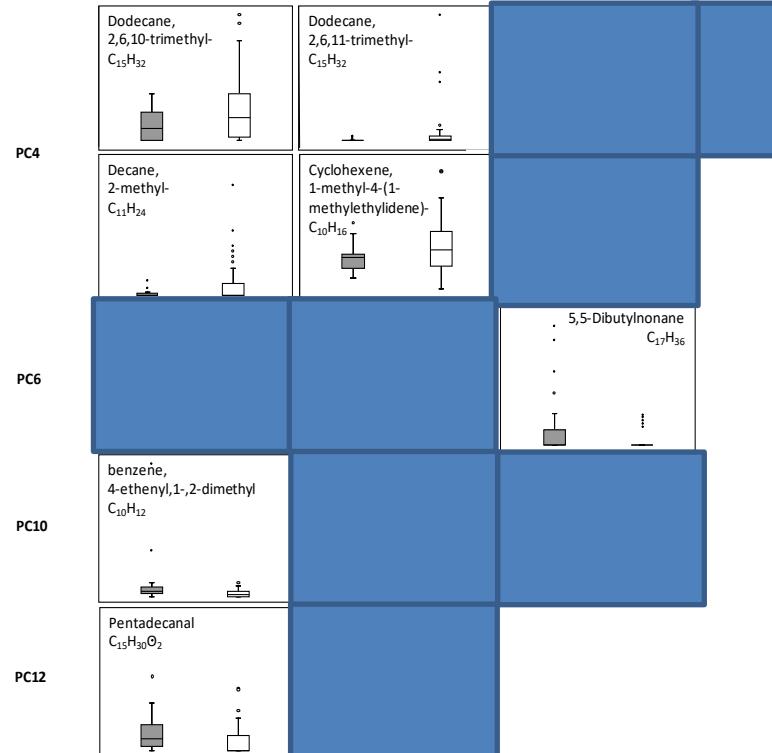
Asthma = airway calibre variability + SYMPTOMS (\pm inflammation)

COPD = not-completely-reversible-airflow obstruction + SYMPTOMS (\pm exposure history)

Are asthma diagnostic studies still useful?



Are asthma diagnostic studies still useful?

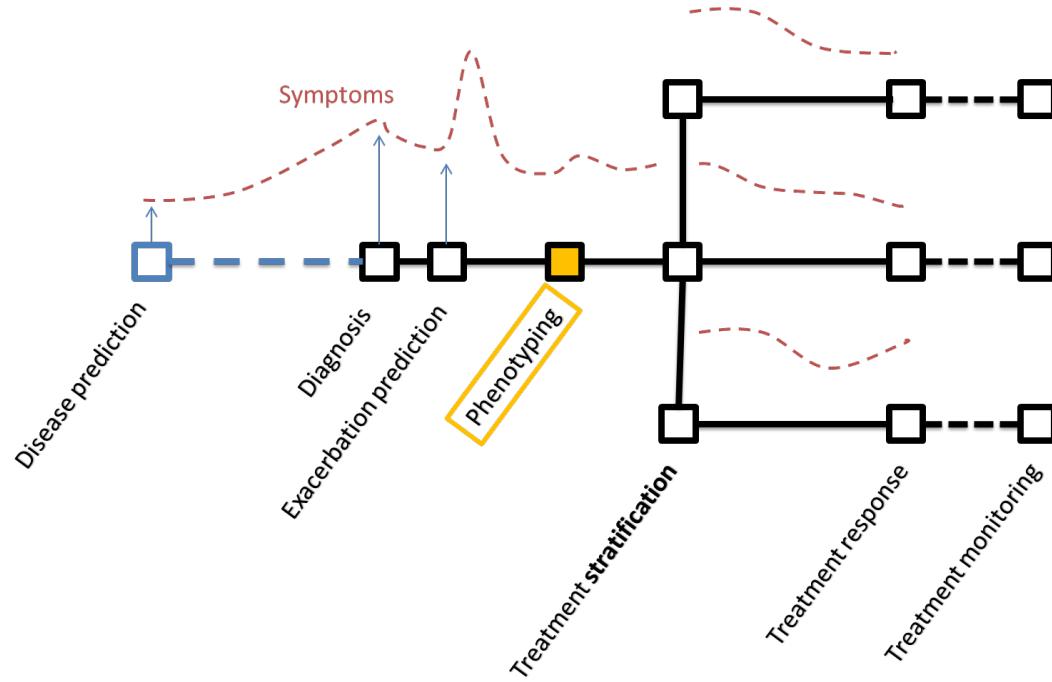


Philips J Lab Clin Chem 2000

VOCs in Asthma – mounting evidence

Compound	Compound type	Number of studies
2,4-dimethylheptane	Alkane	4
acetone	Ketone	3
dodecane	Alkane	3
isoprene	Terpene	3
1,4-dichlorobenzene	Aromatic hydrocarbon	2
2,6,10-trimethyldodecane	Alkane	2
2,6,11-trimethyldodecane	Alkane	2
2-ethyl-1,3-butadiene	Alkane	2
4-methyloctane	Alkane	2
benzene	Aromatic hydrocarbon	2
decane	Alkane	2
ethane	Alkane	2
limonene	Terpene	2
nonanal	Aldehyde	2
octanal	Aldehyde	2
p-xylene	Aromatic hydrocarbon	2
Tetradecane	Alkane	2

Potential uses: Phenotyping



Phenotypes: unbiased clustering in U-BIOPRED by eNose

- Severe asthma adults, U-BIOPRED cohort
- Sampling procedure:
 - Filtered air -> Tedlar bag -> TD tubes
- Analytical: Composite eNose platform (Cyranose / Tor Vergata / Common Invent / Owlstone Lonestar) – 158 data points / patient
- PCA then clustering (Ward -> K-means)



J Allergy Clinical Immunol - JACI-D-18-00626 2
Identification and prospective stability of eNose
derived inflammatory phenotypes in severe asthma.
Brinkman, Wagener, ...Fowler, Sterk

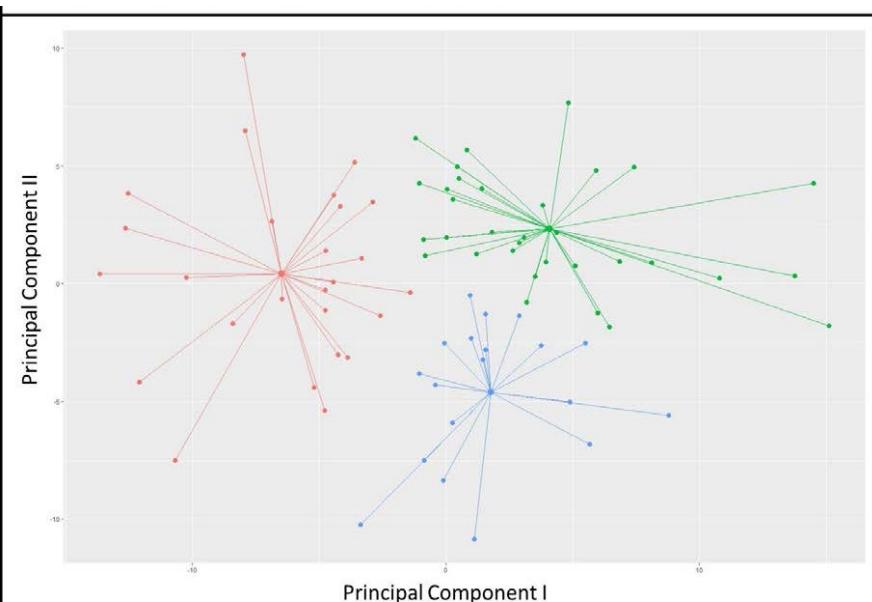
- Samples from 78 patients / 7 sites / 5 countries
- Age 56 (45-64) yrs, 41% male, 13% current smokers, 42% on oral steroids, 68% atopic, FEV₁ 77 (61-89) % pred
- PCA -> 34 PC's Eigenvalue >1



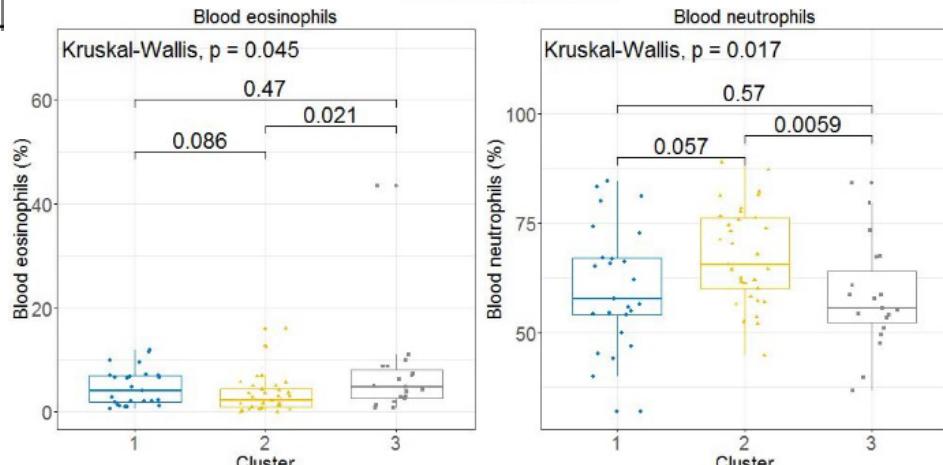
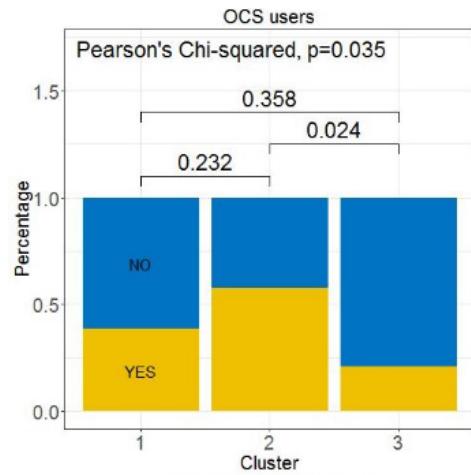
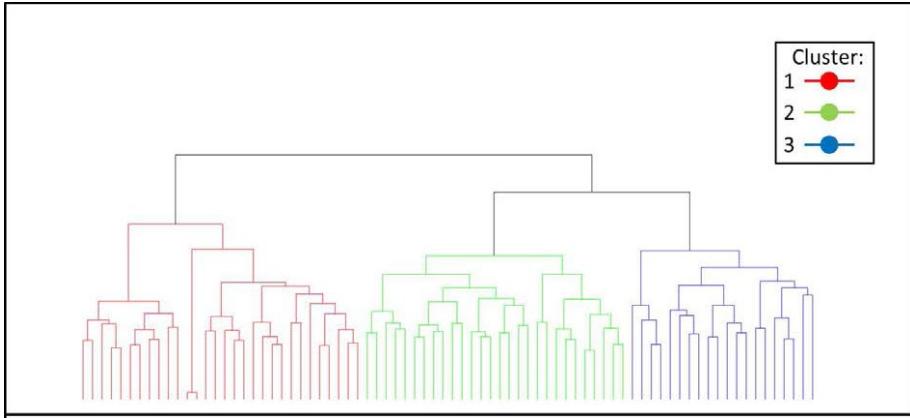
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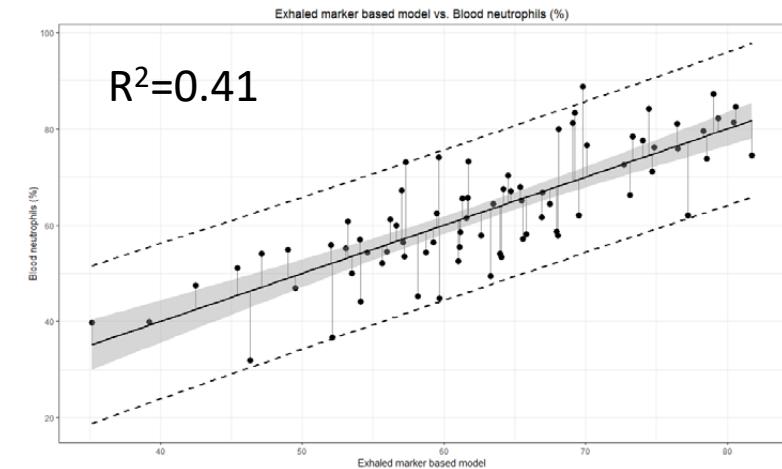
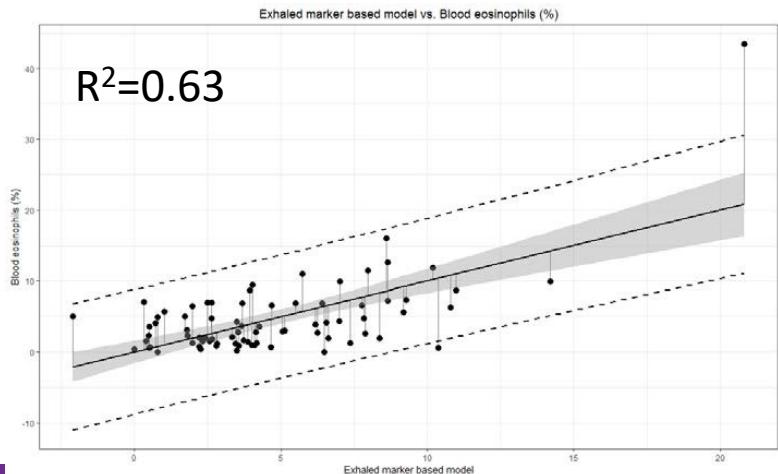
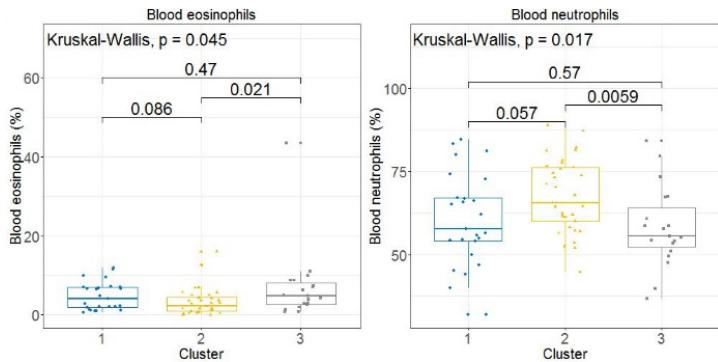
Ward and K-Means clustering outcomes

Cluster:
1 -●-
2 -○-
3 -●-

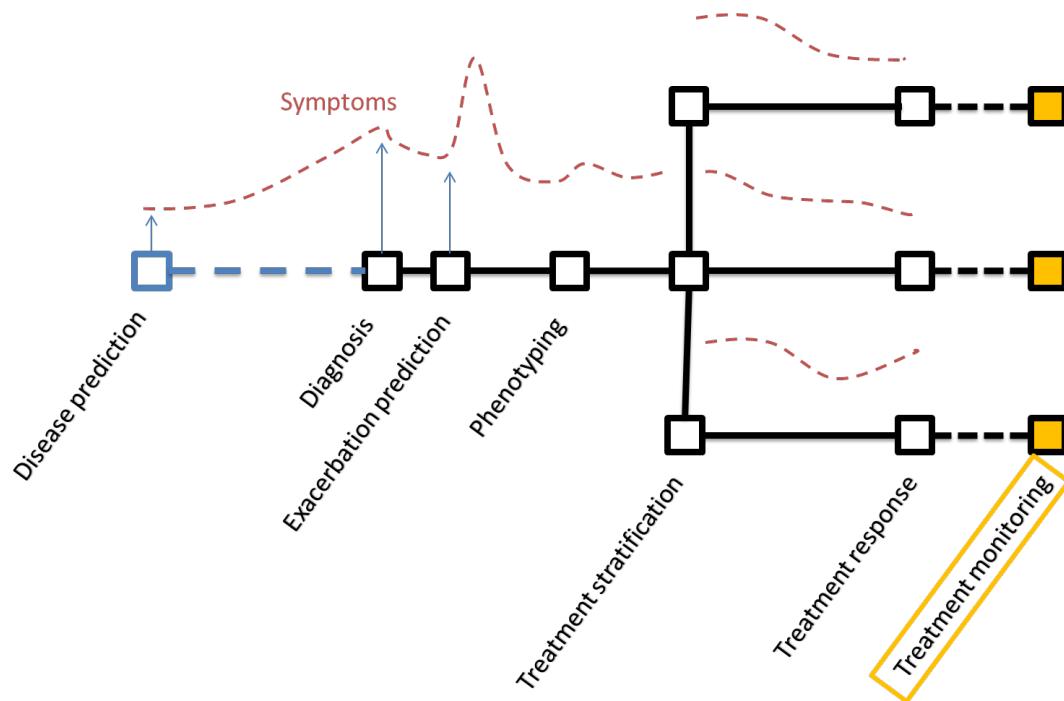


Clinical differences between clusters



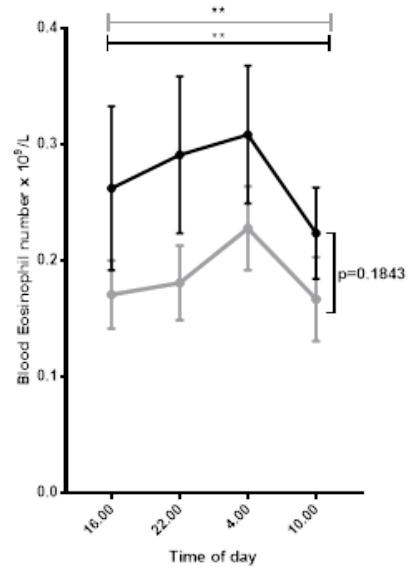
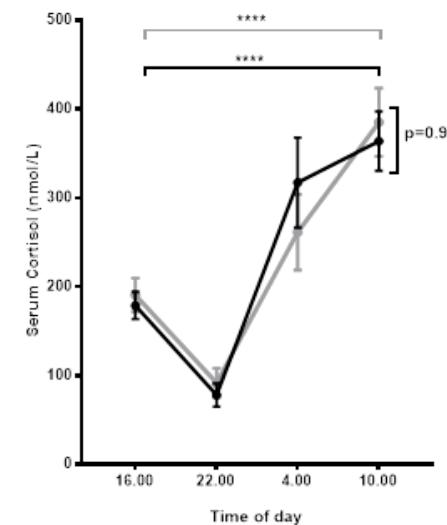


Potential uses: Treatment monitoring



Asthma – special considerations?

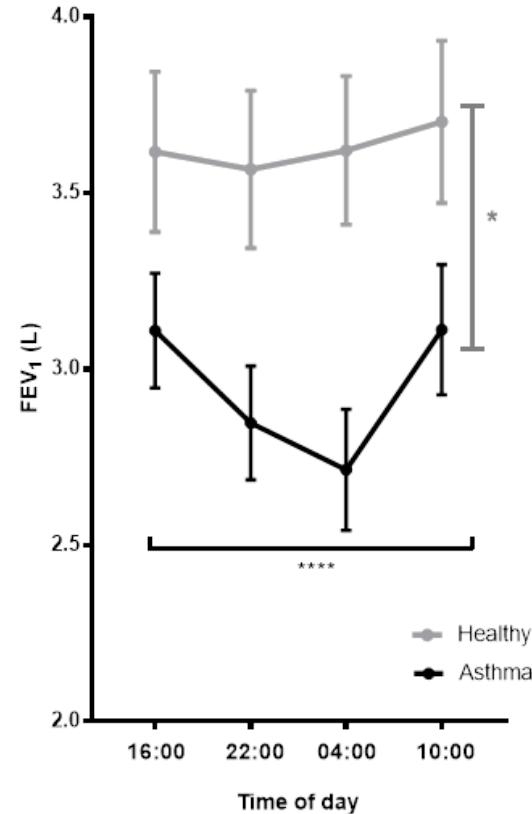
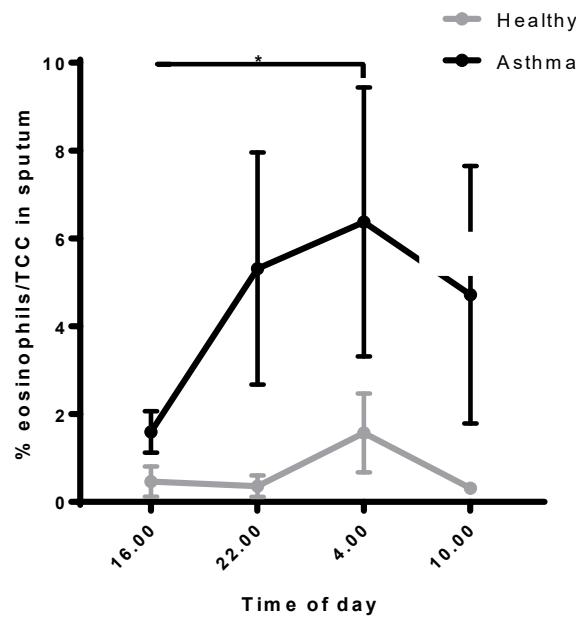
	Healthy (n=10)	Asthma (n=10)
Age (years)	40.2 ± 4.2	42.8 ± 3.17
M:F	7:3	9:1
BMI kg/m ² (\pm SEM)	26.73 ± 1.93	27.03 ± 1.38
FEV ₁ (L)	3.64 ± 0.25	3.16 ± 0.14
FEV ₁ % Predicted	98.67 ± 3.21	81.48 ± 2.94
FEV ₁ /FVC Ratio (%)	80.37 ± 1.95	67.16 ± 2.14
Reversibility (mls)	52 ± 33.86	265 ± 43.85
Skin Prick Positive (HDM, cat, grass)	1	10
ICS mean dose equivalent to BDP (μ g)	-	520 ± 68



Durrington

Am J Respir Crit Care Med on line

Circadian rhythm in asthma



Breath analysis: looking to the future

Follow on studies

-> POC

-> **Validation**

-> **Clinical Effectiveness**

Sampling and Analytic refinements:

- How will the test be used?
- Location / patients
 - Acute
 - Outpatient
 - ICU / ventilator studies



Acknowledgments



Manchester
Biomedical Research Centre



Innovate UK
Technology Strategy Board

