The clinical management of acute asthma

S1 OBESE, NON-EOSINOPHILIC ASTHMA: FREQUENT EXACERBATORS IN A REAL-WORLD SETTING

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Introduction In the UK, asthma deaths are at their highest level this century (1). Increased recognition of at-risk patients is needed. This study phenotyped frequent asthma exacerbators, and used machine learning to predict frequent exacerbators. We hypothesised that frequent exacerbators would have more severe peripheral eosinophilia than infrequent exacerbators.

Methods Patients admitted to Watford General Hospital with an asthma exacerbation between 1st March 2018 – 1st March 2020 were included. Patient data was retrospectively collected from

hospital and primary care records. Patients were organised into two groups: “Infrequent Exacerbator” (1 admission in the previous 12 months) and “Frequent Exacerbator” (≥ 2 admissions in the previous 12 months). Good adherence to inhaled corticosteroids (ICS) was defined as medication possession ratio (MPR) ≥ 0.8 ; poor adherence was defined as MPR ≤ 0.5 . Machine learning models were used to predict frequent exacerbators.

Results 200 patients admitted for asthma exacerbations were randomly selected (73% female; mean age 47.8 ± 19.3 years; table 1). Peripheral eosinophilia was uncommon in either group (19% vs 21%). More frequent exacerbators were being treated with high-dose ICS (46.5% vs 23.2%; $P < 0.001$), and frequent exacerbators used more SABA inhalers (10.9 vs 7.40; $P = 0.01$) in the year preceding the current admission. Good adherence to ICS was similarly low between both groups (40.0% vs 48.3%). BMI was raised in both groups (34.2 vs 30.9). Logistic regression classifier was the most accurate machine learning model for predicting frequent exacerbators (AUC = 0.80).

Abstract S1 Table 1 Characteristics of patients admitted for asthma exacerbations

	Infrequent Exacerbators	Frequent Exacerbators	P Value
n	100	100	
Age, years	46.5 $\pm$ 20.9	49.0 $\pm$ 17.5	0.25
Female (%)	69.0	77.0	0.20
Ethnicity (%)			
	Caucasian 82.0	Caucasian 83.0	0.85
	Asian 15.0	Asian 13.0	0.68
	Afro-Caribbean 1.0	Afro-Caribbean 1.0	1.00
Exacerbations managed in primary care in the last 12 months	0.79 $\pm$ 1.15	1.92 $\pm$ 1.83	<0.001***
FEV1/FVC (%)	71.0 $\pm$ 13.4	70.9 $\pm$ 16.8	0.96
Obstructive lung function (%)	34.5	39.1	0.60
FeNO, ppb	42.3 $\pm$ 57.1	24.8 $\pm$ 13.6	0.97
High FeNO (%)	27.3	12.5	0.44
Blood eosinophils, $\times 10^9/L$	0.27 $\pm$ 0.39	0.32 $\pm$ 0.41	0.45
Eosinophilia (%)	19.0	21.0	0.72
Blood neutrophils, $\times 10^9/L$	7.91 $\pm$ 3.87	7.70 $\pm$ 3.11	0.87
Neutrophilia (%)	45.0	49.0	0.57
Total IgE, kU/L	470.3 $\pm$ 870.3	378.9 $\pm$ 755.1	0.18
High IgE (%)	68.2	52.9	0.11
Patients with CT scan changes (%)	78.0	90.2	0.09
ICS-LABA (%)	60.6	88.9	<0.001***
High-dose ICS (%)	23.2	46.5	<0.001***
Long-term OCS (%)	3.03	10.1	0.04*
OCS courses in past year	0.99 $\pm$ 1.21	2.06 $\pm$ 2.34	0.005**
SABA dispensed in past year	7.40 $\pm$ 7.89	10.94 $\pm$ 9.39	0.01*
SABA overuse (%)	64.8	78.6	0.58
ICS MPR	0.72 $\pm$ 0.44	0.72 $\pm$ 0.40	0.66
Good ICS adherence (%)	48.3	40.0	0.35
Poor ICS adherence (%)	36.7	30.8	0.49
Past Medical History			
	COPD (%)	3.03	0.46
	GORD (%)	46.5	0.02*
	Depression (%)	32.3	0.68
Ex or current smoker (%)	64.5	69.9	0.51
BMI	30.9 $\pm$ 6.06	34.2 $\pm$ 9.48	0.14
Obese (%)	63.4	63.6	0.98
Follow-up within 4 weeks (%)	54.0	67.0	0.06

Data presented as mean $\pm$ standard deviation, unless stated differently.

FEV1/FVC: ratio of Forced Expiratory Volume in 1 second to the Forced Vital Capacity. FeNO: fractional exhaled nitric oxide. ICS: inhaled corticosteroid. LABA: long-acting β_2 -agonist. OCS: oral corticosteroid. SABA: short-acting β_2 -agonist. MPR: medication possession ratio. COPD: chronic obstructive pulmonary disease. GORD: gastro-oesophageal reflux disease.

High FeNO defined as FeNO > 40 . Eosinophilia defined as blood eosinophils $\geq 0.5 \times 10^9/L$. Neutrophilia defined as blood neutrophils $\geq 7.2 \times 10^9/L$. High IgE defined as serum IgE ≥ 81 kU/L. Good ICS adherence defined as ICS MPR ≥ 0.8 . Poor ICS adherence defined as ICS MPR ≤ 0.5 . SABA overuse defined as ≥ 3 SABA inhalers per year.

Conclusions Patients admitted for asthma are predominately female, obese and non-eosinophilic. Patients who require multiple admissions per year have poorer asthma control at baseline. Machine learning algorithms can predict frequent exacerbators using clinical data available in primary care. Instead of simply increasing the dose of corticosteroids, multidisciplinary management targeting Th2-low inflammation should be considered for these patients, including weight loss regimens, reflux management and macrolide therapy.

S2 DERIVATION OF A PROTOTYPE ASTHMA ATTACK RISK SCALE CENTRED ON BLOOD EOSINOPHILS AND EXHALED NITRIC OXIDE

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Rationale Reduction of the risk of asthma attacks is a major goal of clinical management.

Objective To develop a risk scale to predict asthma attacks based on the blood eosinophil count and exhaled nitric oxide.

Methods Trial-level data were extracted from the Novel START, CAPTAIN, Benralizumab phase 2b, PATHWAY, STRATOS 1-2, QUEST and DREAM trials. Attack rates for control arm patients ($n=3051$) were stratified by blood eosinophils and exhaled nitric oxide. Aggregate frequency-weighted biomarker-stratified rate ratios were calculated and applied to reference GINA treatment step attack rates derived from 222,817 patients. Other parameters included were a recent asthma attack history (≤ 1 year), ≥ 2 concurrent clinical risk factors*, and treatment step. We validated the scale by comparing the frequency-weighted predicted versus observed biomarker-stratified asthma attack rates in the derivation trials.

Results Biomarker-stratified asthma attack rate ratios were 0.65 in the lowest type 2 biomarker combination group and 2.29 in the highest. A previous asthma attack and/or having concurrent risk factors independently increased rates 2.8- and/or 1.3-fold, respectively. Predicted annual attack rates ranged from 0.06 in the lowest biomarker step 1&2 patients to 2.6 in the highest biomarker step 5 patients. The resultant scale is shown

Abstract S2 Figure 1 Prototype Oxford asthma attack risk ScaLE (ORACLE). Numbers in each cell are predicted annual asthma attack rates for patients over the age of 12 if treatment is not changed. Blood eosinophil count is contemporaneous or the highest result in last 12 months; exhaled nitric oxide level is contemporaneous. *Risk factors are defined by GINA: poor symptom control, low lung function, non-adherence, reliever over-use, previous intubation/critical asthma attack, selected comorbidities, environmental exposures.

in figure 1. There was close agreement between frequency-weighted observed and predicted asthma attack rates: the intraclass correlation coefficient [95%CI] was 0.83 [0.78–0.86], the weighted least squares regression equation was $y=0.94x - 0.08$ (slope [0.92–0.96], constant [-0.09– -0.07]) with $R^2 = 0.79$, and the Bland-Altman fixed bias estimate was -0.08 [-0.58–0.41].

Conclusion A prototype scale based on biomarkers of type 2 inflammation shows feasibility and potential to predict asthma attacks which may be prevented by treatment.

Please refer to page A188 for declarations of interest related to this abstract.

S3 EMERGENCY ROOM VISITS AND RESCUE MEDICATION USE IN PATIENTS WITH ASTHMA IN THE IRIDIUM STUDY AND THEIR IMPACT ON CARBON FOOTPRINT

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Introduction/Rationale Patients with uncontrolled asthma experience severe exacerbations that may require emergency room (ER) visits associated with substantial CO₂ emissions. Metered-dose inhalers (MDIs) that deliver rescue medications contain greenhouse gases with a substantial carbon footprint. We analyzed the effect of once-daily indacaterol/glycopyrronium/mometasone furoate (IND/GLY/MF) versus twice-daily salmeterol/fluticasone (SAL/FLU) on ER/hospital visits and rescue medication use in the IRIDIUM¹ study, and its impact on carbon footprint.

Methods Patients who received either IND/GLY/MF high-dose (150/50/160 µg) or IND/GLY/MF medium-dose (150/50/80 µg) via Breezhaler® or SAL/FLU high-dose (50/500 µg) via Diskus® for 52 weeks were included. Patients used salbutamol 100 µg/albuterol 90 µg MDI as a rescue medication. The