REFERENCE

1. Brant A, Nightingale S, Berriman J, *et al.* Supermarket baker's asthma: how accurate is routine health surveillance? *Occup Environ Med* 2005;**62**:395–9.

Clinical studies in asthma

S7 ADIPOSITY AND ASTHMA, PULMONARY FUNCTION AND ATOPY IN 11-YEAR OLD CHILDREN: A BIRTH COHORT STUDY

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Background Results of studies investigating the association between obesity and asthma, atopy and lung function have been inconsistent, in part due to the limitation of BMI in evaluating body adiposity.

Objectives To investigate the association between obesity and asthma, wheeze, atopy, lung function and bronchial hyper-responsiveness in children at age 11 years using bioelectrical impedance (BIA) and BMI.

Methods Children from the unselected birth cohort study attending follow-up at age 11 years had percent body fat (PBF) and truncal fat (PTF) assessed using BIA (Tanita BC-418). Weight and height were also measured. Current asthma and wheeze were derived from a validated respiratory questionnaire. Atopy was ascertained using skin prick testing. Lung function was assessed using spirometry and bronchial hyper-responsiveness by 5-step methacholine challenge according to ATS guidelines.

Results 646 children (339 male) completed anthropometric measurements. BMI z-score, PBF and PTF were associated with current wheeze (OR [95% CI]: 1.27 [1.03 to 1.57], $p=0.03$; 1.04 [1.00, 1.08], $p=0.04$; 1.04 [1.00, 1.08], $p=0.04$ respectively). BMI z-score, PBF and PTF were also associated with current asthma (1.30 [1.04 to 1.63], $p=0.02$; 1.04 [1.00 to 1.08], $p=0.06$; 1.04 [1.00 to 1.08], $p=0.04$). However, the effect of PBF and PTF appeared strongest in girls (PBF: 1.12 [1.04 to 1.20], $p=0.004$; PTF: 1.11 [1.04 to 1.20], $p=0.003$; $p=0.05$ and $p=0.04$ for interactions respectively). Children were defined as normal or overweight according to BMI (23% overweight) and PBF (29.8% overweight) cut-offs; overweight children had an increased risk of asthma (BMI: 1.73 [0.99 to 3.02], $p=0.05$; PBF: 2.09 [1.23 to 3.32] $p=0.006$). This was highly significant in girls (BMI: 3.34 [1.43 to 7.83], $p=0.005$; PBF: 4.74 [1.98 to 11.35], $p<0.001$; $p=0.05$ and $p=0.02$ for interactions respectively). Increasing BMI was associated with increases in both FEV₁ and FVC but reductions in FEV₁: FVC ratios. This association was again stronger in girls than boys. No associations between adiposity and atopy or bronchial hyper-responsiveness were found.

Conclusion Higher BMI z-score, PBF and PTF were associated with increased risks of wheeze and asthma. This effect was stronger in girls. BIA measurements appeared to have stronger associations in

girls with outcomes than BMI. This may reflect the ability of BIA to measure adiposity more accurately than BMI.

S8 SENSITIVITY OF IMPULSE OSCILLOMETRY AND SPIROMETRY IN THE ASSESSMENT OF BETA-BLOCKER INDUCED BRONCHOCONSTRICTION AND BETA-AGONIST BRONCHODILATION IN MILD-TO-MODERATE ASTHMATICS

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Introduction and Objectives Impulse oscillometry (IOS) is known to be a sensitive marker of airway dysfunction, but is commonly associated with a wider variation than spirometry. The effects of β -blocker induced bronchoconstriction on IOS have not been studied. We compared the sensitivities of IOS and spirometry in the assessment of bronchoconstriction to propranolol and bronchodilatation to salbutamol.

Methods Mild-to-moderate persistent stable asthmatics taking $\approx 1000 \mu\text{g}$ day budesonide or equivalent, received a single dose of 10 mg or 20 mg of oral propranolol followed by histamine bronchial challenge testing (PC10), with recovery to nebulised salbutamol (5 mg). Spirometry and IOS were measured pre and 2-h post β -blocker, post histamine and 20 min post salbutamol. Pre vs post % change (95% CI) values were compared and standardised response means (SRM) were calculated to assess the "signal to noise" of each test.

Results Thirteen patients (mean age, 34 years) completed per protocol: 11 received 20 mg of oral propranolol. All IOS indices showed a greater magnitude of response to propranolol (ie, as % change) compared to spirometry. After adjustment for test variability, in response to propranolol, SRM's for IOS outcomes were better than spirometry with the highest seen with R5 and *fres*. Likewise for the bronchodilator response to salbutamol the highest SRMs were also seen with R5 and *fres* (see Abstract S8 table 1).

Conclusions IOS is a more sensitive response outcome than spirometry with respect to bronchoconstriction to oral propranolol and bronchodilatation post salbutamol in mild-to-moderate asthmatics.

S9 INHALED AND SYSTEMIC CORTICOSTEROID RESPONSE IN MODERATE-TO-SEVERE ASTHMA ASSESSED BY EXTENDED EXHALED NITRIC OXIDE AND LUNG FUNCTION

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Introduction and Objectives Alveolar nitric oxide (CANO) has been proposed as a potential biomarker of small airway inflammation in

Abstract S8 Table 1

Outcome	Bronchoconstriction		Bronchodilatation	
	Mean % change (95% CI), p Value	Standardised response mean	Mean % change (95% CI), p Value	Standardised response mean
Spirometry				
FEV ₁ (l)	4.6% (1.9 to 7.3), $p=0.009$	0.86	31.5% (18.2 to 44.7), $p<0.001$	1.67
FEF _{25–75} (l)	6.2% (–0.2 to 12.6), $p=0.116$	0.47	57.9% (29.1 to 86.7), $p<0.001$	1.42
Impulse oscillometry				
R5 (Airway Resistance at 5 Hz) (kPa L/s) (Total airway resistance)	30.8% (14.01 to 47.6), $p<0.001$	1.32	45.8% (36.7 to 55), $p<0.001$	1.87
R5-20 (difference) (Small airways resistance)	104.1% (22.6 to 185.6), $p=0.004$	1.05	115.6% (55.6 to 175.7), $p<0.001$	1.43
AX (area) (Respiratory reactance)	118.5% (37.2 to 200), $p=0.007$	0.94	82.6% (73.9 to 91.3), $p=0.001$	1.26
<i>fres</i> (Resonant Frequency) (Hz)	39.4% (16.6 to 54.3), $p=0.002$	1.13	50.7% (40.7 to 60.8), $p<0.001$	2.13

severe asthma. We wished to investigate the effects on CANO of the addition of coarse or fine particle inhaled corticosteroids to standard therapy in severe asthma.

Methods Severe asthmatics taking ≥ 1600 $\mu\text{g/day}$ budesonide or equivalent performed a randomised open-label crossover study. Subjects with $\text{FEV}_1 < 80\%$, gas trapping and elevated CANO (≥ 2 ppb) entered a 6 week dose-ramp run-in of Fluticasone/Salmeterol (FPSM) 250/50 μg twice daily for 3 weeks, then 500/50 μg twice daily for 3 weeks. Patients then received additional HFA-BDP 200 μg twice daily or FP 250 μg twice daily for 3 wks in a crossover. Participants then received prednisolone (PRED) 25 mg/day for 1 week. Nitric oxide, lung function, mannitol challenge, systemic inflammatory markers and urinary cortisol were measured.

Results 15 patients completed per protocol: mean (SD) age, 51 (12) yr; FEV_1 , 58 (13)% predicted; residual volume, 193 (100)% predicted; mannitol PD10177 (2.8) μg . There was no significant difference between FPSM and any add-on therapy for CANO. FPSM/BDP and FPSM/PRED suppressed JawNO and FENO compared to FPSM alone. There was no significant difference between treatments for pulmonary function or bronchial challenge. ECP, e-selectin and ICAM-1 were significantly suppressed by FPSM/PRED compared to FPSM and FPSM/FP but not FPSM/BDP. Plasma cortisol was significantly suppressed by FPSM/PRED only.

Conclusion In severe asthma, alveolar nitric oxide is insensitive to changes in dose and delivery of inhaled corticosteroids and is not suppressed by systemic corticosteroids. Additional inhaled HFA-BDP caused reductions in FENO and JawNO without adrenal suppression. Oral prednisolone reduced FENO and JawNO with suppression of systemic inflammatory markers and urinary cortisol.

S10 IS A HIGH FeNO A MARKER OF NON-ADHERENCE IN DIFFICULT ASTHMA?

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Background Non-adherence to inhaled combination therapy (ICT) is a major contributor to poor control in difficult asthma¹; however identifying non-adherence in this population is challenging. We have shown that suppression of fractional exhaled nitric oxide (FeNO), following directly observed inhaled corticosteroid can identify non-adherence²; it has previously been suggested that a single high FeNO measurement can identify non-adherence in difficult asthma.

Methods We performed a retrospective analysis of patients attending a difficult asthma clinic between January 2007 and December 2010. Prescription refill data, patient demographics, FeNO and lung function were collated. ICT prescription refill ratio % was calculated as the number of doses refilled/number of doses prescribed over 6 months $\times 100$.¹ Non-parametric correlation analysis was performed. Tests for non-adherence defined as ICT prescription refill cut-offs of $<80\%$ and $<50\%$ were assessed.

Results One hundred and forty-six patients underwent systematic evaluation during the time period. Patient characteristics are displayed in Abstract S10 table 1. FeNO level and ICT prescription refill ratio did not correlate significantly ($r = -0.11$, $p = 0.2$). For FeNO > 45 ppb, there was a trend with ICT prescription refill ratio of $<80\%$ ($p = 0.06$); significant in patients not prescribed oral steroids ($n = 99$, $p = 0.016$). No relationship existed between FeNO > 100 ppb at both prescription refill ratio cut-offs. Using FeNO > 45 ppb to define non-adherence, negative (NPV) and positive predictive values (PPV) were: 66% and 61% for $<80\%$ ICT prescription refill ratio; 71% and 33% for $<50\%$ prescription refill ratio. Using FeNO > 100 ppb, NPV and PPV were: 55% and 52% for $<80\%$; 69% and 32% for $<50\%$ prescription refill ratio.

Abstract S10 Table 1 Patient characteristics

Patient characteristic	n = 146
Age (years) †	40.6 $\pm$ 15.1
Sex (F/M)	100/46
Inhaled corticosteroid (BDP equivalent μg)*	1600 (800–2000)
Long acting β -agonist, n (%)	142 (97)
Theophylline, n (%)	75 (51)
Maintenance oral steroids, n (%)	47 (32)
FEV ₁ (L) % predicted †	79 $\pm$ 24
FEV ₁ / FVC ratio % †	69 $\pm$ 13
FeNO (ppb)*	46 (21–89)
ICT prescription refill ratio (%)*	89 (49–103)

*Median (IQR).

†Mean $\pm$ SD.

Conclusion While there is a weak relationship between a single point-in-time FeNO measurement and non-adherence to ICT in difficult asthma, this cannot be used as an alternative to our previously described FeNO suppression test.

REFERENCES

1. Gamble, et al. *AJRCCM* 2010; **180**:817–22.
2. McNicholl, et al. *AJRCCM* 2011; **183**:A437.

S11 INAPPROPRIATE PRESCRIBING OF COMBINATION INHALERS IN ASTHMA IN NORTHERN IRELAND (NI)

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Introduction BTS/SIGN asthma management guidelines recommend a stepwise approach to the use of anti-inflammatory therapy, including the addition of inhaled combination therapy (ICT) at Step 3. In NI, ICT accounts for 47% (£23 million) of the entire respiratory drug spend suggesting excessive utilisation of ICT.

Methods Using data from a large representative sample of GP practices in NI, we looked at subjects who had a new prescription of ICT (Symbicort, Seretide, Fostair). Data were collected from the Information and Registration Unit of the Business Services Organisation for the period January to December 2010 inclusive for subjects aged 5 to 35. We examined treatment prior to ICT, SABA, oral steroid and antibiotic use and, prescription filling in the preceding 6 and 12 months.

Results 42 665 subjects received 2 or more prescriptions for any respiratory drug (BNF categories 3.1, 3.2, 3.3) and of these 12 989 received ICT with 3953 new ICT prescriptions. 2642 (67%) of these had no ICS in study year or 6 month lead in period. A further analysis of a 12-month lead in period showed 39 315 subjects with 2 or more respiratory prescriptions and out of these 11 962 received ICT with 2609 new ICT prescriptions. 1359 (52%) had no ICS in the study year or 12-month lead in. A sub-group analysis ($n = 600$) showed that 51% of first prescriptions for ICT are made in Jan–April but in the previous 6 months only 23% are issued a SABA, 5% receive OCS and 31% receive an antibiotic.

Conclusion ICT is initiated in the majority of young asthmatic subjects without prior inhaled steroid therapy. Most prescriptions are initiated in the January–April period and do not appear to be driven by severe asthma exacerbation (oral steroid prescription) or worsening asthma control (SABA use). Significant reductions in ICT, with associated cost savings, would occur if the BTS/SIGN prescribing guidelines were followed in primary care. We are currently trying to identify the drivers and potential economic impact of poor adherence to national prescribing guidelines and