S12 EFFICACY OF BRONCHIAL THERMOPLASTY IN CLINICAL PRACTICE USING THE BRITISH THORACIC SOCIETY UK DIFFICULT ASTHMA REGISTRY AND HOSPITAL EPISODE STATISTICS

[1]J Burn, [1]AJ Sims, [1]K Keltie, [2]H Patrick, [3]S Welham, [4]RM Niven, [5]LG Heaney. *[1]The Newcastle Upon Tyne Hospitals NHS Foundation Trust (On Behalf of the British Thoracic Society (BTS) UK Difficult Asthma Registry Participants), Newcastle Upon Tyne, UK; [2]National Institute for Health and Care Excellence (On Behalf of the British Thoracic Society (BTS) UK Difficult Asthma Registry Participants), London, UK; [3]British Thoracic Society (On Behalf of the British Thoracic Society (BTS) UK Difficult Asthma Registry Participants), London, UK; [4]The University Hospital of South Manchester NHS Foundation Trust & the University of Manchester (On Behalf of the British Thoracic Society (BTS) UK Difficult Asthma Registry Participants), Manchester, UK; [5]Queen's University Belfast (On Behalf of the British Thoracic Society (BTS) UK Difficult Asthma Registry Participants), Belfast, UK*

10.1136/thoraxjnl-2015-207770.18

Introduction and objectives NICE Guidance encourages further research on the efficacy of bronchial thermoplasty (BT). This study uses data from the British Thoracic Society (BTS) UK Difficult Asthma Registry (DAR) and the Hospital Episodes Statistics (HES) database to assess aspects of efficacy and compares these with previous trials.

Methods Lung function (FEV_1), quality of life (AQLQ), rescue steroid use, healthcare visits and days lost from work/school were compared at BT baseline and 12 month follow-up in patients for whom DAR data were available. In calculating annualised figures, baseline data were assumed to represent 12 months pre-BT, and 12 month follow-up data were scaled according to the time period that the follow-up represented.

Significance testing for differences in FEV_1 and AQLQ used a paired t-test. Differences in event counts were tested using non-parametric bootstrap hypothesis tests.

HES was searched for BT episodes from 1st April 2011 to 31st January 2015. An anonymised matching technique was used to link patients in HES and DAR, and for those whom sufficient time had elapsed since BT, HES A&E attendances were compared in the 12 months pre-BT and the 12 months starting from 30 days post-BT (to exclude any transient increases).

Results 31 patients had 12 month follow-ups in DAR, enabling comparison with BT baseline where data were available. All outcomes from DAR showed improvement at 12 month follow-up compared to BT baseline (Table 1). The mean improvement in AQLQ score (0.92) was smaller than that reported in AIR2 (1.35; n = 190), AIR (1.3; n = 52) and RISA (1.53; n = 15) trials.

From HES, there were 24 A&E attendances (in 5/12 patients) in the 12 months pre-treatment and 15 A&E attendances (in 6/12 patients) in the 12 months post-treatment.

Conclusion To date, efficacy outcomes appear consistent with those observed in previous clinical trials, with a smaller, but statistically significant, improvement in AQLQ score. The reduction in unscheduled healthcare visits and days lost from work/school also reached statistical significance. Although the median number of A&E attendances increased in the 12 patients studied, the annual rate of A&E attendances per patient reduced from 2 to 1.25.

Abstract S12 Table 1 Summary of efficacy outcomes

	BT baseline	12 month follow-up	n	Significance
FEV_1 (DAR)	71.62 ± 19.95	79.14 ± 23.18	21	p = 0.051
AQLQ (DAR)	3.88 ± 1.15	4.80 ± 1.24	13	p = 0.002
Rescue steroid courses (annualised, DAR)	3.0 [0.0–10.0]	1.99 [0.0–14.04]	22	p = 0.236
Unscheduled healthcare visits (annualised, DAR)	4.0 [0.0–15.0]	2.65 [0.0–8.94]	20	p = 0.039
Hospital admissions (annualised, DAR)	2.0 [0.0–6.0]	0.0 [0.0–11.23]	23	p = 0.277
Days lost from work/school (annualised, DAR)	0.0 [0.0–35.0]	0.0 [0.0–0.0]	11	p = 0.013
A&E (all cause) attendances (annualised, HES)	2 [1–10]	2.5 [1–4]	12	p = 0.159

Values reported asmean ± SD or median [min-max]]; $p < 0.05$ for statistical significance

Paediatrics: early life influences on lung health

S13 EARLY PERSISTENT CHILDHOOD WHEEZE IS A RISK FOR MORE TROUBLESOME YOUNG ADULT ASTHMA

[1]C Hodgekiss, [2]SH Arshad, [2]RJ Kurukulaaratchy. *[1]David Hide Asthma and Allergy Research Centre, Isle of Wight, UK; [2]Clinical Experimental Sciences, University Hospitals Southampton, Southampton, UK*

10.1136/thoraxjnl-2015-207770.19

Background Until recently being a wheezy infant was not felt to confer significant respiratory health risks in later life. Using the Isle of Wight Birth Cohort (IOWBC) we assessed the association of persistent childhood wheeze with young adult lung function, wheezing status/morbidity, allergic comorbidity and smoking.

Methods The Isle of Wight Birth Cohort (n = 1,456) was reviewed at 1, 2, 4, 10 and 18-years with recording of current wheeze at each visit. At 10-years, 4 separate childhood wheeze phenotypes were defined. Those who wheezed in the first 4-years of life and at 10-years were labelled Persistent-Wheezers (PW). The outcome of PW was then assessed at 18-years to determine the effects of early life persistent wheeze on adult lung health.

Results Wheezing occurred in 57.7% PW at 18-years. Asthma prevalence in PW fell from 76.0% to 58.2% over adolescence and PW comprised 38% of currently diagnosed asthma at 18-years. PW had significantly impaired lung function at 18-years compared to Non-Wheezers (NW) who never wheezed in the 1st decade of life. This included impaired FEV1, FEV1/FVC ratio and FEF25–75 along with significantly elevated bronchodilator response (BDR), bronchial hyperresponsiveness (BHR), exhaled Nitric Oxide (FeNO) plus significantly reduced gain in FEF 25–75 over adolescence (Table 1).

Compared to NW at 18-years, PW were significantly more likely to have atopy, eczema, and rhinitis (Table1). Of concern, prevalence of current smoking (44.4%) at 18-years was significantly greater in PW than NW as was passive smoke exposure through the life course (Table 1).

Abstract S13 Table 1 18 year outcomes of Childhood Persistent-Wheezers (PW) at 10 years old compared to Non-Wheezers (NW)

Characteristic	OR	P Value	CI
Female Gender	0.60	0.01	0.41–0.89
Atopy	2.78	<0.001	1.69–4.56
Eczema	2.06	0.007	1.21–3.50
Rhinitis	3.05	<0.001	2.01–4.63
Asthma	19.82	<0.001	11.96–32.82
Wheeze in last 12 months	10.28	<0.001	6.53–16.20
Smoking at 18	2.53	<0.001	1.65–3.87
Ever Smoked	2.76	<0.001	1.74–4.39
Cumulative Smoke Exposure 1–18	2.53	<0.001	1.53–4.18
Wheezy During or After Exercise	2.04	0.012	1.17–3.57
Dry Cough At Night	4.78	<0.001	2.88–7.94
Characteristic		**P Value**	**CI**
FEV1		0.031	0.02–0.40
FEV1/FVC Ratio		<0.001	0.04–0.08
FEF 25–75%		<0.001	0.41–0.95
FeNO		<0.001	(-0.38)–(-0.19)
BHR		<0.001	(-3.23) – (-0.16)
FEF growth in mls 10–18 years		0.002	147.28–624.59
Bronchodilator Reversibility		<0.001	(-5.63)–(-2.810)

Discussion Our findings highlight young adult respiratory consequences of PW. While there was some outgrowth of disease over adolescence a considerable proportion of PW showed significant airways disease at 18-years. We previously showed that PW already have impaired lung function by 10-years and these further findings suggest that phenomenon tracks through adolescence with possible additional effects on small airways growth. The longer term consequences of that finding allied to the high smoking prevalence in this phenotype merit attention.

S14* CUMULATIVE GENETIC RISK OF ASTHMA SEVERITY IN CHILDREN AND YOUNG PEOPLE

[1]VL Collis, [1]JO Cunningham, [2]S Dumble, [3]R Tavendale, [4]SJH Vijverberg, [4]AH Maitland-van der Zee, [5]HE Smith, [6]SW Turner, [3]CNA Palmer, [1]S Mukhopadhyay. *[1]Academic Department of Paediatrics, Brighton and Sussex Medical School, Royal Alexandra Children's Hospital, Brighton, UK; [2]Statistical Services Centre, University of Reading, Reading, UK; [3]Population Pharmacogenetics Group, Medical Research Institute, University of Dundee, Ninewells Hospital and Medical School, Dundee, UK; [4]Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, Netherlands; [5]Division of Public Health and Primary Care, Brighton and Sussex Medical School, Brighton, UK; [6]Department of Child Health, University of Aberdeen, Royal Aberdeen Children's Hospital, Aberdeen, UK*

10.1136/thoraxjnl-2015-207770.20

Introduction and objectives Single nucleotide polymorphisms (SNPs) in *Chitinase 3-like-1* (*CHI3L1)*, *Matrix Metalloproteinase 9 (MMP9)* and *Matrix Metalloproteinase* 12 (*MMP12)* act on the biological process of airway remodelling that is linked to asthma exacerbations. The cumulative presence of these SNPs could help identify patients at increased risk of asthma exacerbations. The aim of this study is to assess whether these genetic variants increase the risk of asthma exacerbations in children and young adults and exert a cumulative effect on this risk.

Methods Gene-environmental interactions were investigated in three observational asthma cohorts (BREATHE, PAGES, PACMAN), across three European countries (England, Scotland and the Netherlands), and a pooled dataset including, in total 2,701 patients with asthma, aged between 3 and 22 years (recruited between 2003 and 2011). Participants were genotyped for four biologically related SNPs in three genes (*CHI3L1*, *MMP9 and MMP12*).

Results In single SNP analysis all four investigated SNPs were associated with markers of asthma severity. In the BREATHE study the four investigated SNPs showed a cumulative association with exacerbations involving the use of a course of oral steroids, asthma-related absence from school/college/work, overall asthma exacerbations (OR for overall exacerbations with four risk variants compared to zero risk variants = 3.14, $p < 0.001$) and asthma treatment step (p value for trend = 0.036). Furthermore, a combined meta-regression analysis of the four investigated SNPs in the pooled dataset (n = 2701) replicated this cumulative association with exacerbations requiring hospital admission (OR per genotypic step 1.18; p = 0.046) and

Abstract S14 Table 1 Cumulative effect of number of risk variants *CHI3L1* rs4950928, *MMP9* rs17576, *MMP9* rs6073983, *MMP12* rs652438 on asthma exacerbations

Combined analysis							
	Number of risk variants						
	0 (n = 41)	1 (n = 144)	2 (n = 894)	3 (n = 1453)	4 (n = 137)	Odds ratio (95% CI)	p-value
Hospital admission	3 (8)	15 (10)	102 (12)	197 (14)	17 (13)	1.18 (1.00–1.39)	0.046
OR		1.18	1.39	1.64	1.94		
Oral steroid intake	7 (18)	28 (19)	195 (22)	348 (24)	41 (30)	1.19 (1.05–1.36)	0.008
OR		1.19	1.42	1.69	2.01		

Count (%), odds ratio (95% confidence intervals), p values calculated by binary logistic regression adjusted for age, sex and study membership.