Compared to NW at 18-years, PW were significantly more likely to have atopy, eczema, and rhinitis (Table 1). 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

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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, PAC-MAN), 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.

exacerbations requiring oral steroids (OR per genotypic step 1.19; $p = 0.008$).

Conclusions Analysis of these four SNPs could enable clinicians to identify patients at higher risk of a severe asthma phenotype, potentially helping tailor strategies for improved asthma control.

*S14- BTS Medical Student Award Winner

S15 MEASURING BRONCHODILATOR RESPONSE BY INTERRUPTER TECHNIQUE TO PREDICT RESPONSE TO INHALED STEROID THERAPY IN WHEEZY PRESCHOOL CHILDREN

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Managing recurrent wheezing in preschool children is problematic, with conflicting evidence on the effectiveness of asthma therapy. One reason is the heterogeneous nature of preschool wheeze: distinguishing "transient viral wheeze" from asthma at presentation is currently impossible. Bronchodilator response (BDR) measured by interrupter resistance (Rint) is greater in preschool children with diagnosed asthma than in healthy controls, but the usefulness of Rint in clinical practice has not been studied. We aimed to assess whether measuring BDR using Rint can predict clinical response to inhaled corticosteroids (ICS).

We studied children aged 2 years to 1. Response to ICS was defined as reduction in daily symptom score of at least 0.26.² Association between BDR and ICS response was assessed using chi-square test. We also assessed the relationship between measured BDR and the caregiver's assessment.

121 children were recruited, 59 completed the full study (27 withdrew, 10 were unable to perform Rint, 18 failed to meet 4w symptom threshold, 7 commenced ICS or Montelukast by clinician before 4w). Positive BDR at baseline was demonstrated by 33 children, and was significantly associated with a clinical response to ICS ($p < 0.05$). There was no relationship between objective BDR and caregiver's rating of bronchodilator efficacy.

Our findings suggest that measuring BDR using Rint may help in making pragmatic decisions on commencing asthma preventer therapy in wheezy preschool children. Further work is needed to assess whether Rint BDR measurement may have the potential to distinguish those with transient wheeze from those with asthma.

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S16 OUTCOMES OF MULTIPLE TRIGGER WHEEZE AND EXCLUSIVE VIRAL WHEEZE IN EARLY CHILDHOOD: A COMPARISON ACROSS TWO POPULATION COHORTS

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Introduction Early childhood wheeze has been classified according to triggers; exclusive viral wheeze (EVW) and multiple trigger wheeze (MTW). It has been proposed that these phenotypes differ in their aetiology, severity and prognosis.

Objectives To examine the prevalence and symptom severity of EVW and MTW in 2–6 year olds. To evaluate the stability of these phenotypes over time, and their association with later wheeze.

Method In two longitudinal birth cohorts comprising 18,362 individuals, data on respiratory symptoms were collected at age 2, 4 and 6 years. Parent-reported triggers were used to classify wheeze as EVW or MTW for each 2-year period. Logistic regression analysis was used to estimate odds ratios for current wheeze and relative risk ratios for wheeze phenotypes versus no wheeze, at follow-up compared with baseline.

Results At 2 years 17.6% and 22.6% (cohorts 1 and 2 respectively) had wheeze, of which 55.2% and 56.3% had MTW. At 6 years 69.7% and 75.7% of children with wheeze had MTW.

Among children with wheeze at baseline, 58–76% with EVW and 46–67% with MTW were in remission 2 years later (cohort 1) and 14–20% and 4–11% (cohort 2).

MTW had greater reported symptom-severity at all time-points compared with EVW.

When adjusted for symptom-severity, children with EVW at baseline had relative risk ratios (RRR) of 2.9–7.4 and 4.1–15.5 (cohorts 1 and 2 respectively) for EVW and RRR 1.7–2.9 and 1.6–4.0 for MTW at follow-up. Children with MTW at baseline had RRR of 3.1–6.2 in cohort 1 and 3.6–15.6 in cohort 2 for MTW and 1.1–2.7 and 1.4–7.0 respectively for EVW at follow-up.

Conclusions When adjusted for symptom severity, wheezing phenotypes based on reported triggers remained stable between 2–6 years of age. Symptom-severity may be a more important determinant than triggers of future wheeze classification in young children.

S17 DO PRE-SCHOOL LUNG VENTILATION SCANS PREDICT OUTCOME BY 6 YEARS OF AGE IN CHILDREN WITH CYSTIC FIBROSIS (CF)?

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Introduction and objectives Progressive respiratory disease accounts for most of the mortality and morbidity in CF. Identification of early lung disease is imperative to recognise young patients who are at high risk of developing future lung damage. The London CF collaboration has shown that infant pulmonary function at one and at two years is essentially normal, and one year HRCT has mild abnormalities only, so new markers need to be identified. We have used ventilation scans (VS) at the CF annual assessment in infants too young to perform standard pulmonary function tests; VS are more sensitive than chest radiography, and have been used to guide immediate management. We hypothesised that an abnormal pre-school lung VS predicted worse spirometry by age six years in CF children.

Methods Data from children born after 2000 under the care of the RBH were retrieved from hospital databases and Port CF. We recorded demographics (gender, age, CFTR genotype,