





Table 1 Descriptive characteristics of cases and controls included in Stage 1 (UK Biobank primary and signal prioritisation analyses)

	ACO cases (n=8068)	Healthy controls (n=40360)	Controls with COPD but no asthma (n=16762)	Controls with asthma but no COPD (n=26815)
Age at recruitment (median, IQR)	60 (53-65)	57 (49-63)	62 (56-65)	55 (48-61)
Sex				
Male	4179 (51.8%)	17598 (43.6%)	9147 (54.6%)	9703 (36.2%)
Female	3889 (48.2%)	22762 (56.4%)	7615 (45.4%)	17112 (63.8%)
Smoking status				
Ever smoked	4367 (54.1%)	17316 (42.9%)	11752 (70.1%)	11231 (41.9%)
Never smoked	3701 (45.9%)	23044 (57.1%)	5010 (29.9%)	15584 (58.1%)
Pack-years smoking (median, IQR)*	25.5 (13.5, 39.5)	15.8 (8.3, 26.4)	32.0 (19.0, 45.5)	16.5 (8.5, 28.1)
Allergic rhinitis (including hayfever) or eczema				
Yes	3325 (41.2%)	8468 (21.0%)	2691 (16.1%)	13010 (48.5%)
No	4743 (58.8%)	31892 (79.0%)	14071 (83.9%)	13805 (51.5%)
Eosinophil count (10⁹ cells/Litre) (median, IQR)**	0.20 (0.13, 0.32)	0.13 (0.08, 0.20)	0.16 (0.10, 0.24)	0.21 (0.11, 0.27)
Lung function (median, IQR)				
FEV ₁ /FVC	0.63 (0.58, 0.67)	0.78 (0.75, 0.81)	0.65 (0.61, 0.68)	0.77 (0.74, 0.80)
% predicted FEV ₁	66.1% (56.5%, 73.3%)	97.3% (89.9%, 105.6%)	68.7% (60.0%, 74.8%)	90.8% (81.6%, 100.0%)

* in ever-smokers with non-missing data, 3270/4367 cases, 11196/17316 main controls, 9672/11752 COPD not asthma controls, 7443/11231 asthma not COPD controls

**in those with non-missing data after cleaning as per Astle *et al.* 2016, N=7666 cases, N=38259 main controls, N=15845 COPD not asthma controls, N=25292 asthma but not COPD controls.

Table 2 Eight genome-wide signals for asthma-COPD overlap

rsid	chr:pos (effect/non-effect allele)	Nearest gene	Location	EAF	Stage 1 (UK Biobank, cases=8068, controls=40360)		Stage 2 (12 independent studies, cases=4301, controls =48609)*		Joint analysis of Stage 1 and Stage 2	
					OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
rs80101740	5:98471135 (C/A)	<i>LOC1002892 30</i>	Intergenic	0.015	1.44 (1.24, 1.68)*	1.87E-06*	1.37 (1.10, 1.71)	5.49E-03	1.42 (1.25, 1.61)	3.72E-08
rs35570272	3:33047662 (T/G)	<i>GLB1</i>	Intronic	0.398	1.11 (1.07, 1.15)	1.06E-07	1.08 (1.02, 1.14)	4.67E-03	1.10 (1.06, 1.13)	2.44E-09
rs16903574	5:14610309 (G/C)	<i>FAM105A</i>	Exonic	0.077	1.23 (1.15, 1.32)	4.47E-09	1.13 (1.03, 1.25)	9.96E-03	1.20 (1.13, 1.27)	3.8E-10
rs2584662	17:47470487 (C/A)	<i>PHB</i>	Intergenic	0.42	0.90 (0.86, 0.94)	3.20E-08	0.95 (0.90, 1.00)	5.89E-02	0.92 (0.89, 0.95)	2.21E-08
rs1837253	5:110401872 (C/T)	<i>TSLP</i>	intergenic	0.739	1.22 (1.17, 1.27)	4.22E-21	1.06 (1.00, 1.12)	4.44E-02	1.16 (1.12, 1.20)	1.53E-18
rs6787279	3:57163751 (C/T)	<i>IL17RD</i>	intronic	0.169	0.88 (0.84, 0.92)	2.69E-07	0.91 (0.85, 0.97)	6.51E-03	0.89 (0.86, 0.93)	7.87E-09
rs9273410	6:32627250 (A/C)	<i>HLA-DQB1</i>	UTR3	0.445	1.24 (1.19, 1.29)	4.37E-27	1.11 (1.05, 1.18)	6.42E-04	1.20 (1.16, 1.24)	9.19E-28
rs3749833	5:131799626 (C/T)	<i>C5orf56</i>	ncRNA_intronic	0.263	1.16 (1.11, 1.21)	3.10E-12	1.06 (1.00, 1.12)	4.21E-02	1.12 (1.09, 1.16)	9.37E-12

Variants were annotated with nearest gene and type of region using ANNOVAR software (and genome build hg19). OR, 95% CI and P-value all calculated using score test. Firth test for rs80101740 gave OR 1.40 (95% CI 1.22, 1.60) and P=1.56x10⁻⁶. EAF denotes effect allele frequency.

*Stage 2 studies: CHS, COPDGene, deCODE, ECLIPSE, EPIC-Norfolk, FHS, Generation Scotland, GenKOLS, HUNT, LOVELACE, Rotterdam Study, SPIROMICS.