Supplemental Data

Immunoglobulin E as a Biomarker for the Overlap of Atopic Asthma and Chronic Obstructive Pulmonary Disease

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Supplemental Table 1: Total and specific IgE assays

	No COPD, no asthma (n=598)	Asthma, no COPD (n=541)	COPD, no asthma (n=899)[c]	COPD and asthma (n=832)[c]
Total IgE, median (IQR)	43.0 (17.2-126.8)	76.9 (24.8-205.0)	42.2 (13.9-127.8)	67.0 (21.9-204.0)
Total IgE>30 IU/ml	362 (60.5%)	385 (71.2%)[a]	524 (58.4%)	565 (68.0%)[b]
Cat dander	47 (7.9%)	109 (20.2%)[a]	52 (5.8%)	154 (18.5%)[b]
Dog dander	38 (6.4%)	83 (15.3%)[a]	45 (5.0%)	122 (14.7%)[b]
D. Farinae	104 (17.4%)	166 (30.7%)[a]	123 (13.7%)	201 (24.2%)[b]
D. Pteronyssinus	95 (15.9%)	168 (31.1%)[a]	123 (13.7%)	191 (23.0%)[b]
German cockroach	75 (12.5%)	125 (23.1%)[a]	94 (10.5%)	121 (14.5%)[b]
Mold mix	61 (10.2%)	103 (19.0%)[a]	74 (8.2%)	162 (19.5%)[b]
Mean number of positive specific IgE assays	0.7 (1.3)	1.4 (1.8)[a]	0.6 (1.2)	1.1 (1.6)[b]

[a]P<0.05 for comparison with no COPD, no asthma

[b]P<0.05 for comparison with COPD, no asthma

[c]Two subjects had failed total IgE assays.

Supplemental Table 2: Concordance between elevated total IgE >30 IU/ml and at least one positive specific IgE.

A. No COPD, no asthma

	Low IgE	High IgE
Specific IgE -	223 (37.3%)	194 (32.4%)
Specific IgE +	13 (2.2%)	168 (28.1%)

B. Asthma, no COPD

	Low IgE	High IgE
Specific IgE -	135 (25.0%)	136 (25.1%)
Specific IgE +	21 (3.9%)	249 (46.0%)

C. COPD, no asthma

	Low IgE	High IgE
Specific IgE -	355 (39.5%)	324 (36.1%)
Specific IgE +	19 (2.1%)	200 (22.3%)

D. COPD & asthma

	Low IgE	High IgE
Specific IgE -	238 (28.6%)	231 (27.8%)
Specific IgE +	28 (3.4%)	334 (40.2%)

Supplemental Table 3: Concordance between elevated total IgE >100 IU/ml and at least one positive specific IgE.

A. No COPD, no asthma

	Low IgE	High IgE
Specific IgE -	349 (58.4%)	68 (11.4%)
Specific IgE +	63 (10.5%)	118 (19.7%)

B. Asthma, no COPD

	Low IgE	High IgE
Specific IgE -	217 (40.1%)	54 (10.0%)
Specific IgE +	93 (17.2%)	177 (32.7%)

C. COPD, no asthma

	Low IgE	High IgE
Specific IgE -	562 (62.6%)	117 (13.0%)
Specific IgE +	72 (8.0%)	147 (16.4%)

D. COPD & asthma

	Low IgE	High IgE
Specific IgE -	381 (45.8%)	88 (10.6%)
Specific IgE +	120 (14.4%)	242 (29.1%)

Supplemental Table 4: Concordance between elevated total IgE >100 IU/ml and at least one positive specific IgE, in current smokers.

A. No COPD, no asthma

	Low IgE	High IgE
Specific IgE -	202 (55.5%)	45 (12.4%)
Specific IgE +	33 (9.1%)	84 (23.1%)

B. Asthma, no COPD

	Low IgE	High IgE
Specific IgE -	132 (39.2%)	37 (11.0%)
Specific IgE +	50 (14.8%)	118 (35.0%)

C. COPD, no asthma

	Low IgE	High IgE
Specific IgE -	220 (57.4%)	59 (15.4%)
Specific IgE +	27 (7.0%)	77 (20.1%)

D. COPD & asthma

	Low IgE	High IgE
Specific IgE -	136 (41.1%)	35 (10.6%)
Specific IgE +	42 (12.7%)	118 (35.6%)

Supplemental Table 5: Concordance between elevated total IgE >100 IU/ml and at least one positive specific IgE, in former smokers.

A. No COPD, no asthma

	Low IgE	High IgE
Specific IgE -	147 (62.8%)	23 (9.8%)
Specific IgE +	30 (12.8%)	34 (14.5%)

B. Asthma, no COPD

	Low IgE	High IgE
Specific IgE -	85 (41.7%)	17 (8.3%)
Specific IgE +	43 (21.1%)	59 (28.9%)

C. COPD, no asthma

	Low IgE	High IgE
Specific IgE -	342 (66.4%)	58 (11.3%)
Specific IgE +	45 (8.7%)	70 (13.6%)

D. COPD & asthma

	Low IgE	High IgE
Specific IgE -	245 (49.0%)	53 (10.6%)
Specific IgE +	78 (15.6%)	124 (24.8%)

Supplemental Table 6: Logistic regression models for severe exacerbations in the year prior to enrollment

	Strict ACO vs COPD, no asthma[a]			Broad ACO with atopy vs COPD, no asthma, no atopy[a]			Strict ACO with atopy vs COPD, no asthma, no atopy[a]		
	OR	p-value	C-statistic[b]	OR	p-value	C-statistic[b]	OR	p-value	C-statistic[b]
Severe exacerbation in past year	2.14	<0.001	0.72	2.05	<0.001	0.74	2.23	<0.001	0.73

[a]Strict asthma-COPD overlap is defined by $FEV_1/FVC<0.7$, $FEV_1<80\%$ predicted, and self-report of a doctor's diagnosis of asthma before age 40. Broad ACO is defined by defined by $FEV_1/FVC<0.7$, $FEV_1<80\%$ predicted, and self-report of asthma. Atopy is defined by total IgE >100 IU/ml or at least one positive specific IgE. All models are adjusted for age, sex, race, current smoking, pack-years of smoking and FEV_1 % predicted.

[b]C-statistic from logistic regression corresponds to area under the receiver operating characteristic curve.

Supplemental Table 7: Linear regression models for airway thickening on chest CT scan

	Strict ACO vs COPD, no asthma[a]		Broad ACO with atopy vs COPD, no asthma, no atopy[a]		Strict ACO with atopy vs COPD, no asthma, no atopy[a]	
	β (SE)	p-value	β (SE)	p-value	B (SE)	p-value
Wall area % of segmental airways	2.69 (0.47)	<0.001	2.48 (0.50)	<0.001	2.73 (0.60)	<0.001

[a]Strict asthma-COPD overlap is defined by $FEV_1/FVC<0.7$, $FEV_1<80\%$ predicted, and self-report of a doctor's diagnosis of asthma before age 40. Broad ACO is defined by defined by $FEV_1/FVC<0.7$, $FEV_1<80\%$ predicted, and self-report of asthma. Atopy is defined by total IgE >100 IU/ml or at least one positive specific IgE. Models adjusted for age, sex, race, current smoking, BMI, and chest CT scanner model.