		ARIC			CARDIA			JHS			MESA		
Inital n:	female	1584			503			1141			734		
	male	932			317			751			674		
Selection Criteria													
		total	unique/ removed	remaining	total	unique/ removed	remaining	total	unique/ removed	remaining	total	removed	remaining
Chronic Respiratory Symptoms:	female	892	892	692	364	364	139	615	615	526	14	14	720
	male	547	547	385	197	197	120	368	368	383	12	12	662
Lung Disease other than Asthma:	female	181	27	665	43	1	138	75	14	512	9	7	713
	male	55	7	378	22	1	119	33	4	379	20	17	645
Low Lung Function:	female	217	63	602	54	14	124	69	32	480	28	23	690
	male	175	39	339	56	17	102	45	12	367	69	60	585
CARe Quality Control:	female	1	1	601	16	16	108	4	4	476	7	7	683
	male	0	0	339	18	18	84	1	1	366	4	4	581
Final n:	female	601			108			476			683		
	male	339			84			366			581		

Supplemental Table 1: **Demographics and exclusion criteria for the control group.** Listed in the first row is the starting number of African American subjects without a diagnosis of asthma (subdivided by gender) that were identified from questionnaire data for each of the 4 parent studies used in this analysis. See methods section and Supplemental Table 6 for further details about the questionnaire data that was used to identify subjects with asthma. Moving down the table, next listed for each study is the exclusion criteria that were applied to arrive at the final n for the control group. Chronic respiratory symptoms were determined from the questionnaire data listed in Supplemental Table 7. Lung disease other than asthma was determined from the questionnaire data listed in Supplemental Table 8. Low lung function was defined as FEV_1 < 70% of predicted based on race and sex specific NHANES III prediction equations adjusting for age and height, or FEV1/FVC less than lower limits of normal for age, race and sex (see material and methods). CARe quality control metrics were defined previously (Lettre et al. 2011). The "total" column under each parent study refers to the total number of subjects positive for the associated exclusion criterion. The ""unique/removed" column under each parent study refers to those subjects who had not been filtered due to the presence of other selection criteria - i.e. this is the number of subjects that were positive only for the one associated selection criterion. The "remaining" column under each parent study refers to the number of subjects remaining after that stage of filtering.

		ARIC		CARDIA		JHS		MESA	
Inital n:	female	183		140		178		161	
	male	90		70		92		67	
Selection Criteria									
		removed	remaining	removed	remaining	removed	remaining	removed	remaining
Lung Disease Other Than Asthma:	female	82	101	30	110	38	140	9	152
	male	29	61	14	63	11	81	8	59
CARe Quality Control:	female	2	99	9	101	1	139	2	150
	male	0	61	7	56	1	80	0	59
Final n:	female	100		101		139		150	
	male	61		56		80		59	

Supplemental Table 2: Demographics and exclusion criteria for the asthma group. Listed in the first row is the starting number of African American subjects with asthma (subdivided by gender) that were identified from questionnaire data for each of the 4 parent studies used in this analysis. See methods section and Supplemental Table 6 for further details about the questionnaire data that was used to identify subjects with asthma. Moving down the table, next listed for each study is the exclusion criteria that were applied to arrive at the final n for the asthma group. Lung disease other than asthma was determined from the questionnaire data listed in Supplemental Table 8. CARe quality control metrics were defined previously (Lettre et al. 2011). The "removed" column under each parent study refers to the total number of subjects positive for the associated exclusion criterion. The "remaining" column under each parent study refers to the number of subjects remaining after that stage of filtering.

Locus	Rprtd SNP	Reference	EAF-CARe	CARe SNP	Ancestry specific r2	African Ancestry r2	EAF	Pvalue-one tailed	DOE	I/G	RSQ
PDE4D	rs1588265	Himes et al. 2009	0.7941	rs4700369	0.565054	0.0444644	0.945	1.17E-01	-	I	0.959
DENND1B	rs2786098	Sleiman et al. 2010	0.9032	rs10922238	0.793802	0.0310301	0.92	6.13E-02	+	I	0.977
RAD50/IL13	**rs2244012**	**Moffat et al. 2010**	**0.5943**	**rs17622991**	**0.86971**	**0.117662**	**0.195**	**1.07E-05**	**+**	**I**	**0.950**
IL1RL1/IL18R1	**rs10173081**	**Moffat et al. 2010**	**0.7394**	**rs17027029**	**0.773331**	**0.511213**	**0.688**	**9.97E-05**	**+**	**I**	**0.958**
GSDMB/ORMDL3	**rs2305480**	**Moffat et al. 2010**	**0.8424**	**rs869402**	**0.79411**	**0.570927**	**0.801**	**1.25E-04**	**+**	**G**	**NA**
IL33	rs1342326	Moffat et al. 2010	0.3463	rs10975479	1	0.122753	0.094	9.52E-03	-	I	0.645
RORA	rs11071559	Moffat et al. 2010	0.5983	rs10519068	0.955359	0.158994	0.582	2.00E-01	+	I	0.867
SMAD3	rs744910	Moffat et al. 2010	0.6621	rs12708492	0.76813	0.447359	0.444	6.79E-01	+	G	NA
IL2RB	rs2284033	Moffat et al. 2010	0.5988	rs228954	0.936749	0.0940429	0.574	9.54E-01	+	I	0.829
IL6R	rs4129267	Ferreira et al. 2011	0.1322	rs4133213	0.785035	0.331899	0.217	1.88E-01	+	I	0.738
11q13.5 (C11orf30-LRRC32)	rs7130588	Ferreira et al. 2011	0.2085	rs61894512	0.555977	0.281153	0.199	9.97E-01	+	I	0.954
10p14 (gene desert)	**rs10508372**	**Hirota et al. 2011**	**0.8016**	**rs11255975**	**0.985498**	**0.793969**	**0.777**	**8.49E-04**	**+**	**I**	**0.972**
4q31 (USP38)	rs7686660	Hirota et al. 2011	0.5672	rs11735113	0.942907	0.0931479	0.247	3.37E-02	-	I	0.988
5q22 (TSLP-WDR36)	rs1837253	Hirota et al. 2011	0.7319	Same SNP	-	-	0.732	-	+	I	0.990
6p21 (HLA/NOTCH4)	rs404860	Hirota et al. 2011	0.2835	rs2256594	0.791158	1	0.284	9.11E-02	+	I	0.975
12q13 (IKZF4/EOS)	rs1701704	Hirota et al. 2011	0.1295	rs7955865	0.838692	0.838692	0.464	9.38E-02	+	I	0.903
HLA-DP	rs987870	Noguchi et al. 2011	0.6794	rs4947357	0.538114	0	0.987	9.44E-01	+	I	0.829
PYHIN1	rs1102000	Torgerson et al. 2011	0.7544	rs1102000	0.550829	-	0.272	9.08E-01	+	I	0.790
DPP10	rs1435879	Mathias et al. 2010	0.9298	Same SNP	-	-	0.93	-	+	I	0.995
ADRA1B	rs10515807	Mathias et al. 2010	0.0563	rs35591745	0.83105	same	0.05	2.34E-01	+	I	0.930
PRNP	rs6052761	Mathias et al. 2010	0.3182	rs6052762	0.765314	same	0.241	2.22E-01	-	I	0.871

Supplemental Table 3: Replication of European asthma associated SNPs in the CARe African-American meta-analyses. Reported SNP refers to the top SNP at the particular locus from the referenced GWA studies, and CARe SNP refers the top SNP in the CARe African American cohort. EAF-CARe is the effect allele frequency for the reported SNP in CARe. EAF is the effect allele frequency for the "better" SNP (i.e. the SNP with the strongest signal of replication) in CARe that was found in the analysis. DOE (direction of effect): + indicates that the CARe SNP effect was in the same direction as the reported SNP. I/G indicates whether the CARe SNP was imputed (I) or genotyped (G). RSQ, imputation r2 for imputed CARe SNPs. Bold is used to indicate CARe SNPs that either exceeded the Bonferoni corrected significance threshold or were nominally significant and in the same effect direction as the reported SNP.

Locus	Reported SNP	Reference	EAF-CARe	CARe SNP	Anestry specific r2	African Ancestry r2	EAF	Pvalue-one tailed	Pvalue (local ancestry)	Effect Direction
RAD50/IL13	rs2244012	Moffat et al. 2010	0.5943	rs17622991	0.86971	0.117662	0.195	1.07E-05	1.50E-05	+
IL1RL1/IL18R1	rs10173081	Moffat et al. 2010	0.7394	rs17027029	0.773331	0.511213	0.688	9.97E-05	1.18E-04	+
GSDMB/ORMDL3	rs2305480	Moffat et al. 2010	0.8424	rs869402	0.79411	0.570927	0.801	1.25E-04	1.36E-04	+
10p14 (gene desert)	rs10508372	Hirota et al. 2011	0.8016	rs11255975	0.985498	0.793969	0.777	8.49E-04	1.01E-03	+

Supplemental Table 4: Adjustment of meta-analysis results for local ancestry. Reported SNP refers to the top SNP at the particular locus from the referenced GWA studies, and CARe SNP refers the top SNP in the CARe African American cohort. EAF-CARe is the effect allele frequency for the reported SNP in CARe. EAF is the effect allele frequency for the "better" SNP (i.e. the SNP with the strongest signal of replication) in CARe that was found in the analysis. P-value (local ancestry) is the p-value reported in table 2 adjusted for the confounding effects of admixture by using HAPMIX software. Effect direction: + indicates that the CARe SNP effect was in the same direction as the reported SNP. Bold is used to indicate CARe SNPs that exceeded the Bonferoni corrected significance threshold.

Locus	MarkerName	Allele1	Allele2	Freq1	FreqSE	MinFreq	MaxFreq	Zscore	P-value
RAD50/IL13	rs2244012	a	g	0.4062	0.007	0.3958	0.416	-1.337	0.1811
RAD50/IL13	rs17622991	a	g	0.1958	0.0098	0.1765	0.2052	3.624	**2.90E-04**
IL1RL1/IL18R1	rs10173081	t	c	0.2613	0.0034	0.2558	0.2658	-0.674	0.5006
IL1RL1/IL18R1	rs17027029	c	g	0.3125	0.004	0.3056	0.3182	-1.836	0.06639

Supplemental Table 5: Conditional analysis of signals in the *RAD50/IL13* region and the *IL1RL1/IL18R1* region. Conditioning for the effect of rs17622991 eliminated evidence for association for rs224012. However, conditioning for the effect of rs224012 did not abolish the association signal of rs17622991. Conditional analysis of the signals in *IL1RL1/IL18R1* did not distinguish the signal at the European ancestry SNP from the signal at the African ancestry SNP.

Study	Variable	Question
ARIC	HHXB05F	asthma diagnosed by a doctor
ARIC	HOM10H	asthma ever diangosed
ARIC	PHXA8M	has a doctor said you had asthma
ARIC	PHXB6E	ever told asthma
ARIC	RPAA35	ever had asthma
ARIC	RPAA36	doctor confirmed asthma
CARDIA	A08asma	do you take meds for asthma or other breathing problem (year 1)
CARDIA	A12ASDOC	was asthma confirmed by a doctor (year 1)
CARDIA	A12ASTHM	have you ever had asthma (year 1)
CARDIA	B08ASMA	do you take meds for asthma or other breathing problem (year 2)
CARDIA	B12ASDOC	was asthma confirmed by a doctor (year 2)
CARDIA	B12ASTHM	have you ever had asthma (year 2)
CARDIA	C08ASMA	are you taking meds for asthma or other breathing problem (year 5)
CARDIA	D08asma	are you taking meds for asthma or other breathing problem (year 7)
CARDIA	D08asth	has a doctor or nurse ever said you had asthma (year 7)
CARDIA	E08asma	are you taking meds for asthma or other breathing problem (year 10)
CARDIA	E08asth	has a doctor or nurse ever said you had asthma (year 10)
CARDIA	F08ASTH	has a doctor or nurse ever said you had asthma (year 15)
CARDIA	Y01ASTDR	asthma based on physician diagnosis
JHS	AFUA7h	has a doctor ever told you that you have asthma (exam 1 follow up)
JHS	AFUB7h	has a doctor ever told you that you have asthma (exam 1 follow up)
JHS	AFUI7H	has a doctor ever told you that you have asthma (exam 1 follow up)
JHS	AFUJ7H	has a doctor ever told you that you have asthma (exam 1 follow up)
JHS	AFUK7H	has a doctor ever told you that you have asthma (exam 1 follow up)
JHS	AFUC20	has a doctor ever told you that you have asthma (exam 2 follow up)
JHS	PFHA10A	has a doctor ever told you that you have asthma
JHS	RPAA13	have you ever had asthma
MESA	ASTHMA1	asthma (self report) (exam 1)
MESA	ASTHMA2	asthma (self report) (exam 2)
MESA	ASTHMA3	asthma (self report) (exam 3)
MESA	ASTHMA4	asthma (self report) (exam 4)

Supplemental Table 6: Questionnaire questions to establish asthma diagnosis. Subjects with asthma were defined based on an affirmative response to any of these study questions and included both physician-diagnosed and self-reported asthma.

Study	Variable	Question
ARIC	RPAA01	usually have cough
ARIC	RPAA13	chest wheeze or whistle with a cold
ARIC	RPAA14	chest wheeze or whistle otherwise
ARIC	RPAA17	ever had wheeze with SOB
ARIC	RPAB01	usually have cough
ARIC	RPAB03	3 consecutive months of cough
ARIC	RPAB06	phelgm on most days for 3 months out of the year
ARIC	RPAB07	chest wheeze or whistle with a cold
ARIC	RPAB08	chest wheeze or whistle otherwise
ARIC	RPAB10	ever had wheeze with SOB
CARDIA	A12COLD	chest sound wheezy with a cold (year 1)
CARDIA	A12CONSC	cough for 3 consecutive months or more (year 1)
CARDIA	A12EPISD	periods of cough lasting 3 weeks or more each year (year 1)
CARDIA	A12NCOLD	chest sound wheezy apart from colds (year 1)
CARDIA	A12PCONS	phlegm for 3 consecutive months during the year (year 1)
CARDIA	A12SHTBR	ever had wheeze with SOB (year 1)
CARDIA	A12USUAL	usually have a cough (year 1)
CARDIA	B12COLD	chest sound wheezy with colds (year 2)
CARDIA	B12CONSC	cough for 3 consecutive months or more (year 2)
CARDIA	B12NCOLD	chest sound wheezy apart from colds (year 2)
CARDIA	B12PCONS	phlegm for 3 consecutive months during the year (year 2)
CARDIA	B12SHTBR	ever had wheeze with SOB (year 2)
CARDIA	B12USUAL	usually have a cough (year 2)
CARDIA	E12COLD	wheeze with colds (year 10)
CARDIA	E12CONSC	cough for 3 consecutive months or more (year 10)
CARDIA	E12NCOLD	wheeze apart from colds (year 10)
CARDIA	E12PCONS	phlegm for 3 consecutive months during the year (year 10)
CARDIA	E12SHTBR	ever had wheeze with SOB (year 10)
CARDIA	E12USUAL	usually have a cough (year 10)
CARDIA	F12COLD	wheeze with colds (year 15)
CARDIA	F12NCOLD	wheeze apart from colds (year 15)
CARDIA	F12SHTBR	ever had wheeze with SOB (year 15)
JHS	AFUC19G	usually have some cough or wheezing
JHS	RPAA1	usually have cough
JHS	RPAA10	attacks of wheezing that have made you SOB
JHS	RPAA3	cough most days for 3 consecutive months
JHS	RPAA6	phlegm most days for 3 consecutive months
JHS	RPAA7	wheezing with respiratory infections
JHS	RPAA8	wheezing apart from a cold

Supplemental Table 7: Questionnaire questions to determine history of chronic respiratory symptoms. These symptoms could be consistent with asthma, and so subjects who provided an affirmative answer to these questions were excluded from the control group.

Study	Variable	Question
ARIC	HOM10G	chronic lung disease ever diagnosed
ARIC	PHXA8L	chronic lung disease
ARIC	PHXB6D	Chronic lung disease, such as bronchitis, or emphysema
ARIC	RPAA27	ever had chronic bronchitis
ARIC	RPAA28	still have chronic bronchitis
ARIC	RPAA29	doctor confirmed chronic bronchitis
ARIC	RPAA31	ever had emphysema
ARIC	RPAA32	still have emphysema
ARIC	RPAA33	doctor confirmed emphysema
CARDIA	A12CBDOC	chronic bronchitis confirmed by doctor (year 1)
CARDIA	A12CBRON	ever had chronic bronchitis (year 1)
CARDIA	A12CBSTL	still have chronic bronchitis (year 1)
CARDIA	A12EMDOC	doctor confirmed emphysema (year 1)
CARDIA	A12EMPH	ever had emphysema (year 1)
CARDIA	A12EMSTL	still have emphysema (year 1)
CARDIA	D08BRON	chronic bronchitis (year 7)
CARDIA	D08EMPH	emphysema (year 7)
CARDIA	E08BRON	chronic bronchitis (year 10)
CARDIA	E08EMPH	emphysema (year 10)
CARDIA	F08BRON	chronic bronchitis (year 15)
CARDIA	F08EMPH	emphysema (year 15)
CARDIA	F08EMPYR	emphysema in the past year (year 15)
JHS	AFUA7G	Chronic lung disease such as bronchitis or emphysema (exam 1 follow up)
JHS	AFUB7G	Chronic lung disease such as bronchitis or emphysema (exam 1 follow up)
JHS	AFUC18A	doctor said chronic lung disease, such as bronchitis or emphysema (exam 2 follow up)
MESA	EMPHYS1	Emphysema, self report (exam 1)
MESA	EMPHYS2	Emphysema, self report (exam 2)
MESA	EMPHYS3	Emphysema, self report (exam 3)
MESA	EMPHYS4	Emphysema, self report (exam 4)
SHHS	COPD15	MD said pt had COPD
SHHS	CRBRON15	MD said pt had chronic bronchitis
SHHS	EMPHYS15	MD said pt had emphysema
SHHS	hi201a	doctor ever told you that you have emphysema
SHHS	hi201b	doctor ever told you that you have chronic bronchitis?
SHHS	hi201c	doctor ever told you that you have COPD?

Supplemental Table 8: Questionnaire questions to establish diagnoses consistent with chronic lung disease. Subjects who provided an affirmative answer to these questions were excluded from both the asthma group and the control group.

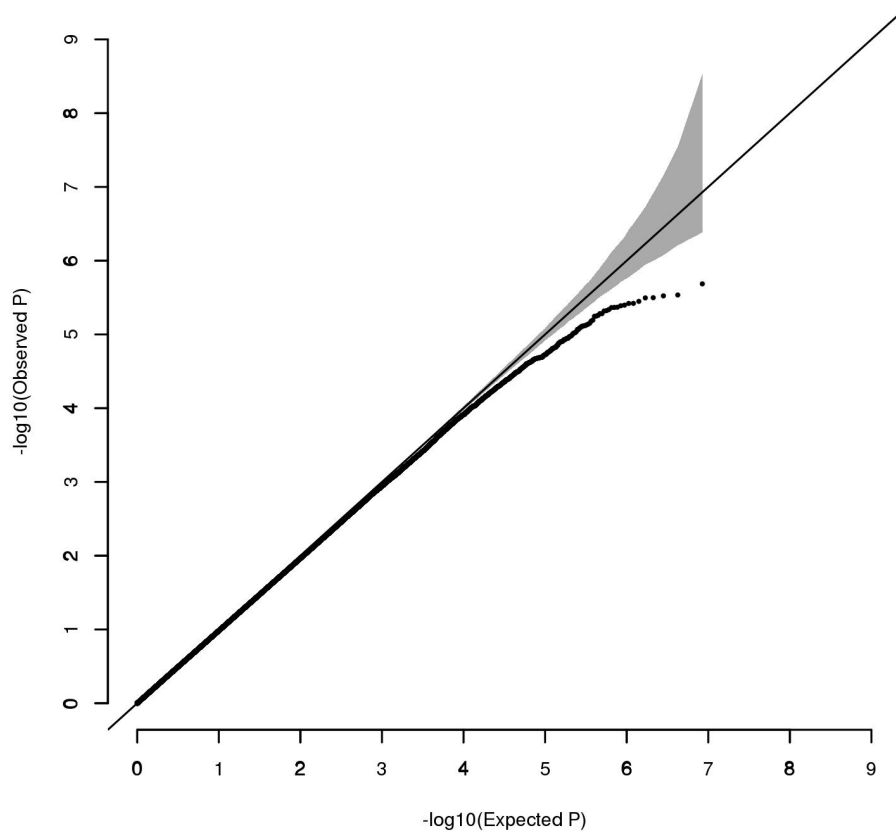|	**Asthma**	**COPD**	**P-value**
Allergic Status			
w/o allergies	117	308	<0.001
with allergies	44	39	
Lung Function			
normal lung function	142	52	<0.001
low lung function	19	292	
Smokng Status			
never smoker	76	97	<0.001
ever smoker	83	247	
Age			
median +/- SD	53.5 +/- 5.9	56.50 +/- 5.7	<0.001

Supplemental Table 9: Comparison of phenotypic variables between subjects with self-reported asthma or self-reported COPD in ARIC. Key variables that distinguish patients with asthma from patients with COPD (allergic status, lung function, smoking status, and age) were compared in order to determine if the asthma subjects identified in ARIC were phenotypically distinct from the COPD subjects identified in ARIC. P-values are determined with Chi-Square or Fisher's exact test, where appropriate. Taken together, these results argue that our method of defining asthma by self-report combined with the exclusion of those with self-reported COPD successfully allowed us to isolate a cohort of asthmatics that was phenotypically distinct from subjects with COPD in ARIC.

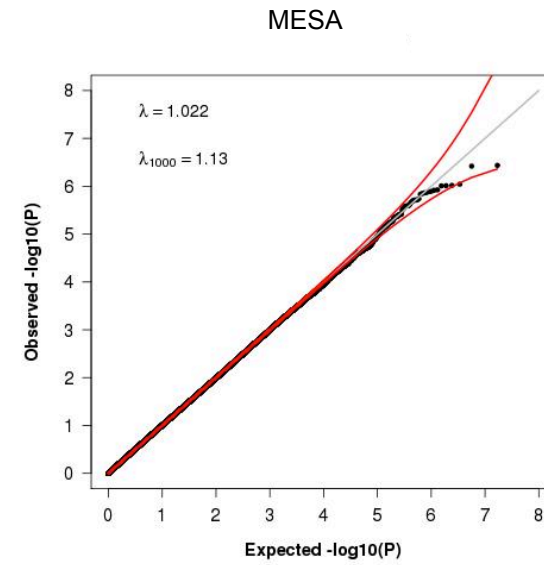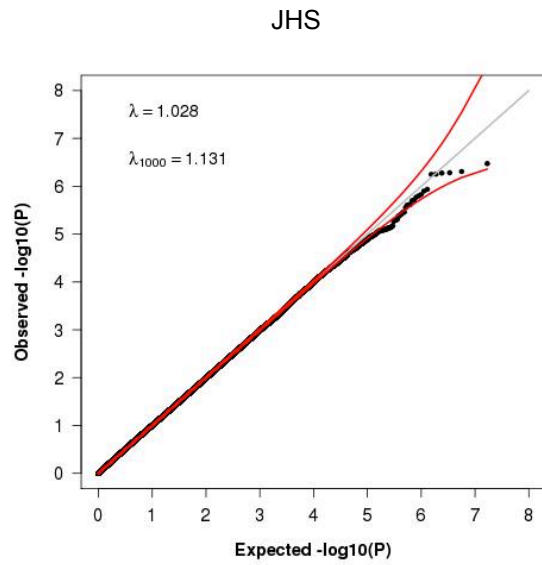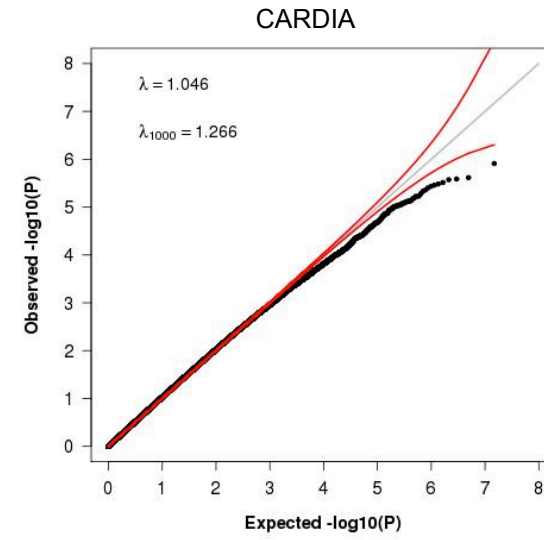|	Asthma	COPD	P-value
Allergic Status			
w/o allergies	71	76	<0.001
with allergies	86	33	
Lung Function			
normal lung function	122	74	0.045
low lung function	33	33	
Smokng Status			
never smoker	80	49	> 0.05
ever smoker	61	60	
Age			
median +/- SD	40 +/- 3.63	40 +/- 3.74	> 0.05

Supplemental Table 10: Comparison of phenotypic variables between subjects with self-reported asthma or self-reported COPD in CARDIA. Key variables that distinguish patients with asthma from patients with COPD (allergic status, lung function, smoking status, and age) were compared in order to determine if the asthma subjects identified in CARDIA were phenotypically distinct from the COPD subjects identified in CARDIA. P-values are determined with Chi-Square or Fisher's exact test, where appropriate. Taken together, these results argue that our method of defining asthma by self-report combined with the exclusion of those with self-reported COPD successfully allowed us to isolate a cohort of asthmatics that was phenotypically distinct from subjects with COPD in CARDIA.

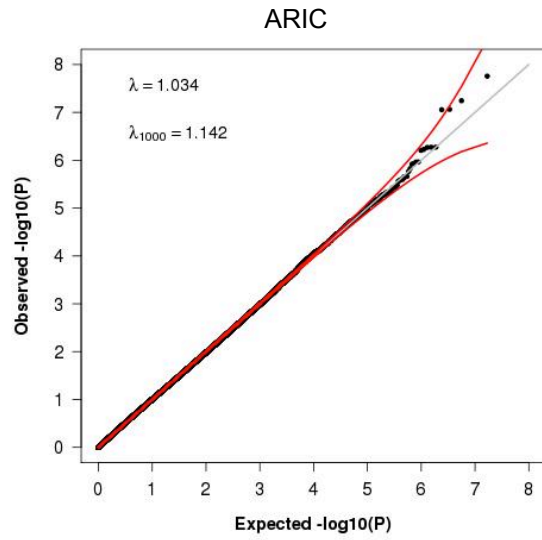|	Asthma	COPD	P-value
Allergic Status			
w/o allergies	n/a	n/a	n/a
with allergies	n/a	n/a	
Lung Function			
normal lung function	198	141	> 0.05
low lung function	18	11	
Smokng Status			
never smoker	141	80	0.038
ever smoker	73	66	
Age			
median +/- SD	51 +/- 12.6	55 +/- 12.3	> 0.05

Supplemental Table 11: Comparison of phenotypic variables between subjects with self-reported asthma or self-reported COPD in JHS. Key variables that distinguish patients with asthma from patients with COPD (lung function, smoking status, and age) were compared in order to determine if the asthma subjects identified in JHS were phenotypically distinct from the COPD subjects identified in JHS. P-values are determined with Chi-Square or Fisher's exact test, where appropriate. Taken together, these results argue that our method of defining asthma by self-report combined with the exclusion of those with self-reported COPD successfully allowed us to isolate a cohort of asthmatics that was phenotypically distinct from subjects with COPD in JHS.

	Asthma	COPD	P-value
Allergic Status			
w/o allergies	127	10	< 0.001
with allergies	82	36	
Lung Function			
normal lung function	189	36	0.004
low lung function	19	8	
Smokng Status			
never smoker	100	5	< 0.001
ever smoker	104	39	
Age			
median +/- SD	59 +/- 10.2	67 +/- 10.0	< 0.001

Supplemental Table 12: Comparison of phenotypic variables between subjects with self-reported asthma or self-reported COPD in MESA. Key variables that distinguish patients with asthma from patients with COPD (allergic status, lung function, smoking status, and age) were compared in order to determine if the asthma subjects identified in MESA were phenotypically distinct from the COPD subjects identified in MESA. P-values are determined with Chi-Square or Fisher's exact test, where appropriate. Taken together, these results argue that our method of defining asthma by self-report combined with the exclusion of those with self-reported COPD successfully allowed us to isolate a cohort of asthmatics that was phenotypically distinct from subjects with COPD in MESA.
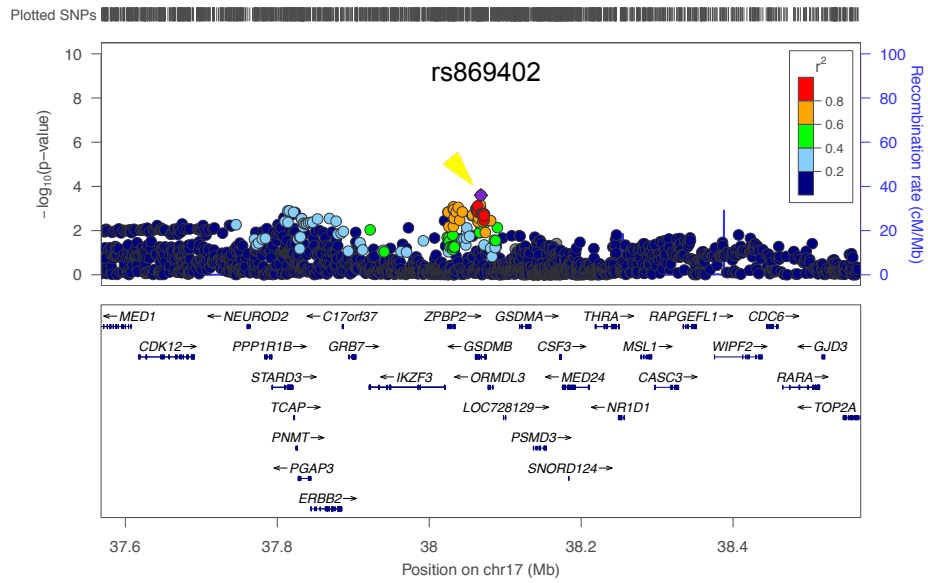
Supplemental Figure 1

ARIC

$\lambda = 1.034$

$\lambda_{1000} = 1.142$

CARDIA

$\lambda = 1.046$

$\lambda_{1000} = 1.266$

JHS

$\lambda = 1.028$

$\lambda_{1000} = 1.131$

MESA

$\lambda = 1.022$

$\lambda_{1000} = 1.13$

Supplemental Figure 2

A *GSDMB/ORMDL3* African Signal

B *GSDMB/ORMDL3* European Signal

Supplemental Figure 3