

## Supplementary Materials

### Admixture Mapping Identifies Novel Loci for Obstructive Sleep Apnea in Hispanic/Latino Americans

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## Supplementary Methods

Replication analysis was conducted using independent European American, African American, and Hispanic/Latino American cohorts. The replication cohorts, chosen because they share one or all ancestries with the HCHS/SOL samples, were the Atherosclerosis Risk in Communities (ARIC), the Cleveland Family Study (CFS), the Cardiovascular Health Study (CHS), the Framingham Heart Study (FHS), the Jackson Heart Study (JHS), the Starr County Health Studies, the Multi-Ethnic Study of Atherosclerosis (MESA) and the Osteoporotic Fractures in Men Study (MrOS).

*The Atherosclerosis Risk in Communities (ARIC)* study is a community based study of atherosclerosis risk factors and cardiovascular outcomes. 11,478 European Americans and 4,266 African Americans were collected from 4 sites: Forsyth County, NC; Jackson, MI; Minneapolis, MN; and Washington County, MD at baseline exam between 19987 and 1989 (1). European Americans from the Maryland and Minnesota centers were recruited in the Sleep Heart Health Study (SHHS) to investigate the impact of sleep disordered breathing (2). Polysomnography data were collected using Compumedics PS-2 system (Compumedics Pty Ltd, Abbotsford, Australia). 1,432 participants genotyped by Affymetrix 6.0 array with available phenotypes were included in this study.

*The Cleveland Family Study (CFS)* is the largest family-based study of laboratory diagnosed sleep apnea patients and family members as well as neighborhood control families. 356 African-and European American families including 2,534 from northern Ohio were followed across five visits till 2006 (3). An Edentrace Type 3 home sleep apnea device was used (Eden Prairie, MN) to assess sleep apnea before 2000. 14-channel polysomnography (Compumedics E

series, Abbotsford, AU) were used in the last exam between 2000 and 2006 (4). This sample was genotyped by Affymetrix 6.0 and Illumina OmniExpress, Exome, and IBC chip arrays. 1,441 African- and European- Americans were included in this study.

*The Cardiovascular Health Study (CHS)* is a population-based study of factors of coronary heart disease and stroke risk factors in senior adults  $\geq 65$  years old from 1989 – 1999 (5). 5,201 European Americans and 687 African Americans were examined from four sites: Allegheny County, PA; Sacramento County, CA; Washington County, MD; and Winston-Salem, NC. Individuals from the first three centers enrolled in SHHS were assessed for polysomnography data. Samples were genotyped by Illumina CNV370, and/or Omni1M plus IBC genotypes. 185 African Americans and 731 European Americans with genotype and polysomnography data were obtained from dbGaP (pht003699.v1.p1).

*The Framingham Heart Study (FHS)* is a long period family-based cohort studying the risk factors and characteristics of cardiovascular disease (CVD) in Framingham, Massachusetts since 1948. The second-generation Offspring cohort of 5,124 individuals and their spouses was established in 1971 (6). A subset of them were enrolled in SHHS and screening for polysomnography by Compumedics PS-2 system (Compumedics Pty Ltd, Abbotsford, Australia). The Offspring cohort was genotyped by Affymetrix 500k and Illumina Omni 5M. 640 European Americans with genotypes and polysomnography were obtained from dbGaP (pht000395.v7.p8).

*The Jackson Heart Study (JHS)* is a African-American community-based cohort investigate the risk factors of cardiovascular diseases (7, 8). 5,306 participants were recruited from three counties MS (Hinds, Madison, and Rankin) of Jackson at baseline (2000-2004). An

ancillary sleep study associated with Exam 3 (2012-2016) was conducted measuring sleep apnea with the Embla Embletta Gold, a 14-channel device that includes an oximeter (Broomfield, CO). The ancillary sleep study occurred from 2012 – 2016, corresponding with Exam 3. Sleep questionnaire and additional anthropometry and phlebotomy were also collected. 496 individuals genotyped by Affymetrix 6.0 with available phenotypes were included for replication.

*The Multi-Ethnic Study of Atherosclerosis (MESA)* is a cohort study of risk effect of subclinical cardiovascular diseases in multiple ethnic groups (Asian, African American, European American, Hispanic/Latino American) (9). 6,814 participants aged from 45 to 84 were recruited from 6 communities: Baltimore MD, Chicago IL, Los Angeles CA, New York NY, Minneapolis/St. Paul MN, and Winston-Salem NC at baseline (2000). An ancillary sleep study of 2,060 individuals associated with Exam 5 (2010-2013) was conducted measuring in-home PSG, actigraphy, and a questionnaire adapted from the SHHS and HCHS sleep questionnaires. Unattended polysomnography was collected using a 15-channel monitor (Compumedics Somte System, Abbotsford, AU). African Americans, European Americans and Hispanic Latino Americans genotyped by Affymetrix 6.0 array were analyzed for SNP association replication. Gene expression data from monocytes of 619 individuals were further analyzed. Gene expression was measured using the Illumina HumanHT-12 v4 Expression BeadChip and Illumina Bead Array Reader followed by standard QC (10).

*The Osteoporotic Fractures in Men Study (MrOS)* is a cohort study of osteoporosis and fractures in older males (11, 12). Around 6,000 men aged  $\geq 65$  years were recruited from six medical centers in Birmingham AL, Minneapolis MN, Palo Alto CA, Monongahela Valley PA, Portland OR, and San Diego between 2000 and 2002. An ancillary sleep study of 3,135 individuals was conducted between 2003 and 2005. Unattended polysomnography was collected

using the Compumedics Safiro system (Abbotsford AU). Anthropometry and sleep questionnaires were also collected. 2,178 European Americans genotyped by Illumina Omi 1M array were included for replication.

*The Starr County Health Studies (Starr)* is a predominantly Mexican-American (97%) cohort examining the risk factors of diabetes in that Texas border county since 1981 (13, 14). Sleep apnea was assessed in 1,200 adults (ages between 30 and 90) using the WatchPAT-200 device (Itamar-Medical Ltd., Caesarea, Israel), with recording of finger pulse oximetry, actigraphy, body position, peripheral arterial tonometry, and snoring. The validation of WatchPAT using polysomnography has been demonstrated in previous publications. Additional questionnaire adapted from the HCHS sleep questionnaires was also collected. 782 individuals genotyped by Affymetrix 6.0 with available phenotypes were included for replication.

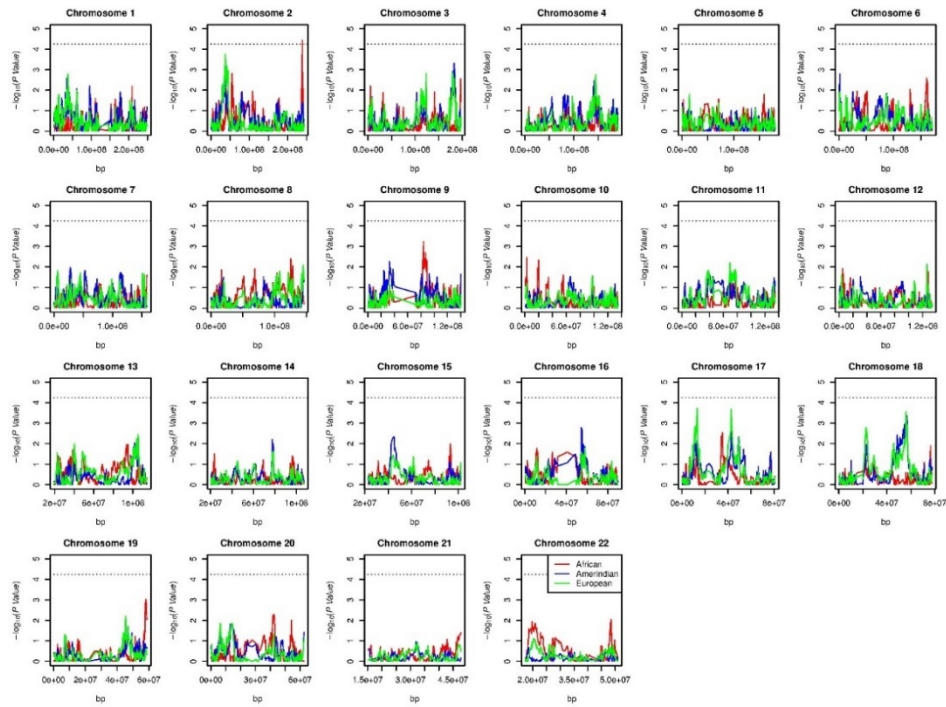
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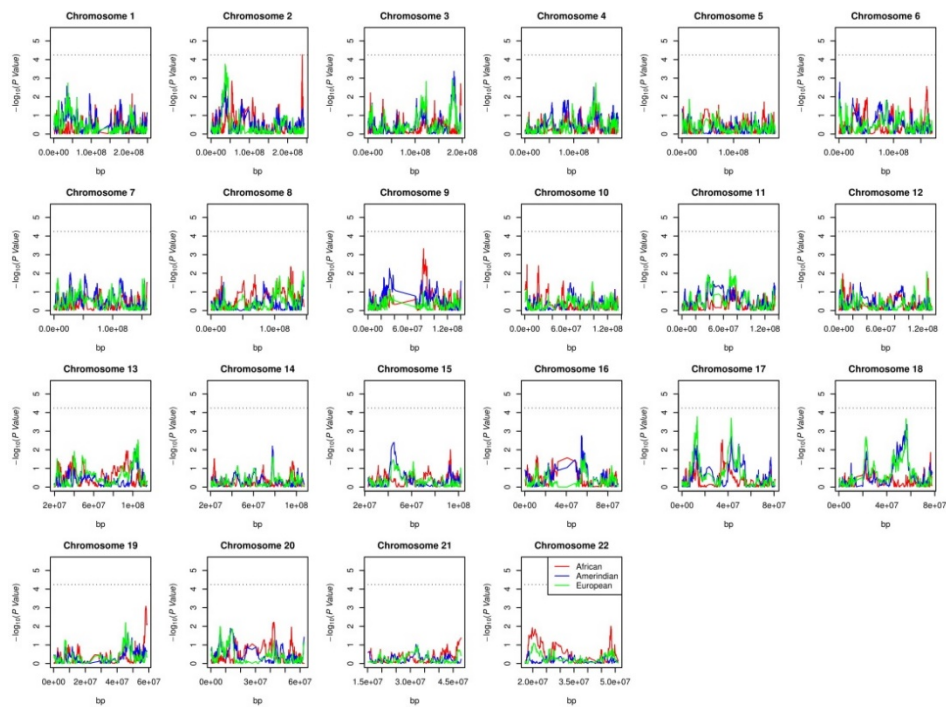
## Supplementary Figures

Supplementary Figure 1. Admixture mapping analysis results of AHI across the genome.

A. Primary model adjusting for sex, age, age<sup>2</sup>, Age×sex, BMI, BMI<sup>2</sup>, five PCs and kinship coefficients.



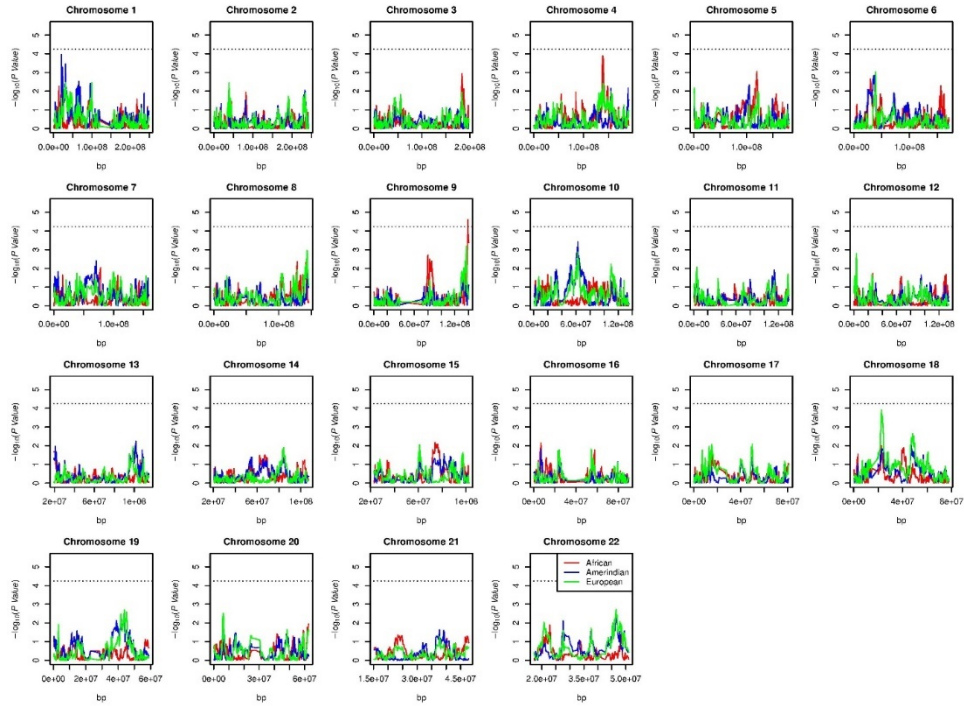
B. Secondary model adjusting for sampling weight, households, census blocks and covariates in A.



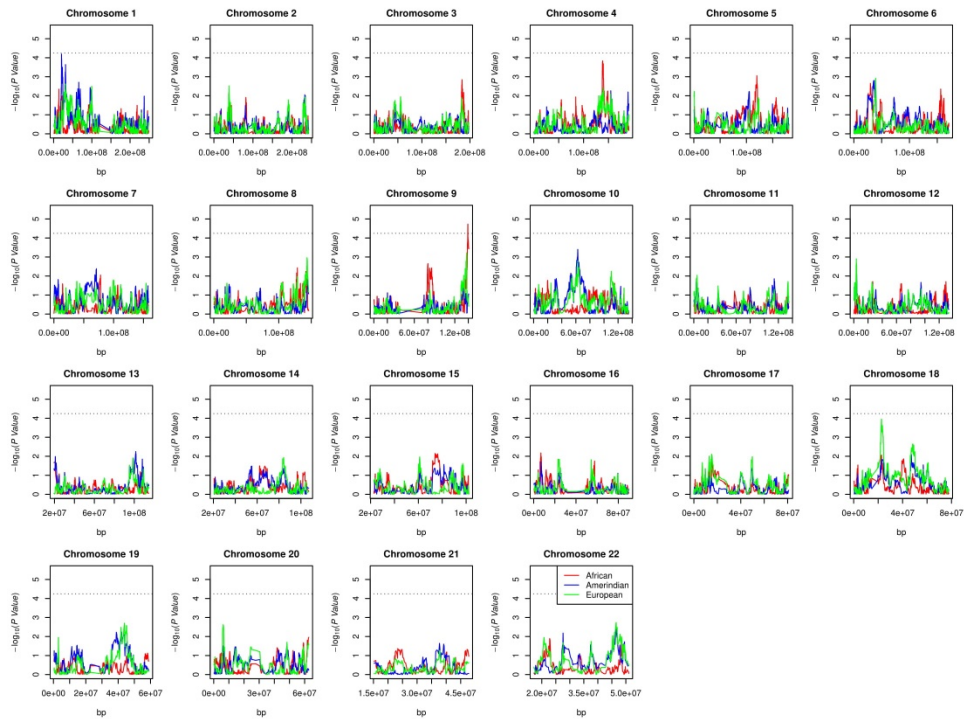


Supplementary Figure 2. Admixture mapping analysis results of average SaO<sub>2</sub> overnight.

A. Primary model adjusting for sex, age, age<sup>2</sup>, Age×sex, BMI, BMI<sup>2</sup>, five PCs and kinship coefficients.

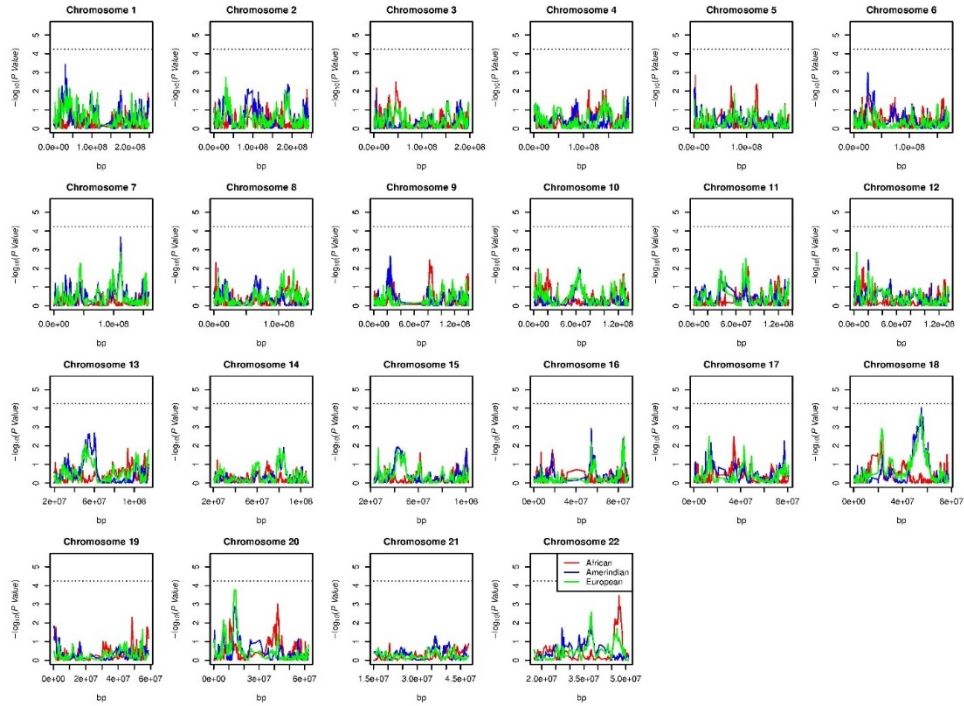


B. Secondary model adjusting for sampling weight, households, census blocks and covariates in A.

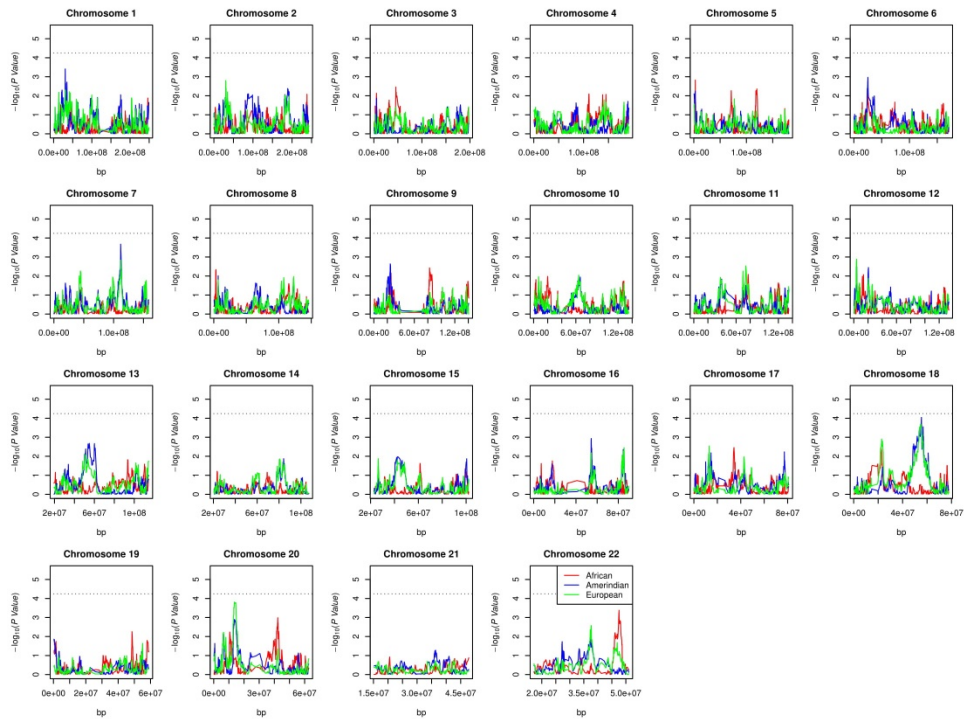


Supplementary Figure 3. Admixture mapping analysis results of percentage time SaO<sub>2</sub><90%.

A. Primary model adjusting for sex, age, age<sup>2</sup>, Age×sex, BMI, BMI<sup>2</sup>, five PCs and kinship coefficients.

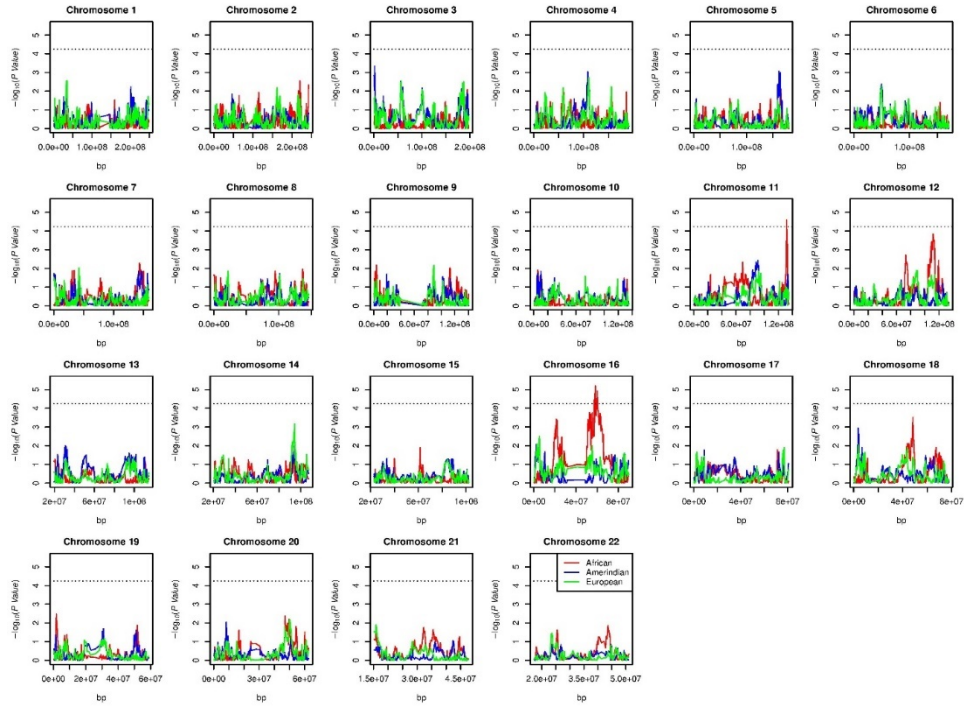


B. Secondary model adjusting for sampling weight, households, census blocks and covariates in A.

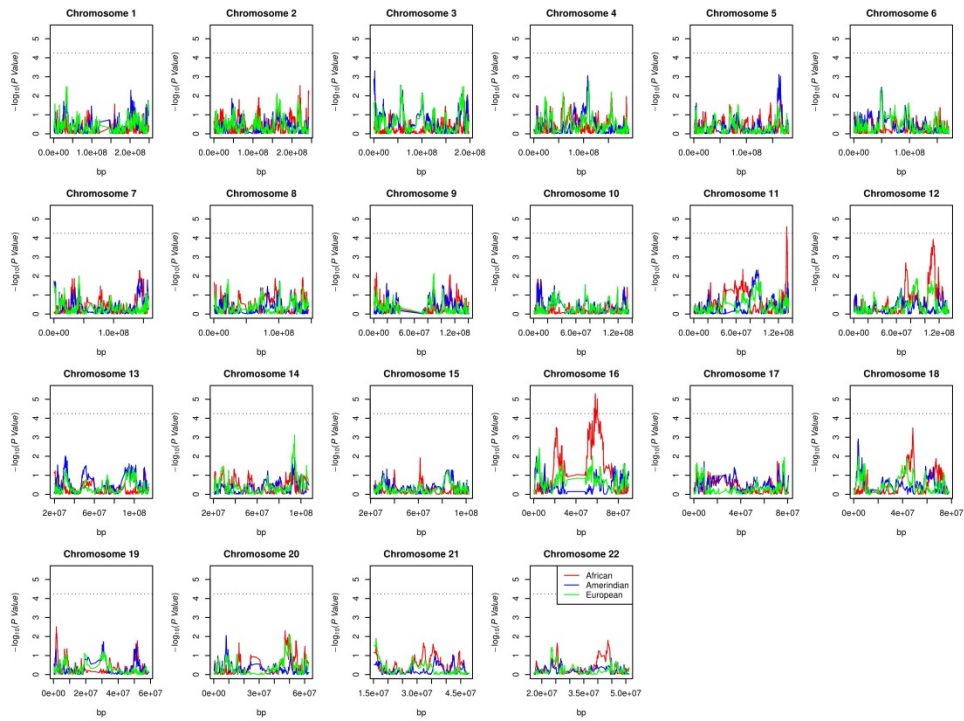


Supplementary Figure 4. Admixture mapping analysis results of average event duration.

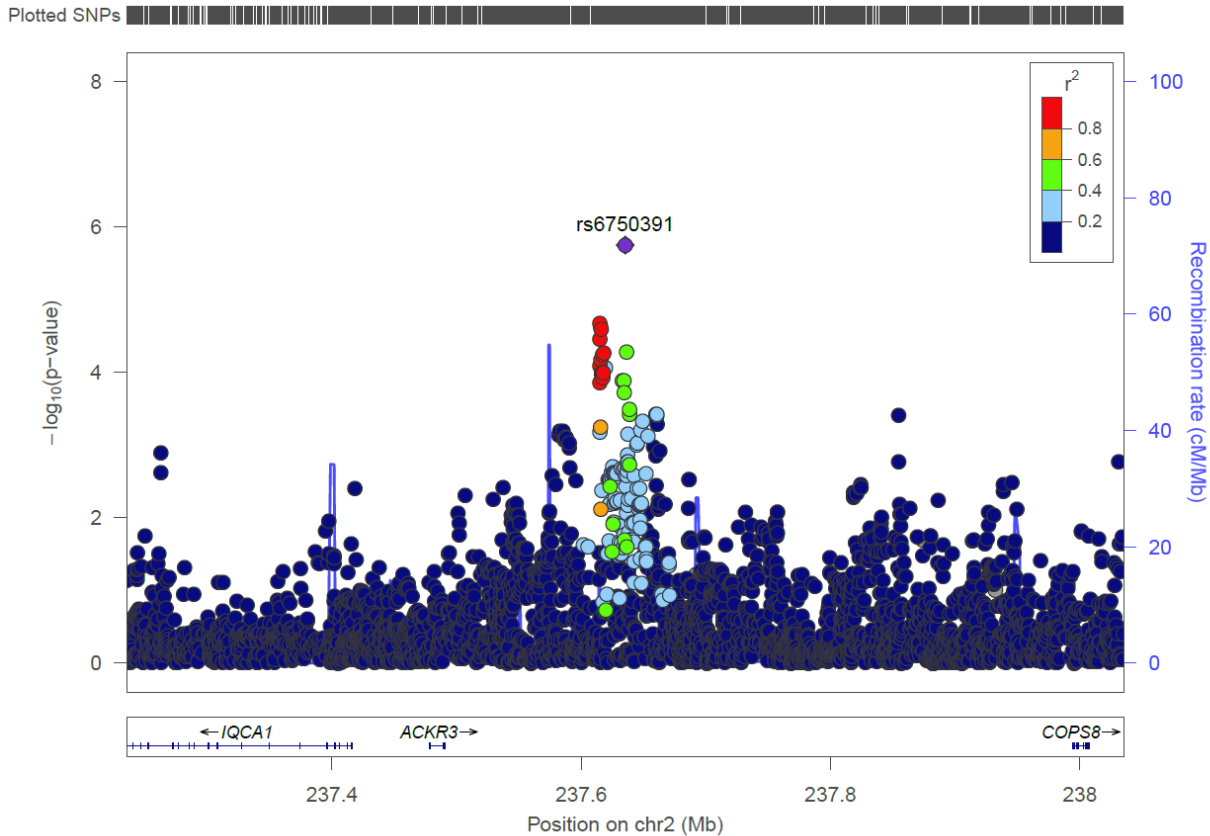
A. Primary model adjusting for sex, age, age<sup>2</sup>, Age×sex, BMI, BMI<sup>2</sup>, five PCs and kinship coefficients.



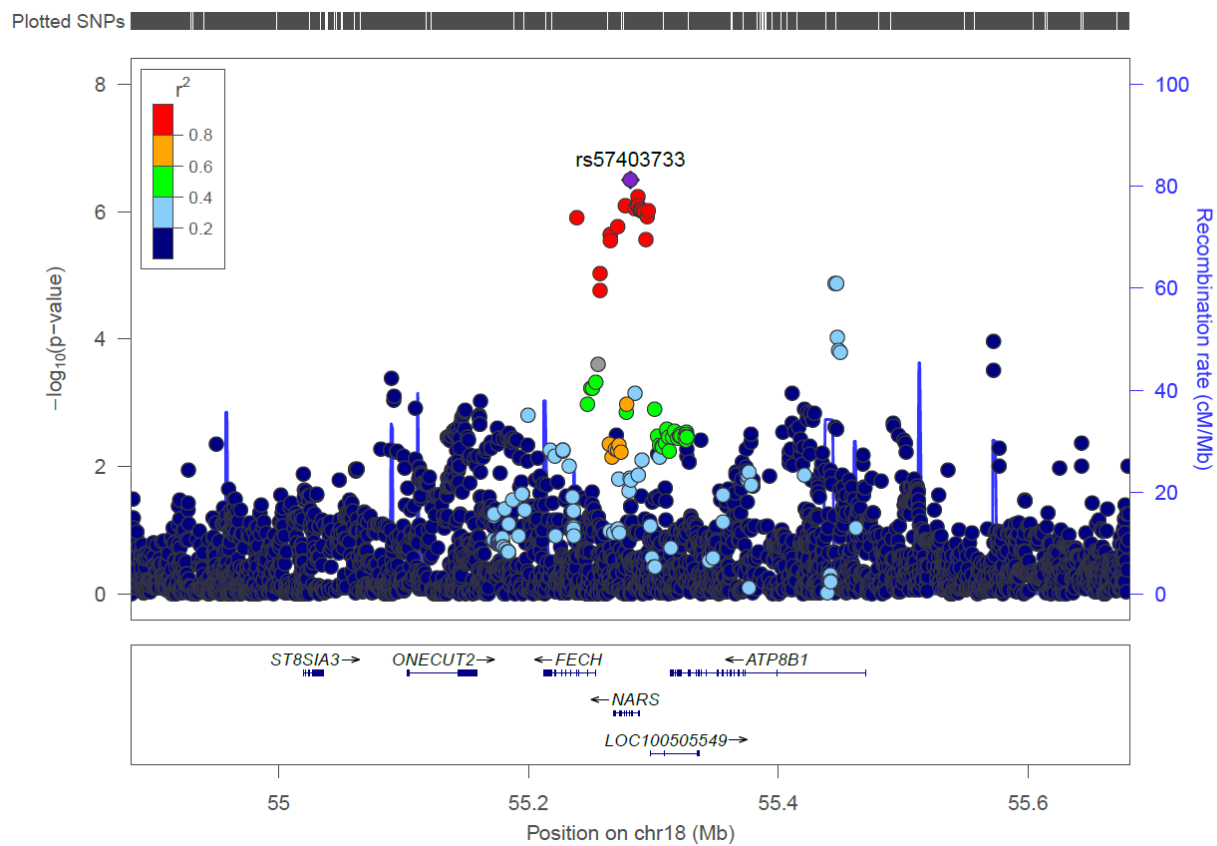
B. Secondary model adjusting for sampling weight, households, census blocks and covariates in A.



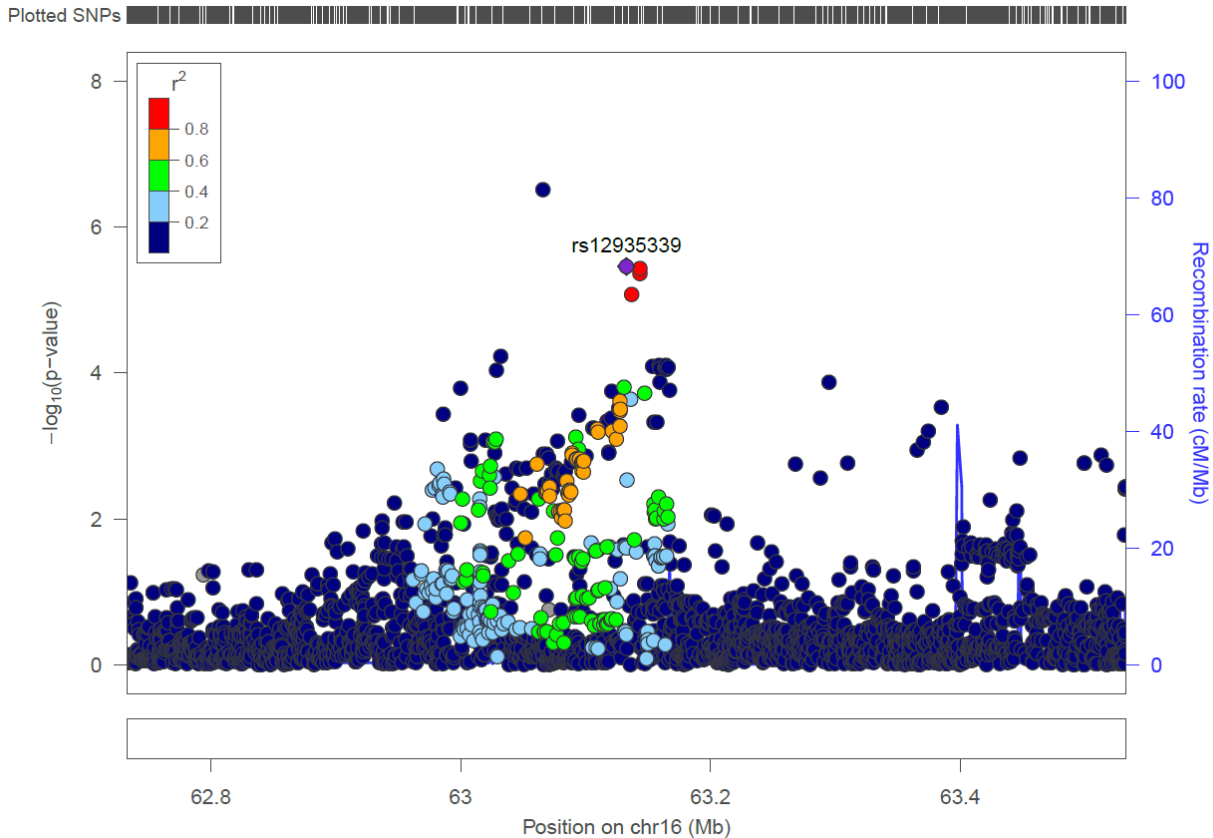
Supplementary Figure 5. Regional association plot of AHI at lincRNA *AC011286.1* on chromosome 2.



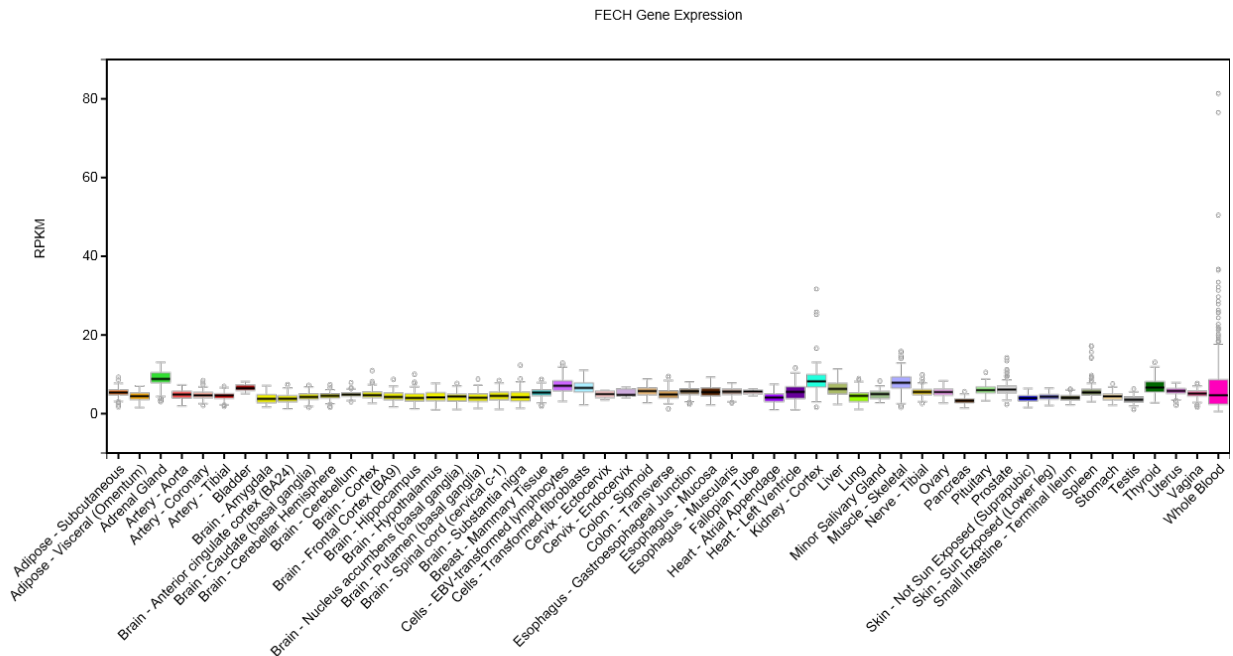
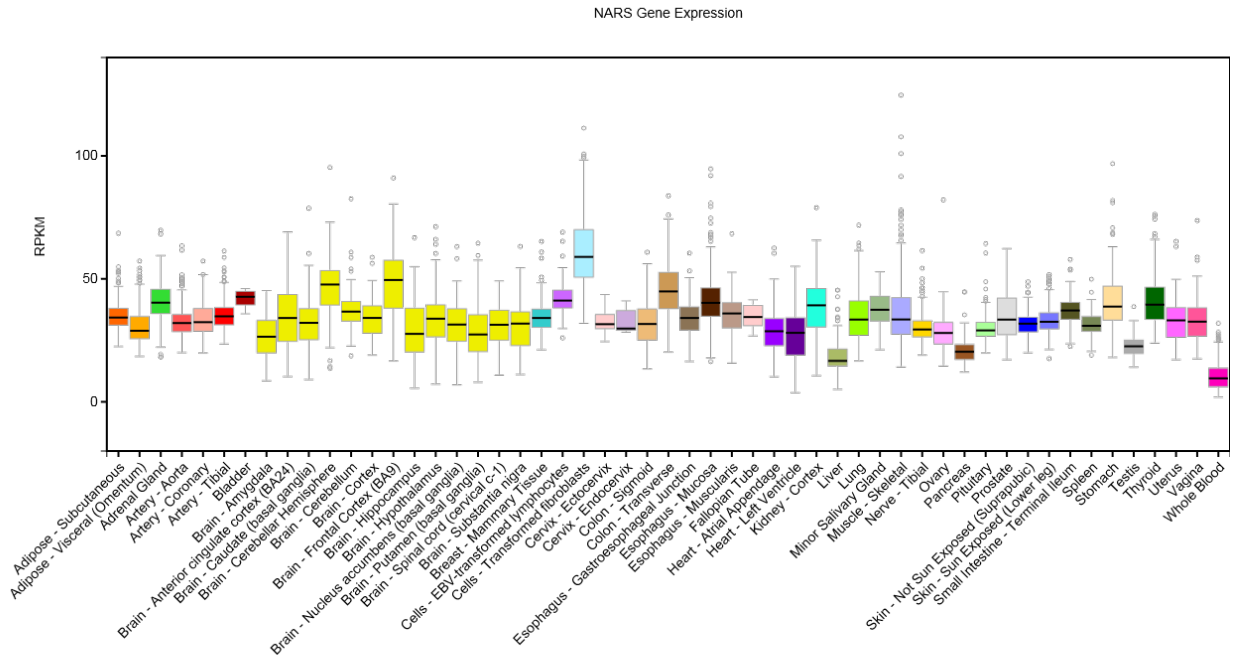
Supplementary Figure 6. Regional association plot of combined AHI and percentage time SaO<sub>2</sub><90% traits at gene *NARS/FECH* on chromosome 18.



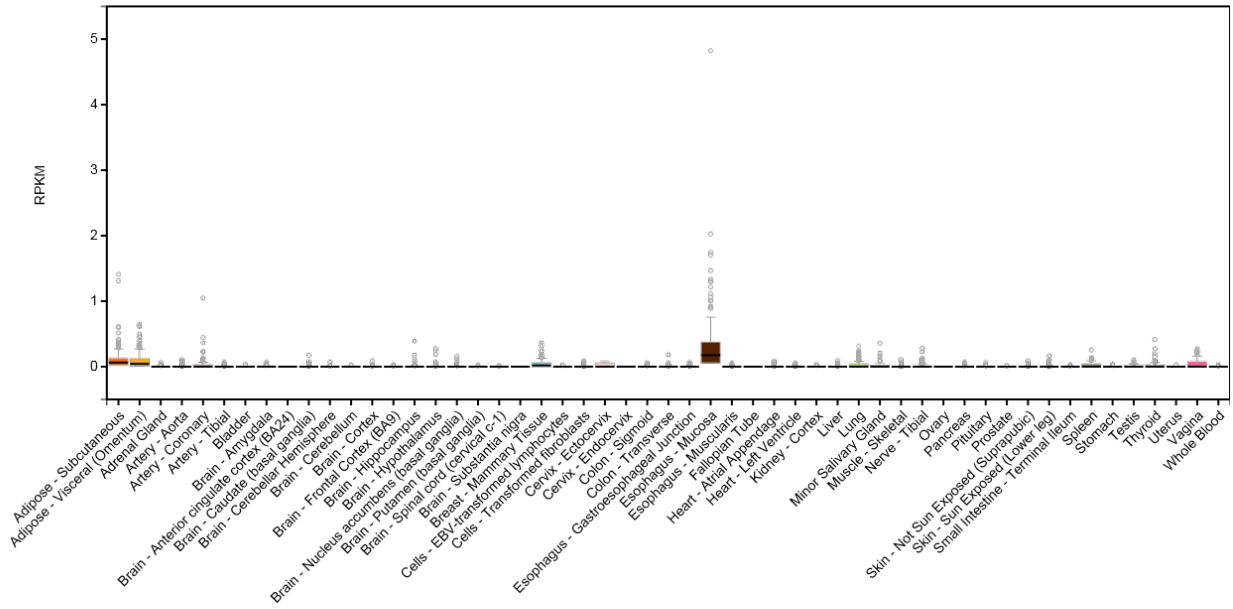
Supplementary Figure 7. Regional association plot of average event duration at lincRNA *RP11-96H17.1* on chromosome 16.



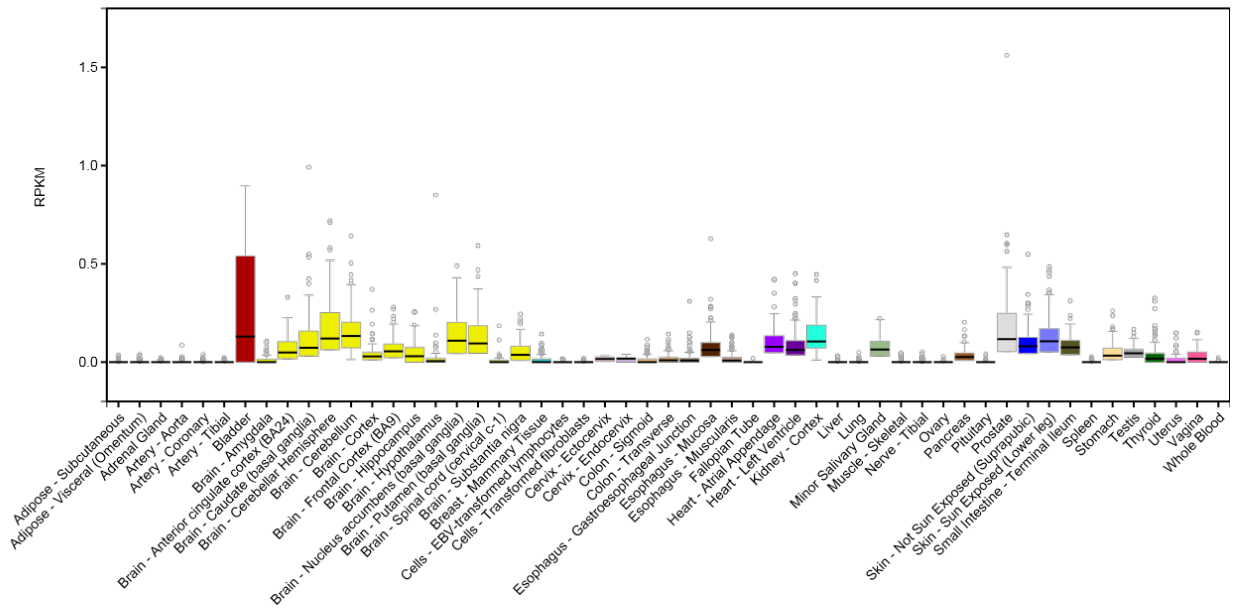
Supplementary Figure 8 Gene expression level in different tissues queried by GTEx.



AC011286.1 Gene Expression



RP11-96H17.1 Gene Expression





Supplementary Table 1. Pairwise correlations among OSA traits and other variables in the HCHS/SOL.

	<b>AHI</b>	<b>Average SaO<sub>2</sub></b>	<b>Percentage time SaO<sub>2</sub>&lt;90%</b>	<b>Average event duration</b>
<b>Average SaO<sub>2</sub></b>	-0.69 (-0.70,-0.68)			
<b>Percentage time SaO<sub>2</sub>&lt;90%</b>	0.77 (0.76,0.78)	-0.72 (-0.73,-0.71)		
<b>Average event duration</b>	0.07 (0.05,0.09)	-0.04 (-0.064,-0.02)	0.09 (0.06,0.11)	
<b>Age</b>	0.24 (0.22,0.25)	-0.30 (-0.32,-0.28)	0.14 (0.12,0.16)	0.18 (0.15,0.20)
<b>Male</b>	0.16 (0.14,0.18)	-0.15 (-0.16,-0.13)	0.10 (0.08,0.12)	0.12 (0.10,0.14)
<b>BMI</b>	0.30 (0.28,0.32)	-0.28 (-0.30,-0.27)	0.22 (0.20,0.24)	-0.15 (-0.17,-0.13)
<b>African Ancestry</b>	-0.01 (-0.03, 0.01)	0.02 (0.00,0.04)	-0.01 (-0.02,0.01)	-0.06 (-0.08,-0.04)
<b>Amerindian Ancestry</b>	-0.04 (-0.05,-0.02)	0.05 (0.03,0.07)	-0.02 (-0.04,0.00)	0.03 (0.01,0.05)
<b>European Ancestry</b>	0.05 (0.03,0.07)	-0.07 (-0.09,-0.05)	0.03 (0.01,0.05)	0.01 (-0.01,0.03)

Supplementary Table 2. Associations between each OSA trait with African and Amerindian global ancestries in one regression model, adjusting for sex, age, age<sup>2</sup>, age×sex, BMI, and BMI<sup>2</sup>.

	African Ancestry			Amerindian Ancestry		
	Estimate per 1% change of ancestry	SE	P	Estimate per 1% change of ancestry	SE	P
AHI	-0.0009	0.0006	0.105	0.0002	0.0004	0.538
Average SaO <sub>2</sub>	0.0022	0.0006	3.21×10 <sup>-4</sup>	0.0012	0.0004	0.003
Percentage time SaO <sub>2</sub> <90%	0.0001	0.0006	0.836	-0.0001	0.0004	0.738
Average event duration	-0.002	0.0007	8.27×10 <sup>-3</sup>	0.0023	0.0005	4.79×10 <sup>-6</sup>

Supplementary Table 3. Significant admixture mapping regions ( $P < 10^{-3}$ ).

Trait	Position (Mb)	Ancestry	Est	SE	P*
<b>AHI</b>	2:36.76-38.72	European	0.05	0.013	1.77E-04
N=10242	<b>2:237.54-238.39</b>	<b>African</b>	<b>-0.079</b>	<b>0.019</b>	<b>3.70E-05</b>
	3:182.34-182.54	Amerindian	-0.052	0.015	4.83E-04
	17:12.55-13.38	European	0.049	0.013	1.88E-04
	17:42.55-42.75	European	-0.048	0.013	2.06E-04
	<b>18:55.82-56.17</b>	<b>European</b>	<b>0.048</b>	<b>0.013</b>	<b>2.74E-04</b>
	<b>18:56.68-56.88</b>	<b>Amerindian</b>	<b>-0.052</b>	<b>0.015</b>	<b>4.46E-04</b>
<b>Average SaO<sub>2</sub></b>	1:20.48-31.29	Amerindian	0.063	0.016	1.07E-04
N=10267	4:137.49-139.75	African	0.079	0.021	1.29E-04
	5:119.80-120.00	African	0.071	0.021	8.85E-04
	6:39.13-39.33	European	0.046	0.014	9.20E-04
	9:137.20-137.62	European	0.048	0.014	6.28E-04
	10:62.50-62.79	Amerindian	-0.057	0.016	3.79E-04
	18:22.12-24.19	European	-0.055	0.014	1.22E-04
<b>Percentage time SaO<sub>2</sub>&lt;90%</b>	1:30.15-30.60	Amerindian	-0.054	0.015	3.82E-04
N=10267	7:111.59-112.47	Amerindian	0.056	0.015	2.12E-04
	<b>18:51.81-57.12</b>	<b>Amerindian</b>	<b>-0.058</b>	<b>0.015</b>	<b>9.15E-05</b>
	<b>18:53.54-56.17</b>	<b>European</b>	<b>0.049</b>	<b>0.013</b>	<b>2.01E-04</b>
<b>Average event duration</b>	3:1.70-1.90	Amerindian	-0.067	0.019	4.60E-04
N=8862	4:108.29-108.49	Amerindian	-0.065	0.02	8.97E-04
	5:161.67-161.96	Amerindian	0.065	0.02	8.71E-04
	12:108.22-113.79	African	0.097	0.025	1.43E-04
	14:94.14-94.34	European	-0.057	0.017	6.86E-04
	16:21.18-22.11	African	-0.09	0.025	3.77E-04
	<b>16:51.14-64.12</b>	<b>African</b>	<b>-0.113</b>	<b>0.025</b>	<b>6.42E-06</b>
	18:47.99-48.44	African	0.09	0.025	3.12E-04

\* Minimum P-value in each region.

Supplementary Table 4. All significant SNPs ( $p < 8 \times 10^{-6}$ ) under the candidate regions associated with OSA traits in HCHS/SOL.

SNP	B37 position	Alleles (E/A)	EAF	Trait	$\beta$ (se)	P	Combined P*
rs6750391	2:237635300	T/C	0.898	AHI	0.090 (0.019)	$1.78 \times 10^{-6}$	
rs56874481	2:237648772	TTG/T	0.133	AHI	-0.081 (0.018)	$4.76 \times 10^{-6}$	
rs74021948	16:63065908	A/C	0.984	Duration	0.302 (0.059)	$3.07 \times 10^{-7}$	
rs12935339	16:63132772	G/A	0.308	Duration	-0.074 (0.016)	$3.44 \times 10^{-6}$	
rs34398460	16:63133581	T/TA	0.339	Duration	-0.076 (0.016)	$3.58 \times 10^{-6}$	
rs11647443	16:63143791	A/G	0.299	Duration	-0.075 (0.016)	$3.71 \times 10^{-6}$	
rs57403733	18:55281709	G/A	0.803	AHI	0.066 (0.015)	$1.47 \times 10^{-5}$	$3.20 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.078 (0.015)	$3.98 \times 10^{-7}$	
rs388644	18:55287739	A/C	0.237	AHI	-0.059 (0.014)	$1.53 \times 10^{-5}$	$5.95 \times 10^{-7}$
				SaO <sub>2</sub> <90%	-0.068 (0.014)	$1.16 \times 10^{-6}$	
rs72627250	18:55277787	T/C	0.787	AHI	0.062 (0.015)	$2.25 \times 10^{-5}$	$7.98 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.072 (0.015)	$1.29 \times 10^{-6}$	
rs3745063	18:55287527	C/T	0.787	AHI	0.062 (0.015)	$1.97 \times 10^{-5}$	$8.02 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.071 (0.015)	$1.50 \times 10^{-6}$	
rs388644	18:55287739	A/T	0.787	AHI	0.062 (0.015)	$1.98 \times 10^{-5}$	$8.07 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.071 (0.015)	$1.51 \times 10^{-6}$	
rs56687381	18:55290397	AG/A	0.768	AHI	0.060 (0.014)	$1.62 \times 10^{-5}$	$8.77 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.067 (0.014)	$2.17 \times 10^{-6}$	
rs12458303	18:55285288	C/A	0.786	AHI	0.061 (0.015)	$2.82 \times 10^{-5}$	$9.09 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.071 (0.015)	$1.26 \times 10^{-6}$	
rs72627251	18:55289415	T/C	0.768	AHI	0.060 (0.014)	$1.75 \times 10^{-5}$	$9.26 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.067 (0.014)	$2.20 \times 10^{-6}$	
rs59479795	18:55290771	C/G	0.787	AHI	0.062 (0.015)	$1.97 \times 10^{-5}$	$9.28 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.071 (0.015)	$1.95 \times 10^{-6}$	
rs72627253	18:55296033	A/T	0.787	AHI	0.064 (0.015)	$1.43 \times 10^{-5}$	$9.55 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.070 (0.015)	$2.88 \times 10^{-6}$	
rs28555130	18:55290092	C/G	0.768	AHI	0.060 (0.014)	$1.76 \times 10^{-5}$	$9.81 \times 10^{-7}$
				SaO <sub>2</sub> <90%	0.067 (0.014)	$2.42 \times 10^{-6}$	
rs12454523	18:55292454	C/T	0.787	AHI	0.063 (0.015)	$1.99 \times 10^{-5}$	$1.00 \times 10^{-6}$
				SaO <sub>2</sub> <90%	0.070 (0.015)	$2.20 \times 10^{-6}$	
rs12454416	18:55292605	G/A	0.787	AHI	0.063 (0.015)	$2.01 \times 10^{-5}$	$1.01 \times 10^{-6}$
				SaO <sub>2</sub> <90%	0.070 (0.015)	$2.22 \times 10^{-6}$	
rs72627252	18:55295314	A/G	0.212	AHI	0.063 (0.015)	$2.26 \times 10^{-5}$	$1.22 \times 10^{-6}$
				SaO <sub>2</sub> <90%	0.070 (0.015)	$2.74 \times 10^{-6}$	
rs2272783	18:55238820	A/G	0.788	AHI	0.058 (0.015)	$6.78 \times 10^{-5}$	$1.24 \times 10^{-6}$
				SaO <sub>2</sub> <90%	0.073 (0.015)	$8.06 \times 10^{-7}$	
rs78641697	18:55271627	A/C	0.806	AHI	0.061 (0.015)	$5.80 \times 10^{-5}$	$1.72 \times 10^{-6}$
				SaO <sub>2</sub> <90%	0.074 (0.015)	$1.76 \times 10^{-6}$	
rs72627249	18:55265698	T/C	0.802	AHI	0.060 (0.015)	$6.29 \times 10^{-5}$	$2.28 \times 10^{-6}$
				SaO <sub>2</sub> <90%	0.072 (0.015)	$2.68 \times 10^{-6}$	
rs8095804	18:55294197	C/G	0.76	AHI	0.058 (0.014)	$2.51 \times 10^{-5}$	$2.74 \times 10^{-6}$
				SaO <sub>2</sub> <90%	0.062 (0.014)	$1.00 \times 10^{-5}$	

rs4940483	18:55265856	C/G	0.198	AHI	-0.060 (0.015)	$7.70 \times 10^{-5}$	$2.90 \times 10^{-6}$
				SaO <sub>2</sub> <90%	-0.071 (0.014)	$3.30 \times 10^{-6}$	
rs10559003	18:55295414	CTT/C	0.76	AHI	0.058 (0.014)	$2.68 \times 10^{-5}$	$3.07 \times 10^{-6}$
				SaO <sub>2</sub> <90%	0.062 (0.014)	$1.15 \times 10^{-6}$	

AHI: apnea hypopnea index

Duration: average respiratory event duration

SaO<sub>2</sub><90%: percentage time SaO<sub>2</sub><90%

\*For variants on chromosome 18 associated with both AHI and Per90, we performed CPASSOC to combine the effect of both traits.

Supplementary Table 5. Variants annotation queried from Haploreg.

Variant	Ref	Alt	AFR Freq of Alt	AMR Freq of Alt	EUR freq of Alt	Promoter histone marks	Enhancer	DNase	Proteins bound	Motifs changed	GRASP QTL hits	Selected eQTLhits	GENCODE genes	dbSNP func annot
<a href="#">rs6750391</a>	T	C	0.51	0.07	0.05		KID			SRF			6.7kb 5' of AC011286.1	
<a href="#">rs56874481</a>	TGT	T					BLD, HRT						AC011286.1	
<a href="#">rs74021948</a>	A	C	0.09	0.01	0					Cdx,FAC1,Hmbox1			25kb 3' of RP11-96H17.1	
<a href="#">rs12935339</a>	G	A	0.29	0.7	0.75					5 altered motifs		3 hits	RP11-96H17.1	
<a href="#">rs34398460</a>	T	TA								12 altered motifs			RP11-96H17.1	
<a href="#">rs11647443</a>	A	G	0.29	0.71	0.76					4 altered motifs		3 hits	RP11-96H17.1	
<a href="#">rs57403733</a>	G	A	0.01	0.21	0.04					Pbx3,VDR		1 hit	NARS	intronic
<a href="#">rs388644</a>	A	C,T	0.85	0.98	1	12 tissues	17 tissues						NARS	intronic
<a href="#">rs72627250</a>	T	C	0.01	0.23	0.07					HEN1,Nkx2,Tel2		1 hit	NARS	intronic
<a href="#">rs3745063</a>	C	T	0.01	0.23	0.07	5 tissues	14 tissues	MUS		Irf	1 hit	3 hits	NARS	intronic
<a href="#">rs56687381</a>	AG	A	0.1	0.24	0.08	SKIN	6 tissues	BLD,OVRY		AhR,Zbtb3		1 hit	1.2kb 5' of NARS	
<a href="#">rs12458303</a>	C	A	0.01	0.23	0.07		BLD			5 altered motifs		1 hit	NARS	intronic
<a href="#">rs72627251</a>	T	C	0.1	0.23	0.08	24 tissues		53 tissues	4 bound proteins	SMC3		1 hit	237bp 5' of NARS	
<a href="#">rs59479795</a>	C	G	0.01	0.23	0.07		BRST	BLD,MUS		HMG-IY		1 hit	1.6kb 5' of NARS	

Variant	Ref	Alt	AFR freq	AMR freq	EUR freq	Promoter histone marks	Enhancer	DNase	Proteins bound	Motifs changed	GRASP QTL hits	Selected eQTLhits	GENCODE genes	dbSNP func annot
<a href="#">rs72627253</a>	A	T	0.02	0.22	0.07		VAS			8 altered motifs		1 hit	6.9kb 5' of NARS	
<a href="#">rs28555130</a>	C	G	0.1	0.23	0.08	13 tissues	13 tissues	KID		5 altered motifs		1 hit	914bp 5' of NARS	
<a href="#">rs12454523</a>	C	T	0.01	0.23	0.07		4 tissues	21 tissues	TCF4			3 hits	3.3kb 5' of NARS	
<a href="#">rs12454416</a>	G	A	0.01	0.23	0.07		BRN	SKIN	TCF4	4 altered motifs		1 hit	3.4kb 5' of NARS	
<a href="#">rs72627252</a>	A	G	0.01	0.23	0.07		11 tissues	ESDR,SKIN		8 altered motifs		1 hit	6.1kb 5' of NARS	
<a href="#">rs2272783</a>	A	G	0.02	0.22	0.05					RFX5	2 hits	21 hits	FECH	intronic
<a href="#">rs78641697</a>	A	C	0.01	0.19	0.03		BLD			10 altered motifs		1 hit	NARS	intronic
<a href="#">rs72627249</a>	T	C	0.01	0.2	0.04							2 hits	2.2kb 3' of NARS	
<a href="#">rs8095804</a>	C	G	0.12	0.24	0.08		LIV	BLD			1 hit	1 hit	5kb 5' of NARS	
<a href="#">rs4940483</a>	G	C	0.01	0.2	0.04					5 altered motifs		2 hits	2kb 3' of NARS	
<a href="#">rs10559003</a>	CTT	C	0.12	0.24	0.08							1 hit	6.2kb 5' of NARS	

Supplementary Table 6. Characteristics of replication cohorts

	<b>ARIC</b>	<b>CFS</b>	<b>CFS</b>	<b>CHS</b>	<b>CHS</b>	<b>FHS</b>	<b>JHS</b>	<b>MESA</b>	<b>MESA</b>	<b>MESA</b>	<b>MrOS</b>	<b>Starr</b>
Population	EA	AA	EA	AA	EA	EA	AA	AA	HA	EA	EA	HA
N	1,432	731	710	185	731	640	496	490	458	707	2,178	782
Male%	48%	43%	47%	39%	38%	47%	38%	45%	47%	47%	100%	28%
Age, yrs, mean (SD)	62.43 (5.69)	37.78 (19.46)	41.55 (19.45)	75.67 (4.7)	77.78 (4.33)	58.82 (9.37)	63 (10.83)	69.15 (9.15)	68.64 (9.32)	68.94 (9.28)	76.67 (5.66)	52.34 (11.29)
BMI, kg/m <sup>2</sup> , mean (SD)	28.83 (5.13)	31.73 (9.89)	30.24 (8.66)	28.71 (4.86)	27.16 (4.43)	27.85 (5.09)	32.44 (7.49)	30.47 (5.7)	30.1 (5.54)	28.07 (5.37)	27.22 (3.74)	32.15 (6.78)
AHI, events/h, mean (SD)	14.13 (15.48)	17.52 (26.43)	16.32 (24.2)	15.38 (14.91)	15.3 (15.14)	12.94 (14.67)	15.39 (15.57)	20.09 (19.85)	21.99 (18.78)	18.69 (18.05)	17.32 (15.49)	15.75 (17.07)
Average SaO <sub>2</sub> , %, mean (SD)	94.47 (1.99)	94.58 (3.77)	93.74 (3.66)	95.01 (2.07)	94.14 (1.9)	94.68 (1.96)	94.73 (2.06)	94.44 (1.96)	94.33 (1.56)	93.93 (1.75)	93.85 (1.73)	94.65 (2.09)
Percentage time SaO <sub>2</sub> <90%, mean (SD)	3.4 (10.35)	4.85 (13.87)	4.42 (12.68)	3.08 (8.64)	4.42 (12.17)	2.87 (8.48)	3.17 (9.15)	4.01 (9.46)	3.83 (7.35)	4.36 (10.83)	4.42 (9.93)	2.83 (8.79)
Average event duration, s, mean (SD)	23.71 (6.55)	20.3 (5.5)	20.57 (6.12)	20.97 (4.7)	21.4 (4.88)	24.07 (6.26)	18.49 (3.79)	19.73 (4.84)	21.2 (5.92)	21.63 (5.52)	26.87 (6.86)	NA



Supplementary Table 7. Replication analysis of lead SNPs in independent cohorts.

SNP	A1/A2	TRAIT	AA				EA				HA			
			Effect	P-value	Direction	N	Effect	P-value	Direction	N	Effect	P-value	Direction	N
rs6750391	T/C	AHI	0.018	0.539	+++	1935	-0.045	0.257	++++	6490	-0.051	0.473	--	1240
rs74021948	A/C	Duration	-0.004	0.479	+++	1606								
rs12935339	G/A	Duration	-0.003	0.696	---	1606	0.227	0.079	+++++	6066	0.004	0.257	+?	454
rs34398460	T/TA	Duration	0.006	0.522	+??	690								
rs11647443	A/G	Duration	0.004	0.639	+++	1606	0.232	0.076	+++++	6066	0.003	0.432	+?	454
rs57403733	A/G	AHI	0.126	0.381	+++	1935	0.015	0.777	++?+-	5727	-0.026	0.571	--	1240
		SaO <sub>2</sub> <90%	-0.079	0.533	+++	1935	0.012	0.836	++?+-	5272	-0.052	0.272	--	1240
rs388644	A/C	AHI	0.006	0.880	+++	1935	0.026	0.511	?++++	5027	-0.029	0.503	--	1240
		SaO <sub>2</sub> <90%	0.011	0.793	---	1935	0.077	0.050	?++++	5027	-0.065	0.141	--	1240
rs72627250	T/C	AHI	0.081	0.438	+++	1935	-0.052	0.130	-----	6490	0.032	0.469	++	1240
		SaO <sub>2</sub> <90%	0.157	0.147	+++	1935	-0.109	0.002	-----	6490	0.043	0.355	++	1240
rs3745063	C/T	AHI	0.078	0.450	+++	1935	-0.048	0.164	-----	6490	0.029	0.509	++	1240
		SaO <sub>2</sub> <90%	0.163	0.129	+++	1935	-0.110	0.002	-----	6490	0.042	0.361	++	1240
rs388644	A/T	AHI	0.005	0.969	-+?+	1427	-0.031	0.443	?-----	5027	0.029	0.509	++	1240
		SaO <sub>2</sub> <90%	0.101	0.438	-+?+	1427	-0.081	0.042	?-----	5027	0.042	0.360	++	1240
rs56687381	AG/A	AHI	0.056	0.252	++++	1935	-0.046	0.176	-----	6490	0.043	0.318	++	1240
		SaO <sub>2</sub> <90%	0.069	0.181	+++	1935	-0.069	0.075	-----	6490	0.035	0.427	++	1240

rs12458303	C/A	AHI	0.058	0.570	----+	1935	-0.054	0.117	-----	6490	0.031	0.488	++	1240
		SaO <sub>2</sub> <90%	0.144	0.172	----+	1935	-0.107	0.002	-----	6490	0.043	0.351	++	1240
rs72627251	T/C	AHI	0.059	0.233	++++	1935	-0.045	0.189	-----	6490	0.043	0.320	++	1240
		SaO <sub>2</sub> <90%	0.067	0.190	+++	1935	-0.097	0.004	-----	6490	0.035	0.431	++	1240
rs59479795	C/G	AHI	0.076	0.464	----+	1935	-0.053	0.129	-----	6490	0.030	0.499	++	1240
		SaO <sub>2</sub> <90%	0.163	0.128	----+	1935	-0.105	0.003	-----	6490	0.043	0.348	++	1240
rs72627253	A/T	AHI	0.037	0.708	----+	1935	-0.056	0.110	-----	6490	0.029	0.515	++	1240
		SaO <sub>2</sub> <90%	0.118	0.255	----+	1935	-0.104	0.003	-----	6490	0.044	0.336	++	1240
rs28555130	C/G	AHI	0.058	0.236	++++	1935	-0.045	0.186	-----	6490	0.043	0.318	++	1240
		SaO <sub>2</sub> <90%	0.068	0.186	----+	1935	-0.096	0.005	-----	6490	0.035	0.429	++	1240
rs12454523	T/C	AHI	-0.075	0.472	+++	1935	0.053	0.123	+++++	6490	-0.030	0.494	--	1240
		SaO <sub>2</sub> <90%	-0.164	0.127	+++	1935	0.104	0.003	+++++	6490	-0.043	0.342	--	1240
rs12454416	G/A	AHI	0.074	0.472	----+	1935	-0.054	0.120	-----	6490	0.030	0.493	++	1240
		SaO <sub>2</sub> <90%	0.164	0.127	----+	1935	-0.103	0.003	-----	6490	0.044	0.341	++	1240
rs72627252	A/G	AHI	0.081	0.433	----+	1935	-0.057	0.100	-----	6490	0.030	0.502	++	1240
		SaO <sub>2</sub> <90%	0.164	0.126	----+	1935	-0.104	0.003	-----	6490	0.042	0.364	++	1240
rs2272783	A/G	AHI	-0.189	0.144	--?-	1427	-0.019	0.637	--?++	5727	-0.002	0.966	-+	1240
		SaO <sub>2</sub> <90%	0.007	0.951	--?-	1427	-0.037	0.336	--?++	5727	0.031	0.495	++	1240
rs78641697	A/C	AHI	-0.196	0.193	--?-	1427	0.001	0.991	--?++	5727	0.024	0.592	++	1240

		SaO <sub>2</sub> <90%	0.010	0.938	--?-	1427	-0.031	0.608	--?-++	5727	0.051	0.279	++	1240
rs72627249	T/C	AHI	-0.152	0.276	--?-	1427	-0.018	0.728	--?-++	5727	0.025	0.582	++	1240
		SaO <sub>2</sub> <90%	0.055	0.658	--?-	1427	0.026	0.610	--?+++	5727	0.047	0.314	++	1240
rs8095804	C/G	AHI	0.044	0.321	+++	1935	-0.045	0.181	----++	6490	0.051	0.232	++	1240
		SaO <sub>2</sub> <90%	0.022	0.644	+++	1935	-0.096	0.005	----+-	6490	0.035	0.421	++	1240
rs4940483	C/G	AHI	0.152	0.275	+?-+	1427	0.018	0.728	++?+--	5727	-0.025	0.582	--	1240
		SaO <sub>2</sub> <90%	-0.055	0.658	+?-+	1427	-0.026	0.609	++?+--	5727	-0.047	0.314	--	1240
rs10559003	CTT/C	AHI	0.051	0.259	+++	1935	-0.049	0.150	----++	6490	0.049	0.252	++	1240
		SaO <sub>2</sub> <90%	0.024	0.604	+++	1935	-0.064	0.104	----++	6490	0.034	0.436	++	1240

AHI: apnea hypopnea index

Duration: average respiratory event duration

SaO<sub>2</sub><90%: percentage time SaO<sub>2</sub><90%