Support Vector Machine Prediction of Obstructive Sleep Apnea in a Large-Scale Chinese Clinical Sample

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Supplemental material

1. Table S1

2. Table S2

3. Table S3

4. Table S4

5. Table S5 (Supplementary Excel). Results of Forward stepwise feature selection. Feature marked in yellow was selected in each iteration. Features included in the red rectangle were used for SVM training.

6. Table S6

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8. Figure S1

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Table S1. Summary of published OSA prediction models

(A) Key information

Author year	Source	Training set			Validation set			AHI cutoff (/hr)	Preva (%)	AUROC	Sen (%)	Spec (%)	PPV (%)	NPV (%)
		No.	Age (y/o)	Man (%)	No..	Age (y/o)	Male (%)							
Kirby 1999 [1]	S	405	47.2	72.3	150	51	66	≥10	65.00	0.94	98.90	80.00	88.10	98.00
Rowley 2000 [2]	S	370	46.5	51.6	370	46.5	51.6	[1] ≥10 [2] ≥20	[1] 67.02 [2] 48.65	[1] 0.67-0.74 [2] 0.70-0.76	[1] 76-96 [2] 33-39	[1] 13-54 [2] 87-93	[1] 66-77 [2] 72-85	N/A
Rodsutti 2004 [3]	S	837	N/A	68.2	243	51.0	63.0	≥5	72.02	0.79	100.00	30.88	80.66	84.50
Sharma 2006 [4]	S	102	N/A	68.6	104	NA	77.9	≥15	48.08	NA	82.00	90.70	89.13	84.50
Takegami 2009 [5]	S	307	49.9	66.1	308	43.8	99.0	[1] ≥15* [2] ≥30	[1] 22.40 [2] 6.81	[1] 0.78 [2] 0.85	[1] 73.9 [2] 95.2	[1] 66.1 [2] 61.00	[1] 38.62 [2] 93.09	[1] 89.77 [2] 85.62
Caffo 2010 [6]	C	4,147	N/A	N/A	1,383	65.0	47.3	≥7*	37.80	0.75	66.00	70.00	57.00	77.21
Bouloukaki 2011 [7]	S	538	N/A	N/A	2,690	50.7	79	≥15	79.00	0.78	70.00	73.10	81.00	62.00
Zou 2013 [8]	S	2032	43	82.4	784	41.0	83.2	≥5	83.80	I:0.84 II:0.98	I:86.91 II:94.22	I:74.80 II:85.83	I:94.69 II:97.17	I:52.49 II:74.15
Marti-Soler 2016 [9]	C	2,121	59.0	48.0	1,042	42.0	45.0	>20	11.52	0.74	85.00	77.001	33.0	98.0
Shah 2016 [10]	C	12,158	48.1	39.4	12,158	48.1**	39.4	≥15	9.02	0.83	77.00	75.00	23.39	97.05
Ustun 2016 [11]	S	1,922	50.2	58.7	1,922	50.2	58.7	>5 or >10 *	76.90	[1] 0.77 [2] 0.79	[1] 82.80 [2] 83.20	[1] 56.20 [2] 58.90	[1] 86.29 [2] 87.08	[1] 49.53 [2] 51.29
Liu 2017 [12]	S	5,245	45.3	76.3	1,154	47.4	70.7	[1] ≥15 [2] ≥30	[1] 61.87 [2] 44.04	N/A	[1] 68.35 [2] 68.32	[1] 82.55 [2] 79.85	[1] 86.40 [2] 64.99	[1] 61.65 [2] 77.45
Shin 2017 [13]	SW	108,781	54.4	44.4	108,781	54.4	44.4	>5	2.08	0.82	72.30	76.20	6.06	99.23
Tan 2017 [14]	C	N/A	N/A	N/A	242	48.3	50.4	[1] ≥15 [2] ≥20 [3] ≥25 [3] ≥30	[1] 28.10 [2] 20.20 [3] 14.50 [3] 10.70	[1] 0.70 [2] 0.74 [3] 0.73 [3] 0.71	[1] 60.30 [2] 69.40 [3] 71.40 [3] 69.20	[1] 79.70 [2] 78.20 [3] 75.4 [3] 73.1	[1] 53.90 [2] 44.70 [3] 32.90 [3] 23.70	[1] 83.70 [2] 91.00 [3] 94.00 [3] 95.20
Traxdorf 2017 [15]	S	60	48.8	81.7	100	48.1	76.0	[1] ≥5 [2] ≥15 [3] >30	[1] 70.00 [2] 55.50 [3] 26.00	N/A	[1] 94.30 [2] 92.70 [3] 92.30	[1] 50.00 [2] 33.30 [3] 22.90	[1] 81.50 [2] 62.90 [3] 29.60	[1] 78.90 [2] 78.90 [3] 89.50
Duarte 2018 [16]	S	2,037	45.0	55.9	2,035	44.0	53.2	[1] ≥5	[1] 76.40	[1] 0.78	[1] 83.10	[1] 58.20	[1] 86.50	[1] 51.60

	Algorithm						Threshold						
							2. ≥15	2. 54.70	2. 0.76	2. 88.70	2. 45.30	2. 66.20	2. 76.80
							3. ≥30	3. 35.80	3. 0.75	3. 91.50	3. 36.80	3. 44.60	3. 88.60
Present study	S	6,875	47.8	76.0	6,875	47.8	76.0	1. ≥5	1. 82.47	1. 0.82	1. 74.90	1. 73.97	1. 93.14	1. 38.56
								2. ≥15	2. 61.26	2. 0.80	2. 76.21	2. 68.66	2. 79.36	2. 64.63
								3. ≥30	3. 40.60	3. 0.78	3. 70.65	3. 70.06	3. 61.97	3. 78.23

(B) Algorithm and feature details

Author year	Algorithm	Feature no.	Feature detail
Kirby 1999 [1]	GRNN	23	Age, gender, frequent awakening, witnessed apnea, observed chocking, excessive daytime sleepiness, ESS, HTN, alcohol consumption, smoking (pack-year), height, weight, BMI, SBP≥140, DBP≥90, tonsillar enlargement, soft palate enlargement, crowding of the oral pharynx, sum of the clinical score for the binary categorical values
Rowley 2000 [2]	LR	4-6	Witnessed apnea, HTN, BMI, age, gender, snoring, gasping, neck
Rodsutti 2004 [3]	LR	5	Age, sex, BMI, snoring, witnessed apnea
Sharma 2006 [4]	LR	4	Gender, BMI, snoring index, chocking index
Takegami 2009 [5]	LR	4	Gender, BP, BMI, snoring
Caffo 2010 [6]	Boosting	10	Neck circumference, BMI, age, snoring frequency, waist circumference, snoring loudness, gender, SOL, response to "What is the chance that you would doze off or fall asleep while sitting and reading?", and presence or absence of a heart attack.
Bouloukaki 2011 [7]	LR	4	Gender, EDS, neck circumference, and BMI
Zou 2013 [8]	LR	I. 5 II. 4	I. Age, BMI, waist circumference, gender II. Age, waist circumference, ESS score, and minimum oxygen saturation (SaO2)
Marti-Soler 2016 [9]	LR	5	Neck circumference, BMI, snoring, age, and gender
Shah 2016 [10]	LR	4	Gender, age, BMI, and snoring frequency
Ustun 2016 [11]	SLIM	1. 5 2. 10	1. Age, HTN, BMI, and gender 2. Age, BMI, DM, HTN, smoker, and gender
Liu 2017 [12]	SVM	4	BMI, neck circumference, waist circumference, and age
Shin 2017 [13]	LR	14	BMI, ASA score, age, dyslipidemia, chronic pulmonary disease, liver disease, HTN, CHF, pulmonary HTN, AF, DM, CAD, and hemiplegia/paraplegia
Tan 2017 [14]	LR	5	Neck circumference, BMI, snoring, age, and gender
Traxdorf 2017 [15]	LR	5	ESS score, age, gasping, cardiovascular risk factors (e.g. CHF, CAD, myocardial infarction, AF, stroke), and witnessed apneas
Duarte 2018 [16]	LR	2	Neck circumference, and age
Present study	SVM	1. 2 2. 6	1. Waist, and age 2. Waist, age, snoring, neck circumference, witnessed apnea, and SOL <30 min

3

		[3.] 6	[3.] Waist, witnessed apnea, age, neck circumference, snoring, and SOL <30 min

* respiratory disturbance index.

Abbreviations: S: sleep clinic; C, community; SW, surgical ward; GRNN, generalized regression neural network; Acc, accuracy; Sen, sensitivity; Spec, specificity; OSA, obstructive sleep apnea; AHI, apnea-hypopnea index; N/A, not available; LR, logistic regression; SLIM, Supersparse Linear Integer Model; SVM, support vector machine; SBP, systolic blood pressure; DBP, diastolic blood pressure; ESS, Epworth Sleepiness Scale; HTN, hypertension; SOL, sleep onset latency; EDS, excessive daytime sleepiness; DM, diabetes mellitus; ASA: American Society of Anesthesiologists; CHF, congestive heart failure; AF, atrial fibrillation; CAD, coronary artery disease;

Table S2. Comparison of the clinical features of subgroups categorized by gender and age

Feature name	Male (N=5223)	Female (N=1652)	P	Age <65 (N=5985)	Age ≥65 (N=890)	P
Age (y/o)	47.2±14.3	49.7±15.2	<0.001	44.3±11.8	71.7±6.0	<0.001
Man, n (%)	-	-	-	4580 (76.5)	643 (72.2)	0.006
BMI (kg/m2)	27.4±4.8	25.4±5.2	<0.001	27.1±5.1	26.0±4.1	<0.001
Neck circumference (cm)	39.0±3.4	33.6±3.4	<0.001	37.8±4.1	37.3±4.1	0.002
Waist circumference (cm)	94.1±12.0	82.7±12.5	<0.001	91.3±13.2	91.9±11.5	0.046
Current smoker, n (%)	1029 (19.7)	75 (4.5)	<0.001	1045 (17.5)	59 (6.6)	<0.001
Alcohol consumption, n (%)	648 (12.4)	40 (2.4)	<0.001	618 (10.3)	70 (7.9)	0.022
Hypnotic, n (%)	383 (7.3)	251 (15.2)	<0.001	450 (7.5)	184 (20.7)	<0.001
Comorbidity						
Hypertension, n (%)	1623 (31.1)	398 (24.1)	<0.001	1498 (25)	523 (58.8)	<0.001
Diabetes, n (%)	431 (8.3)	149 (9)	0.328	391 (6.6)	184 (20.7)	<0.001
CAD, n (%)	207 (4.0)	41 (2.5)	0.005	159 (2.7)	89 (10.0)	<0.001
CHF, n (%)	79 (1.5)	22 (1.3)	0.594	47 (0.8)	54 (6.1)	<0.001
CVA, n (%)	98 (1.9)	26 (1.6)	0.421	73 (1.2)	51 (5.7)	<0.001
COPD, n (%)	53 (1.0)	14 (0.8)	0.546	31 (0.5)	36 (4.0)	<0.001
Asthma, n (%)	336 (6.4)	154 (9.3)	<0.001	412 (6.9)	78 (8.8)	0.050
Hypothyroidism, n (%)	72 (1.4)	84 (5.1)	<0.001	110 (1.8)	46 (5.2)	<0.001
Sleep History						
Habitual SOL (min)	18.9±18.6	27.3±31.1	<0.001	19.8±20.8	28.3±31.1	<0.001
Habitual SOL<30 min, n (%)	3808 (72.9)	986 (59.7)	<0.001	4303 (71.9)	491 (55.2)	<0.001
Habitual sleep duration (hr)	6.6±3.4	6.5±3.2	<0.001	6.6±3.3	6.3±3.2	<0.001
Unrefreshed sleep, n (%)	2738 (52.4)	947 (57.3)	<0.001	3369 (56.3)	316 (35.5)	<0.001
Freq. of awakening in sleep (times/night)	0.6±1.5	0.6±1.5	0.172	0.5±1.4	0.9±1.8	<0.001
Awakening in sleep ≥3 times/night, n (%)	1128 (21.6)	376 (22.8)	0.319	1173 (19.6)	331 (37.2)	<0.001
ESS	10.4±4.8	10.0±5.1	0.006	10.4±4.8	9.9±5.4	0.001
EDS, n (%)	2900 (55.5)	864 (52.3)	0.022	3321 (55.5)	443 (49.8)	0.001
Symptom suggestive of OSA						
Snoring, n (%)	4292 (82.2)	1188 (71.9)	<0.001	4815 (80.5)	665 (74.7)	<0.001
Witnessed apnea, n (%)	926 (17.7)	140 (8.5)	<0.001	945 (15.8)	121 (13.6)	0.092
Freq. of nocturia (times/night)	1.1±1.2	1.3±1.2	<0.001	1±1.1	2±1.3	<0.001
Nocturia ≥2 times/night, n (%)	1695 (32.5)	657 (39.8)	<0.001	1744 (29.1)	608 (68.3)	<0.001

Witnessed leg jerks in sleep, n (%)	2458 (47.1)	820 (49.6)	0.0680	2805 (46.9)	473 (53.1)	<0.001
Morning headache, n (%)	484 (9.3)	315 (19.1)	<0.001	729 (12.2)	70 (7.9)	<0.001
Dry throat at waking up, n (%)	2923 (56.0)	933 (56.5)	0.731	3333 (55.7)	523 (58.8)	0.085
AHI (/h)	33.0±26.1	18.9±22.6	<0.001	29.3±26.5	31.9±22.1	<0.001

The demographics data were presented as mean ± SD or n (percentage).

Abbreviations: BMI, body mass index; ESS, Epworth sleepiness scale; EDS, excessive daytime sleepiness; CAD, coronary artery disease; CHF, congestive heart failure; CVA, cerebrovascular disease; COPD, chronic obstructive pulmonary disease; SOL, sleep onset latency; AHI, apnea-hypopnea index

The independent tests were analyzed by t-test and Chi-square test.

Table S3. Description and definition of sleep pattern parameters and OSA symptoms

Parameter	Description	Domain	Definition in SVM
Habitual sleep pattern			
Habitual SOL (min)	During the past month, how long (in minutes) does it usually take you to fall asleep at night?		
Habitual SOL <30 min			<30 min =1, ≥30 min = 0
Habitual sleep duration (hr)	During the past month, how many hours of actual sleep did you get at night?		
Category of habitual sleep duration			<6 hr = -1, 6-8 hr＝0, ≥8 hr =1
Unrefreshed sleep	Do you feel unrefreshed after waking up in the morning?	Yes, No	Yes =1, No =0
Freq. of wakening in sleep (times/night)	How many times do you wake up during the night?		
Awakening in sleep ≥3 times/night			≥3 times/night =1, <3 times/night = 0
EDS			ESS ≥10 =1, ESS<10=0
Symptom suggestive of OSA			
Snoring	Do you snore?	Ye, No, don't know	Yes=1, No=0, don't know=0
Witnessed apnea	How often in the past month have you been told to have long pauses between breaths while in sleep?	no, <1tme/week, 1-2 times/week, ≥3 times/week	no=0, <1tme/week=0, 1-2 times/week=0, ≥3 times/week=1
Freq. of nocturia (times/night)	How many times do you need to get out of bed to go to the bathroom during your sleep period?		
Nocturia ≥2 times/night			≥2 times/night = 1, <2 times/night = 0
Witnessed leg jerks in sleep	How often in the past month have you been told to have had leg twitching or jerking while in sleep?	no, <1tme/week, 1-2 times/week, ≥3 times/week	no=0, <1tme/week=0, 1-2 times/week=0, ≥3 times/week=1
Morning headache	Do you experience headaches while waking up in the morning?	Yes, No	Yes=1, No=0
Dry throat at waking up	Do you experience dry throat at waking up?	Yes, No	Yes=1, No=0

Abbreviations: ESS, Epworth sleepiness scale; EDS, excessive daytime sleepiness; OSA, obstructive sleep apnea; SOL, sleep onset latency
The independent tests were analyzed by t-test and Chi-square test

Table S4. Details of SVM prediction model training and testing procedures

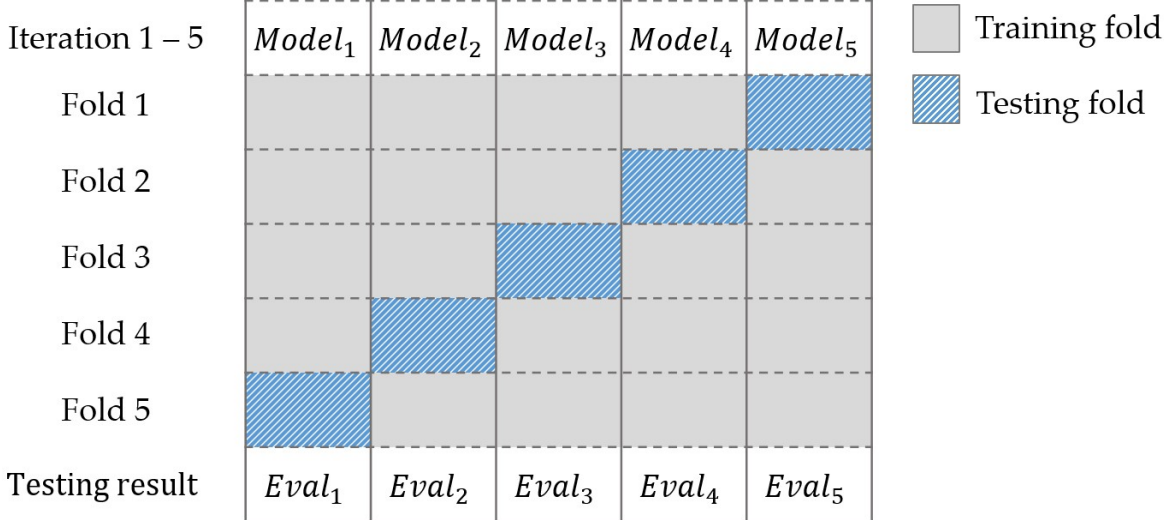| Task	Task name	Comment	Criterion	Cutoff	Corresponding table or figure
1	Data input		N/A	N/A	Table 2 and S3
2	Data exclusion		PSG total recording time	<240 min	Table 1
			Not Chinese	N/A	
			Any missing value in 32 features	N/A	
3	Data splitting for 5-fold CV		Each fold's prevalence rate is nearly same	N/A	Figure S1
4	First feature selection (continuous feature)	Use 4 folds for these tasks	Median of single-feature-SVM's AUROC	≥ Median value	Table 3
	First feature selection (categorical feature)		Median of MCC	≥ Median value	Figure 2
5	Forward stepwise feature selection		AUROC	≥ 0.8	Figure 3, Table S5 and 4
6	SVM optimization		AUROC		
7	Testing on hold out fold		N/A	N/A	N/A
8	Averaging the results of five test folds		N/A	N/A	N/A
9	Plotting learning curve	To evaluate model for overfitting	No significant difference between training and testing curve	N/A	Figure S2
10	Repeating task 3-8 for five times		N/A	N/A	N/A
11	Averaging results from task 10	Calculate mean and 95% confidence interval	N/A	N/A	Table 5 and 6

Table S6. The result of multivariable logistic regression.

AHI≥5/h			AHI≥15/h			AHI≥30/h		
Variable	OR (95%CI)	P-value	Variable	OR (95%CI)	P-value		OR (95%CI)	P-value
Snoring	2.732 (2.231-3.345)	<.0001	Snoring	1.846 (1.543-2.208)	<.0001	Witnessed apnea	2.036 (1.684-2.460)	<.0001
Gender	1.640 (1.244-2.163)	0.0005	Witnessed apnea	1.873 (1.506-2.329)	<.0001	Gender	1.751 (1.376-2.227)	<.0001
Age	1.046 (1.039-1.053)	<.0001	Dry throat	1.451 (1.259-1.674)	<.0001	Snoring	1.471 (1.222-1.770)	<.0001
Neck	1.081 (1.030-1.134)	0.0014	Gender	1.640 (1.301-2.066)	<.0001	Hypertension	1.416 (1.202-1.667)	<.0001
SOL	0.992 (0.988-0.996)	<.0001	Hypnotic	0.635 (0.494-0.817)	0.0004	Dry throat	1.343 (1.168-1.544)	<.0001
BMI	1.131 (1.079-1.186)	<.0001	Age	1.040 (1.034-1.046)	<.0001	Waist	1.013 (0.999-1.027)	<.0001
Waist	1.029 (1.010-1.048)	0.0026	Waist	1.024 (1.009-1.039)	<.0001	Age	1.028 (1.022-1.034)	<.0001
			Neck	1.082 (1.043-1.122)	<.0001	Neck	1.078 (1.041-1.116)	<.0001
			SOL	0.991 (0.988-0.995)	<.0001	BMI	1.141 (1.103-1.181)	<.0001
			BMI	1.126 (1.086-1.168)	<.0001	SOL	0.988 (0.984-0.992)	<.0001

The logistic regression was conducted with forward selection.
Abbreviation: BMI, body mass index; SOL, sleep onset latency

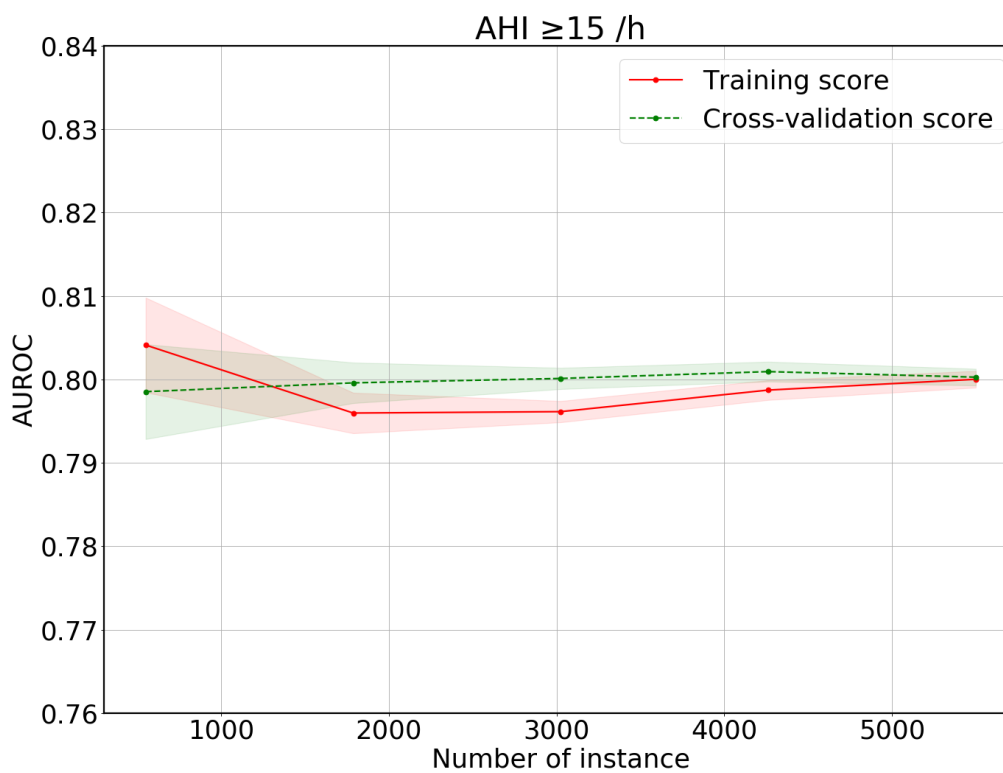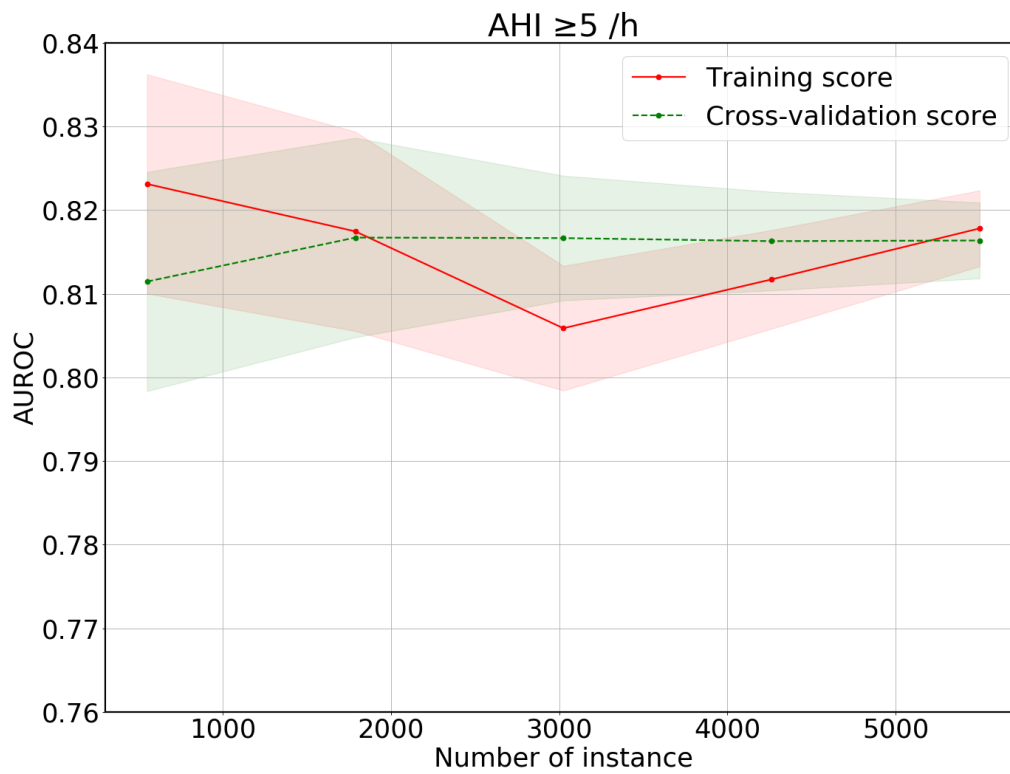**Table S7.** Confusion matrices of different AHI cutoff points

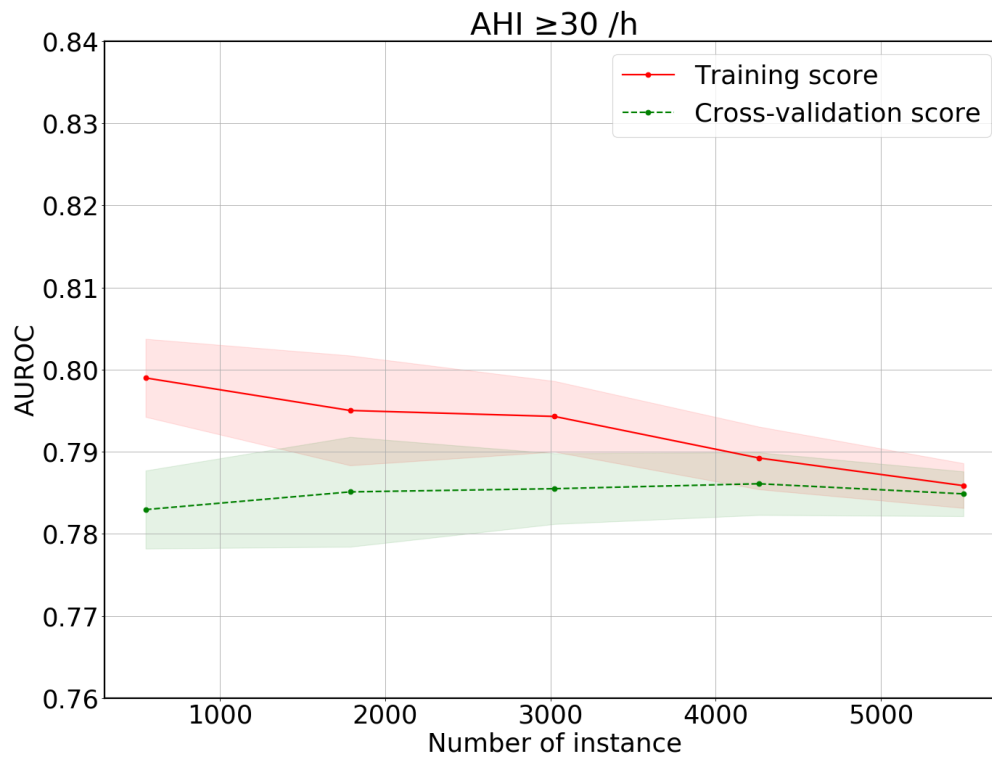| AHI cutoff	Prediction model	
	No OSA	OSA
<5/h	901	1466
≥5/h	305	4203
<15/h	1831	1045
≥15/h	833	3166
<30/h	2871	830
≥30/h	1213	1961

Figure S1. Illustration of procedures of the 5-fold cross validation (CV). First, the whole dataset was separated into 5 folds randomly. Second, in the first iteration, fold 5 was an isolated testing fold, and fold 1-4 were the training folds for feature selection and model optimization. Third, after 5 iterations, the CV result is the average of the testing results from all iterations.

$$CV\ result\ of\ 5\ testing\ fold = \frac{(Eval_1 + Eval_2 + Eval_3 + Eval_4 + Eval_5)}{5}$$

Figure S2. Learning curve of the prediction model with two, six, and six features for prediction of AHI ≥5/h, ≥15/h, and ≥30/h. The red line indicates the training score and the green line indicates the cross-validation score. The colored area represents the 95% confidence interval (CI). The training and testing curves showed similar results and they converged in the end. The 95% CI also showed the convergence of training and testing curves as the training data increased.

AHI ≥30 /h

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