# **Supplemental Material 1**

# List of Supplemental Materials

1. Supplemental Material 1 – Additional results with the following: 1) A Parallel Analysis was done with the AASM criterion of PLM ≥ 15, showing very similar results to what the main article has presented. 2) A sensitivity analysis of each component of arousal threshold definition, showing their effects on PLMS.

# Tables using the AASM criteria with PLM ≥ 15 as Cut-off

|  |
| --- |
| Table S1 Subject characteristics in OSA-PLMS and OSA-only group |
|  | OSA-PLMS | OSA-only | Z/𝛘2 | *p* |
|  | (n = 116) | (n = 604) |
| Age | 60.5 (48.5-69) | 42 (35 - 53) | -8.842 | < 0.001\*\* |
| Sex(male) | 98 (84.4%) | 515 (85.2%) | 0.047 | 0.828 |
| BMI | 26.4 (24.2 - 28.7) | 26.1 (24.2 - 28.1) | -1.013 | 0.311 |
| ESS | 9 (5 - 13) | 8 (4 - 12) | -1.632 | 0.103 |
| Hypertension | 62 (53.4%) | 195 (32.3%) | 18.988 | < 0.001\*\* |
| Diabetes | 21 (18.1%) | 27 (4.5%) | 29.068 | < 0.001\*\* |
| Arrhythmia | 11 (9.5%) | 44 (7.3%) | 0.666 | 0.414 |
| Stroke | 22 (19.0%) | 44 (7.3%) | 15.946 | < 0.001\*\* |
| CAD | 2 (1.7%) | 8 (1.3%) | 0.000 | 1.00 |
| Asthma | 1 (0.86%) | 8 (1.3%) | 0.000 | 1.00 |
| COPD | 1 (0.86%) | 8 (1.3%) | 0.000 | 1.00 |

Data are presented as median (fifirst quartile, third quartile), or n (%)

Abbreviation: BMI, body mass index; ESS, Epworth Sleepiness Scale; CAD: coronary artery disease; COPD, chronic obstructive pulmonary disease; GERD, Gastroesophageal reflux disease; Values were expressed as median (interquartile range in brackets)or n(%); \*p≤0.05 \*\*p≤0.01

Table S2 Polysomnography parameters in the OSA-PLMS and OSA-only group

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | OSA-PLMS | OSA-only | Z | *p* |
|   | (n = 116) | (n = 604) |
| TST, min | 416.5(333.4 - 470.4) | 428 (369.6 - 471) | -1.437 | 0.151 |
| Sleep Efficiency % | 81.3 (69.63 - 88.33) | 86.4 (76.5 - 92.7) | -4.398 | < 0.001\*\* |
| Sleep Latency, min | 4.5 (1 - 15.1) | 4.5 (1.5 - 11) | -0.350 | 0.727 |
| REM Latency, min | 97.5(60.6 - 160.6) | 92.5 (69 - 138) | -0.527 | 0.598 |
| NREM I sleep % | 20.2(12.7 - 32.8) | 13.1 (8.3 - 19.4) | -6.143 | < 0.001\*\* |
| NREM II sleep % | 44.8 (35.7 - 53.4) | 51.6(45.2 - 58.1) | -5.081 | < 0.001\*\* |
| NREM III sleep % | 14.0(6.8 - 20.3) | 14.7 (10.0 - 19.5) |  -1.545 | 0.122 |
| REM sleep % | 18.0 (12.7 - 23.0) | 18.8 (14.6 - 22.7) | -1.1 | 0.271 |
| ODI | 17.4 (6.6 - 35.7) | 19.4 (12.7 - 26.6) | -0.869 | 0.385 |
| AHI | 24.1(10.8 - 42.9) | 24.5 (14.5 - 33.1) | -0.726 | 0.468 |
| minSaO2 | 83.5% (74% - 87%) | 81% (77% - 84%) | -2.004 | 0.045\* |
| avgSaO2 | 95% (94% - 96%) | 95% (95% - 96%) | -2.912 |  0.004\*\* |
| TS90 | 2.3% (0.2% - 12.0%) | 2.8% (1.2% - 5.1%) | -0.438 | 0.661 |
| Arousal Index | 17.8(9.3 - 30.4) | 15.7 (9.8 - 24.0) | -1.898 | 0.058 |

Data are presented as median (first quartile, third quartile)

Abbreviations: TST, total sleep time; REM, rapid eye movement; NREM, non-rapid eye movement; ODI, oxygen desaturation index; AHI, apnea-hypopnea index; minSaO2, lowest arterial oxygen saturation; avgSaO2, mean arterial oxygen saturation; TS90, percentage of total sleep time at oxygen saturation level < 90%. Values were expressed as median (interquartile range in brackets). \*p≤0.05 \*\*p≤0.01

Table S3 Arousal Threshold and its predictors in OSA patients in the OSA-PLMS and OSA-only groups.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | OSA-PLMS | OSA-only | 𝛘2 | *p* |
|  | (N = 116) | (N = 604) |  |  |
| Low ArTH | 54(46.6%) | 119(19.7%) | 58.89 | < 0.001\*\* |
| AHI < 30 | 69 (59.5%) | 364 (60.3%) | 0.025 | 0.875 |
| minSaO2 > 82.5% | 62 (53.4%) | 211(34.9%) | 14.17 | < 0.001\*\* |
| FHypopnea > 58.3% | 29 (25%) | 68 (11.3%) | 15.763 | < 0.001\*\* |

Data are presented as n (%)

Abbreviations: OSA, obstructive sleep apnea; AHI, apnea-hypopnea index; minSaO2, lowest arterial oxygen saturation; ArTH, arousal threshold; FHypopnea, Fraction of hypopnea in all respiratory events; \*p≤0.05 \*\*p≤0.01

Table S4 Regression analyses of factors associated with PLMS among OSA participants

|  |  |  |
| --- | --- | --- |
|  | Univariate analysis | Multivariate analysis |
|  | β | p | OR (95% CI) | β | p | OR (95% CI) |
| Age | 0.071 | <0.001 | 1.073 (1.056 - 1.091) | 0.051 | <0.001 | 1.052(1.032 - 1.072) |
| Hypertension | 0.879 | <0.001 | 2.408(1.610 - 3.602) | 0.092 | 0.721 | 1.096 (0.661 - 1.818) |
| Diabetes | 1.553 | <0.001 | 4.724 (2.566 - 8.696) | 0.944 | 0.016 | 2.570 (1.189 - 5.554) |
| Stroke | 1.091 | <0.001 | 2.979 (1.708 - 5.196) | 0.070 | 0.844 | 1.073(0.534- 2.156) |
| SleepEff | -0.028 | <0.001 | 0.972 (0.961 - 0.985) | 0.012 | 0.164 | 1.012(0.995 - 1.030) |
| NREM1 | 0.053 | <0.001 | 1.054 (1.038 - 1.071) | 0.036 | 0.002 | 1.037 (1.014- 1.061) |
| NREM2 | -0.039 | <0.001 | 0.962 (0.946 - 0.978) | -0.001 | 0.956 | 0.999 (0.979 - 1.020) |
| AvgSaO2 | -0.731 | <0.001 | 0.690(0.598 - 0.796 | -0.374 | <0.001 | 0.688 (0.587 - 0.806) |
| minSaO2 | -0.009 | 0.451 | 0.991(0.969 - 1.014) | Not included |
| Low ArTH | 1.543 | <0.001 | 4.679(3.086 - 7.096) | 1.706 | <0.001 | 5.509(3.352-9.053) |

Abbreviations: NREM1, proportion of NREM-1 sleep; NREM2, proportion of NREM-2 sleep; ArTH, arousal threshold; avgSaO2, mean arterial oxygen saturation; SleepEff，Sleep Efficiency

Table S5 Risk of PLMS by arousal threshold in the MrOS Dataset

|  |  |  |  |
| --- | --- | --- | --- |
|  | High ArTH | Low ArTH | *p* |
| Model 1: Age + BMI | Ref | 1.30 (1.05 - 1.61) | 0.014\* |
| Model 2: Model 1 + SleepEff + NREM1 + NREM2 + NREM3 + Arousal Index | Ref | 1.66 (1.32 - 2.09) | ＜0.001\*\* |
| Model 3: Model 2 + avgSaO2 + TS90 | Ref | 1.60 (1.26 - 2.02) | ＜0.001\*\* |
| Model 4: Model 3 + Hypertension + Diabetes + Arrhythmia + Asthma + Stroke | Ref | 1.62 (1.28 - 2.06) | ＜0.001\*\* |

Abbreviations: Ref, reference; ArTH, arousal threshold; SleepEff, sleep efficiency; NREM1, proportion of NREM-1 sleep; NREM2, proportion of NREM-2 sleep; NREM3, proportion of NREM-3 sleep; avgSaO2, average arterial oxygen saturation; \*p≤0.05 \*\*p≤0.01

# Sensitivity Analysis of the three components of the low ArTH classifier

Table S6 sensitivity analysis on each component of arousal threshold definition in our study cohort.

|  |  |  |  |
| --- | --- | --- | --- |
| Low ArTH | β | OR (95% CI) | p |
| AHI < 30 | 0.305 | 1.36 (0.86 - 2.14) | 0.188 |
| MinSaO2 > 82.5% | 0.993 | 2.70 (1.74 - 4.20) | <0.001\*\* |
| FHypopnea > 58.3% | 0.866 | 2.38 (1.40 - 4.04) | <0.001\*\* |

Table S7 sensitivity analysis on each component of arousal threshold definition in the MrOS cohort.

|  |  |  |  |
| --- | --- | --- | --- |
| Low ArTH | β | OR (95% CI) | p |
| AHI < 30 | 0.173 | 1.19 (0.98 - 1.44) | 0.081 |
| MinSaO2 > 82.5% | 0.163 | 1.18 (0.99 - 1.40) | 0.068 |
| FHypopnea > 58.3% | 0.225 | 1.18 (0.99 - 1.41) | 0.069 |

Odd ratios are presented as estimate (95% confidence interval)

Abbreviations: AHI, apnea-hypopnea index; minSaO2, lowest arterial oxygen saturation; ArTH, arousal threshold; FHypopnea, Fraction of hypopnea in all respiratory events; \*p≤0.05 \*\*p≤0.01