Supplemental Methods

Definition of study endpoints

Cardiovascular death

Death related to proximate cardiovascular causes (eg, myocardial infarction, cardiogenic shock, stroke, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm or other causes), procedure-related complications, or any death unless an unequivocal non-cardiovascular cause could be established.

Myocardial infarction

Myocardial infarction is defined as spontaneous ST-segment elevation myocardial infarction or non-ST-segment elevation myocardial infarction according to the third universal definition.\(^1\)

Any one of the following criteria meets the diagnosis of myocardial infarction:

- Detection of a rise and/or fall of cardiac biomarker values (preferably cardiac troponin) with at least one value above the 99th percentile URL and with at least one of the following:
  - Symptoms of ischemia
  - (Presumed) new significant ST-T wave changes or new LBBB
  - Development of pathological Q waves
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
  - Identification of an intracoronary thrombus by angiography or autopsy

- Cardiac death with symptoms suggestive of myocardial infarction and presumed new ischemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased

Stroke
Stroke is defined as an acute symptomatic episode of neurological dysfunction, more than 24 hours in duration in the absence of therapeutic intervention or death, due to cerebral, spinal or retinal tissue injury as evidenced by neuroimaging or lumbar puncture. It includes the following subclassifications:

- Ischemic stroke
- Intracerebral hemorrhage
- Stroke of undetermined etiology

**Hospitalization for heart failure**

Hospitalization for heart failure (HF) is defined as an event where the patient is admitted to the hospital with a primary diagnosis of HF where the length of stay is at least 24 h, where the patient exhibits new or worsening symptoms of HF (dyspnea, decreased exercise tolerance, fatigue, worsened end-organ perfusion, or volume overload) on presentation, has objective evidence of new or worsening HF, and receives initiation or intensification of treatment specifically for HF.

**Hospitalization for unstable angina**

Hospitalization for unstable angina is defined as unscheduled hospitalization for the management of unstable angina, occurring within 24 h of the most recent symptoms. Hospitalization is defined as an admission to an inpatient unit or a visit to an emergency department that results in at least a 24-h stay. This classification requires that 4 separate criteria be met: a) worsening ischemic discomfort; b) unscheduled hospitalization; c) objective evidence of myocardial ischemia; d) negative cardiac biomarkers.

**Ischemia-driven revascularization**

Ischemia-driven revascularization was defined as any repeat PCI or CABG performed for either: myocardial infarction, unstable angina, stable angina, or documented silent ischemia. Repeat revascularization was further classified into target vessel or non-target vessel revascularization as well as PCI or CABG.

**Sample size**
According to our prior data\(^2\), the prevalence of obstructive sleep apnea (OSA) was 50.1% based on an apnea hypopnea index ≥15. Assuming a 5% absolute increase\(^2,3\) in the event rate for ACS patients with OSA compared with those without OSA, the expected event rate for acute coronary syndrome (ACS) patients with OSA is 20% and that for ACS without OSA is 15% at a median follow-up of 2 years. A sample size of 1,812 patients in OSA (n=906) and non-OSA (n=906) groups would have 80% power at a two-sided \(\alpha\) level of 0.05. With a dropout rate of 10% (failed sleep study, regular CPAP therapy, loss to follow-up, etc), a total of 2,014 patients will be required.

**Reference:**

1. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Circulation. 2012;126(16):2020-35.

2. Fan J, Wang X, Ma X, Somers VK, Nie S, Wei Y. Association of Obstructive Sleep Apnea With Cardiovascular Outcomes in Patients With Acute Coronary Syndrome. J Am Heart Assoc. 2019;8(2):e010826.

3. Lee CH, Sethi R, Li R, Ho HH, Hein T, Jim MH, et al. Obstructive Sleep Apnea and Cardiovascular Events After Percutaneous Coronary Intervention. Circulation. 2016;133(21):2008-2017.
## Supplemental Table S1. Baseline Demographic, Clinical, and Procedural Characteristics by Sex

| Variables                                | Women (n=298) | Men (n=1,629) | P value |
|------------------------------------------|---------------|---------------|---------|
| **Demographics**                         |               |               |         |
| Age, mean±SD, years                      | 64.0±8.2      | 55.0±10.3     | <0.001  |
| BMI, mean±SD, kg/m²                      | 26.8±3.9      | 27.1±3.6      | 0.04    |
| Waist-to-hip ratio, median (IQR)         | 0.96 (0.92-1.00) | 0.98 (0.95-1.02) | <0.001  |
| Neck circumference, median (IQR), cm     | 37 (35-39)    | 41 (39-43)    | <0.001  |
| Systolic BP, median (IQR), mmHg          | 130 (120-141) | 126 (116-137) | <0.001  |
| Diastolic BP, median (IQR), mmHg         | 72 (68-80)    | 77 (70-85)    | <0.001  |
| **Medical history**                      |               |               |         |
| Diabetes                                 | 121 (40.6)    | 488 (30.0)    | <0.001  |
| Hypertension                             | 240 (80.5)    | 1007 (61.8)   | <0.001  |
| Hyperlipidemia                           | 122 (40.9)    | 515 (31.6)    | 0.002   |
| Family history of premature CAD          | 17 (5.7)      | 87 (5.3)      | 0.80    |
| Prior stroke                             | 42 (14.1)     | 165 (10.1)    | 0.04    |
| Prior myocardial infarction              | 25 (8.4)      | 291 (17.9)    | <0.001  |
| Prior PCI                                | 54 (18.1)     | 345 (21.2)    | 0.23    |
| Prior CABG                               | 6 (2.0)       | 23 (1.4)      | 0.44    |
| Smoking                                  |               |               | <0.001  |
| No                                       | 262 (87.9)    | 392 (24.1)    |         |
| Current                                  | 28 (9.4)      | 885 (54.3)    |         |
| Previous                                 | 8 (2.7)       | 352 (21.6)    |         |
| **Drinking**                             |               |               | <0.001  |
| No                                       | 283 (95.0)    | 898 (55.1)    |         |
|                        | Current       | Previous      | p-value |
|------------------------|---------------|---------------|---------|
| Baseline tests         |               |               |         |
| eGFR                   | 106.6 (85.9-122.8) | 104.7 (89.8-120.9) | 0.74    |
| Hs-CRP, median (IQR), mg/L | 2.1 (0.8-5.7)   | 2.0 (0.8-6.2)  | 0.85    |
| LVEF, median (IQR), %  | 63 (60-67)     | 61 (55-65)    | <0.001  |
| Diagnosis              |               |               | <0.001  |
| STEMI                  | 40 (13.4)     | 390 (23.9)    |         |
| NSTEMI                 | 51 (17.1)     | 314 (19.3)    |         |
| Unstable angina        | 207 (69.5)    | 925 (56.8)    |         |
| Procedures             |               |               |         |
| Coronary angiography   | 288 (96.6)    | 1589 (97.5)   | 0.37    |
| Revascularization      | 176 (59.1)    | 1159 (71.1)   | <0.001  |
| PCI                    | 157 (52.7)    | 1052 (64.6)   | <0.001  |
| DES use                | 138/157 (87.9)| 913/1052 (86.8)| 0.70    |
| Baseline TIMI 0 or 1   | 40/157 (25.5) | 382/1052 (36.3)| 0.008   |
| Final TIMI 3           | 153/157 (97.5)| 1036/1052 (98.5)| 0.32    |
| CABG                   | 19 (6.4)      | 111 (6.8)     | 0.78    |
| Sleep study            |               |               |         |
| OSA (AHI≥15)           | 128 (43.0)    | 886 (54.4)    | <0.001  |
| AHI, median (IQR), events·h⁻¹ | 12.5 (6.2-25.8)| 16.9 (8.3-31.4)| <0.001  |
| ODI, median (IQR), events·h⁻¹ | 14.2 (7.2-25.5)| 16.5 (8.9-29.0)| 0.015   |
| Sadir SaO₂, median (IQR), % | 85 (81-88)  | 85 (81-88)   | 0.94    |
| Mean SaO₂, median (IQR), % | 94 (92-95) | 94 (93-95)  | 0.15    |
| Time with SaO2<90%, median (IQR), % | 3.0 (0.4-11.0) | 2.0 (0.3-9.8) | 0.20 |
| Epworth Sleepiness Scale, mean±SD | 6.0 (3.0-10.0) | 7.0 (4.0-11.5) | 0.002 |

**Medications on discharge**

| Medication            | n (%), or n/N (%), or n (%) | p-value |
|-----------------------|-----------------------------|---------|
| Aspirin               | 287 (96.3)                  | 1590 (97.6) | 0.20 |
| P2Y12 inhibitors      | 269 (90.3)                  | 1499 (92.0) | 0.31 |
| β-Blockers            | 226 (75.8)                  | 1262 (77.5) | 0.54 |
| ACEIs/ARBs            | 192 (64.4)                  | 1003 (61.6) | 0.35 |
| Statins               | 291 (97.7)                  | 1606 (98.6) | 0.21 |

Data are presented as mean±SD, median (IQR), n (%), or n/N (%). ACEI, angiotensin-converting enzymes inhibitor; AHI, apnea-hypopnea index; ARB, angiotensin receptor blocker; BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass grafting; CAD, coronary artery disease; DES, drug eluting stent; Hs-CRP, high-sensitivity C-reactive protein; IQR, interquartile range; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-segment elevation myocardial infarction; ODI, oxygen desaturation index; OSA, obstructive sleep apnea; PCI, percutaneous coronary intervention; SaO2, arterial oxygen saturation; SD, standard deviation; STEMI, ST-segment-elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction.
## Supplemental Table S2. Association Between Hypoxemia Indicators and Sleepiness with MACCE by Sex

| Indicators                        | Women                          | Men                           |
|----------------------------------|--------------------------------|-------------------------------|
|                                  | HR (95% CI)                    | P value                       | HR (95% CI)                    | P value   |
| Nadir SaO$_2$ <median vs. >median| 1.20 (0.74-1.94)               | 0.46                          | 0.89 (0.71-1.10)               | 0.28       |
| Mean SaO$_2$ <median vs. >median | 0.78 (0.48-1.27)               | 0.31                          | 0.95 (0.75-1.19)               | 0.62       |
| Time with SaO$_2$<90% >median vs. <median | 0.93 (0.56-1.93) | 0.77                          | 1.19 (0.95-1.49)               | 0.13       |
| Epworth Sleepiness Scale >10 vs. ≤10 | 1.59 (0.71-3.58)               | 0.26                          | 1.13 (0.84-1.53)               | 0.42       |

CI, confidence interval; HR, hazard ratio; MACCE, major adverse cardiovascular and cerebrovascular event; OSA, obstructive sleep apnea.
### Supplemental Table S3. Crude Number of Events by Sex and OSA Categories.

| Variables                                         | Women (n=298) | Men (n=1,629) |
|---------------------------------------------------|---------------|---------------|
|                                                   | OSA (n=128)   | OSA (n=886)   | Non-OSA (n=170) | Non-OSA (n=743) |
| MACCE                                             |               |               |                 |                 |
| Cardiovascular death                              | 2 (1.6)       | 17 (1.9)      | 1 (0.6)         | 13 (1.7)        |
| Myocardial infarction                             | 5 (3.9)       | 28 (3.2)      | 3 (1.8)         | 15 (2.0)        |
| Stroke                                            | 3 (2.3)       | 22 (2.5)      | 7 (4.1)         | 11 (1.5)        |
| Ischemic                                          | 3 (2.3)       | 18 (2.0)      | 4 (2.4)         | 10 (1.3)        |
| Hemorrhagic                                       | 0 (0.0)       | 4 (0.5)       | 3 (1.8)         | 1 (0.1)         |
| Hospitalization for unstable angina               | 30 (23.4)     | 125 (14.1)    | 22 (12.9)       | 95 (12.8)       |
| Hospitalization for heart failure                 | 0 (0.0)       | 11 (1.2)      | 2 (1.2)         | 8 (1.1)         |
| Ischemia-driven revascularization                 | 17 (13.3)     | 77 (8.7)      | 10 (5.9)        | 55 (7.4)        |
| Composite for cardiovascular death, myocardial infarction, or ischemic stroke | 10 (7.8) | 62 (7.0) | 8 (4.7) | 34 (4.7) |
| Composite for cardiac events                      | 33 (25.8)     | 172 (19.4)    | 27 (15.9)       | 121 (16.3)      |
| All-cause death                                   | 4 (3.1)       | 19 (2.1)      | 5 (2.9)         | 18 (2.4)        |
| All repeat revascularization                      | 21 (16.4)     | 108 (12.2)    | 11 (6.5)        | 87 (11.7)       |
| Target vessel revascularization                   | 11 (8.6)      | 53 (6.0)      | 9 (5.3)         | 40 (5.4)        |
| Non-target vessel revascularization               | 13 (10.2)     | 73 (8.2)      | 4 (2.4)         | 52 (7.0)        |
| PCI                                               | 21 (16.4)     | 100 (11.3)    | 10 (5.9)        | 82 (11.0)       |
| CABG                                              | 0 (0.0)       | 8 (0.9)       | 1 (0.6)         | 7 (0.9)         |

Data are presented as n (%). CABG, coronary artery bypass grafting; MACCE, major adverse cardiovascular and cerebrovascular event; PCI, percutaneous coronary intervention; OSA, obstructive sleep apnea.
Supplemental Table S4. Association of OSA with Risk of MACCE According to Subgroups.

| Subgroups          | OSA (n=1,014) | Non-OSA (n=913) | Adjusted HR (95% CI)* | P value | P for interaction |
|-------------------|---------------|-----------------|-----------------------|---------|------------------|
| Age               |               |                 |                       |         |                  |
| <65               | 159/769 (20.7)| 118/714 (16.5)  | 1.31 (1.02, 1.68)     | 0.037   | 0.73             |
| ≥65               | 68/245 (27.8) | 44/199 (22.1)   | 1.30 (0.88, 1.93)     | 0.19    |                  |
| Hypertension      |               |                 |                       |         |                  |
| Yes               | 167/691 (24.2)| 105/556 (18.9)  | 1.35 (1.05, 1.74)     | 0.022   | 0.30             |
| No                | 60/323 (18.6) | 57/357 (16.0)   | 1.17 (0.81, 1.71)     | 0.41    |                  |
| Diabetes mellitus |               |                 |                       |         |                  |
| Yes               | 89/319 (27.9) | 54/290 (18.6)   | 1.58 (1.11, 2.24)     | 0.011   | 0.12             |
| No                | 138/695 (19.9)| 108/623 (17.3)  | 1.15 (0.88, 1.50)     | 0.30    |                  |
| Hyperlipidemia    |               |                 |                       |         |                  |
| Yes               | 68/343 (19.8) | 43/294 (14.6)   | 1.40 (0.93, 2.10)     | 0.11    | 0.84             |
| No                | 159/671 (23.7)| 119/619 (19.2)  | 1.25 (0.98, 1.61)     | 0.77    |                  |
| Prior CAD         |               |                 |                       |         |                  |
| Yes               | 100/445 (22.5)| 67/372 (18.0)   | 1.37 (0.99, 1.89)     | 0.06    | 0.91             |
| No                | 127/569 (22.3)| 95/541 (17.6)   | 1.21 (0.91, 1.60)     | 0.18    |                  |
| Clinical presentation |         |                 |                       |         |                  |
| UAP               | 118/572 (20.6)| 90/560 (16.1)   | 1.30 (0.98, 1.73)     | 0.07    | 0.98             |
| AMI               | 109/442 (24.7)| 72/353 (20.4)   | 1.27 (0.92, 1.73)     | 0.14    |                  |
Data are presented as n/N (%). AMI, acute myocardial infarction; CAD, coronary artery disease; CI, confidence interval; HR, hazard ratio; MACCE, major adverse cardiovascular and cerebrovascular event; OSA, obstructive sleep apnea; UAP, unstable angina pectoris. *Adjusted for age, body mass index, smoking (no [referent], past, current), hypertension, diabetes mellitus, hyperlipidemia, prior myocardial infarction, prior stroke, and clinical presentation (unstable angina [referent], acute myocardial infarction).
Supplemental Figure S1. Cumulative Incidence of CV Death, MI, Ischemic Stroke, and Composite of These Outcomes by Sex and OSA Categories.

A. Women-CV death
Adjusted HR 3.73 (0.24-50.99), P=0.35

B. Men-CV death
Adjusted HR 0.88 (0.40-1.85), P=0.70

C. Women-MI
Adjusted HR 2.69 (0.55-12.10), P=0.23

D. Men-MI
Adjusted HR 1.35 (0.69-2.64), P=0.39
Kaplan-Meier estimates and fully-adjusted HR for CV death, MI, ischemic stroke, and composite of these outcomes between OSA and non-OSA groups in women (A, C, E, G) and men (B, D, F, H). CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction; OSA, obstructive sleep apnea.