Co-morbid Insomnia and Sleep Apnea Is Associated with Uncontrolled Hypertension in a Middle-aged Population

Mio Kobayashi Frisk[1], Joel Bergqvist[1,2], Sven Svedmyr[1,2], Philippe Diamantis[1], Göran Bergström[3,4], Ding Zou[1]

[1]Center for Sleep and Vigilance Disorders, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

[2]Department of Sleep Medicine, Respiratory Medicine and Allergology, Sahlgrenska University Hospital, Gothenburg, Sweden

[3]Department of Molecular and Clinical Medicine, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden

[4]Department of Clinical Physiology, Sahlgrenska University Hospital, Gothenburg, Sweden

Author Contributions:

Study concept and design: MKF, PD, DZ

Data acquisition: GB, DZ

Data analysis and interpretation: MKF, JB, PD, DZ Drafting of the manuscript: MKF Critical revision of the manuscript: MKF, JB, SS, PD, GB, DZ Approval of final version of the manuscript: MKF, JB, SS, PD, GB, DZ Agreement to be accountable for all aspects of the work: MKF, JB, SS, PD, GB, DZ

Artificial Intelligence Disclaimer: No artificial intelligence tools were used in writing this manuscript

This article has a data supplement, which is accessible at the Supplements Tab

Correspondence:

Mio Kobayashi Frisk, MD

Center for Sleep and Vigilance Disorders
Department of Internal Medicine and Clinical Nutrition
University of Gothenburg
Medicinaregatan 8b Box 421
SE-40530, Gothenburg
Sweden
E-mail: mio.kobayashi.frisk@vgregion.se

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Abstract

Introduction: Co-morbid insomnia and sleep apnea (COMISA) has been linked to poorer health outcomes and increased all-cause mortality compared with either insomnia or obstructive sleep apnea (OSA) alone.

Materials and Methods: We investigated the relationship between COMISA and uncontrolled hypertension in the Swedish CardioPulmonary BioImage Study (SCAPIS). A cross-sectional analysis including participants from the SCAPIS Gothenburg cohort (n=3832, 46% males, age 57.5±4.3 years, body mass index 26.6±4.3 kg/m^2) was performed. Subjects underwent a comprehensive examination, including functional tests and a home polygraph sleep recording. COMISA was defined as an apnea-hypopnea index (AHI) >10 events/h and an Insomnia Severity Index score ≥15. Blood pressure (BP) status was characterized as uncontrolled hypertension (office systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg), controlled hypertension (antihypertensive medication-treated hypertension with systolic/diastolic BP < 140/90 mmHg) or normotension with systolic/diastolic BP <140/90 mmHg.

Results: The prevalence of COMISA was 3.1% in the population and 14.5% among OSA patients (AHI >10 events/h). AHI was comparable between OSA-only and COMISA patients (18±9 vs. 19±9 events/h, P=0.86). Uncontrolled hypertension was found in 4.4%, 4.5%, 7.9% and 10.2% of the control group, insomnia-only, OSA-only, and COMISA group, respectively (**p<0.001**). Compared to the control group, the risk of uncontrolled hypertension was significantly increased in the OSA-only group (odds ratio[95%CI]: OR 1.31[1.05 - 1.64], **p=0.02**) and the COMISA group (OR 1.88[1.23 -

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

2.89, **p=0.004**) after controlling for anthropometrics, lifestyle, comorbidities, Epworth sleepiness scale and nocturnal hypoxic exposure (T90, % recording time with oxygen saturation ≤ 90%). T90 was found to be a significant mediator in the relationship between both OSA and COMISA to uncontrolled hypertension.

Conclusions: This study is the first to demonstrate an independent association between COMISA and uncontrolled hypertension in the general population. These findings provide novel insights for identifying subgroups of OSA patients at risk of adverse cardiovascular consequences. Furthermore, our results underscore the importance of recognizing sleep health as a multidimensional construct and advocate for personalized treatment strategies to effectively combat the burden of this common sleep disorder. (See data supplement for graphical abstract and summary of key findings)

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide[1]. Yet, up to 90% of CVD cases are preventable [2]. High blood pressure is a leading modifiable risk factor for cardiovascular and all-cause mortality, with systolic hypertension accounting for nearly 20% of all global deaths[3]. Considering that every 20 mmHg increase in systolic blood pressure above 115 mmHg is associated with a two-fold increase in cardiovascular mortality among adults aged 40-69 years[4], there is an urgent need to gain a better understanding of blood pressure control. Sleep disorders have garnered increasing attention to this end due to evidence suggesting that they are associated with hypertension and CVD[5].

Obstructive sleep apnea (OSA), which can give symptoms such as daytime sleepiness and sleep disturbances [6, 7], is highly prevalent, affecting up to 1 billion people worldwide[8]. It is also intimately linked to cardiovascular health, with related underlying pathophysiological mechanisms caused by intermittent hypoxia and arousals, in addition to shared confounders such as obesity [9]. OSA is highlighted in the European guidelines for the management of elevated blood pressure, especially in relationship to resistant hypertension, non-dipping or reverse-dipping blood pressure[10].

Insomnia is another prevalent sleep disorder, with up to 50% of the adult population experiencing symptoms such as difficulty falling asleep, staying asleep, or poor quality of sleep, with 25% and 15% suffering from clinical and chronic insomnia, respectively [11]. Multiple observational studies point to an association between insomnia and hypertension[12], while European guidelines highlight the link between this type of sleep disturbance with nocturnal hypertension[10]. Co-morbid Insomnia

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

and Sleep Apnea (COMISA) is a condition in which both sleep disorders co-occur, with a potential bidirectional causal relationship between them[13]. There is evidence suggesting COMISA is associated with greater all-cause mortality compared to either disorder alone [14, 15]. The relationship between COMISA and uncontrolled hypertension, however, is not clear, as studies on this topic are sparse.

In the present study we have aimed to determine the relationship between OSA, insomnia, COMISA, and uncontrolled hypertension in a middle-aged Swedish population-based cohort. In addition, we aimed to identify potential mediators to gain insight on plausible pathophysiological mechanisms that may contribute to this relationship.

Methods

Study population

The Swedish CArdioPulmonary BioImage Study (SCAPIS), which has previously been described in detail[16, 17], was initiated to improve the understanding of CVD, chronic obstructive pulmonary disease, and associated metabolic disease. 30154 men and women aged 50-64 years were randomly recruited to 6 centers in Sweden between 2013 and 2018, with 6265 included at the Gothenburg study center. Inability to understand spoken and written Swedish was the sole exclusion criteria, for purposes of informed consent. The participants underwent extensive examination with imaging and functional testing, blood sampling, assessment of physical activity, anthropometric measurements, and questionnaires assessing health and lifestyle.

Written informed consent was obtained from all study participants. The Swedish Ethical Review Authority has approved the SCAPIS study (Dnr 2010-228-31M), as

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

well as the current analysis (Dnr 2020–02113, amendment 2022-02638-02). Data collection was performed at the SCAPIS center, Sahlgrenska University Hospital, Gothenburg, Sweden and data analysis was performed at the Center for Sleep and Vigilance Disorders, University of Gothenburg, Sweden.

Assessment of sleep disorders

OSA was assessed by a home sleep apnea testing (HSAT) device which participants applied at home (SomnoCheck Micro Cardio, Weinmann, Hamburg, Germany). Nasal airflow and puls oximetry were analyzed to determine the number of apneas and hypopneas per hour of recording time (apnea-hypopnea index AHI) as defined by Sommermeyer et.al. [18] and validated by Bailer et. al.[19], number of oxygen desaturations ≥4 % per hour of recording time (oxygen desaturation index, ODI), and % time ≤ 90% oxygen saturation during the recording time (T90). Participants with AHI over 10 events/hour were considered to have OSA, which is the suggested cut-off to optimize diagnostic sensitivity and specificity according to the European Respiratory Society technical standards for HSAT devices [20]. An additional sensitivity analysis was performed utilizing an AHI cutoff of AHI ≥ 15 events/hour.

Insomnia was assessed by the Insomnia Severity Index (ISI) questionnaire, with a score range of 0 to 28 [21]. A score greater than or equal to 15, the cutoff we used in this analysis, is considered clinical insomnia by the developers of the questionnaire as well as in global studies of insomnia[11, 21]. Participants with both ISI score of at least 15 and AHI over 10 events/hour were considered to have COMISA.

Excessive daytime sleepiness (EDS) was determined by Epworth Sleepiness Scale, with a score of 11 or more equating to EDS [22].

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Hypertension classification

Systolic and diastolic blood pressure was measured twice in each arm after 5 minutes of rest in the supine position with an automatic device (Omron M10-IT; Omron Health Care Co., Kyoto, Japan). The mean blood pressure in the arm with the highest systolic blood pressure was used in the analysis.

Pressure under 140/90 mmHg without reported use of antihypertensive medication was considered normotensive. Pressure under 140/90 mmHg with reported use of antihypertensive medication in the past two weeks was considered controlled hypertensive. Participants with pressure greater than or equal to 140/90 mmHg were considered to be uncontrolled hypertensive regardless of medication use.

Other variables

Anthropometric data (height, weight, waist circumference) and questionnaire data were collected at a study visit.

A multiple-choice questionnaire was used to determine education level {(not completed primary school/ completed primary school / completed secondary school / completed university degree) converted to a tertiary variable (no secondary school / secondary school / university degree)}, employment status (income-related work: yes/no), civil status{ (single and living alone / married or living with partner / divorced or separated / widowed / other) converted to a binary variable (married or living with partner /not married or living with partner)}, and smoking status (never smoker / ex-smoker / current smoker).

The Alcohol Use Disorders Identification Test for consumption (AUDIT-C) was used to assess alcohol consumption, where a total score of 5 or higher in men and 4 or higher in women was classified as unhealthy drinking [23, 24].

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Sleep duration under 6 hours was based on a multiple-choice question {(4 hours or less / 5 hours / 6 hours / 7 hours / 8 hours / 9 hours / 10 hours or more) converted to a binary variable (under 6 hours/6 hours or more)}. Depression symptoms (yes/no) was based on the question: “During the past 12 months, have you experienced a period of two weeks or more of feeling sad, downhearted or depressed?”. Feelings of stress was determined by a multiple-choice question (“never experienced stress” / “have experienced some stressful periods” / “some stressful periods in the past 5 years” / constant stress in the past year” / “constant stress during the past five years”), with the last two responses qualifying as chronic stress.

Participants were determined to have diabetes mellitus if they had a fasting venous blood glucose ≥7 mmol/L, HbA1c ≥ 48 mmol/L, or self-reported diabetes diagnosis.

Statistics

Statistical analyses were performed similarly to as previously described [25] using SPSS 29.0.0.0 (IBM, Armonk, NY, USA). Data are shown as percentage, mean ± standard deviation (SD) or 95 % confidence interval (CI). Chi-square tests and independent samples t-tests were applied for categorical and continuous variables respectively for between-groups comparisons. The association between sleep disorder status and hypertensive status was analyzed using a generalized ordinal regression model, adjusting for gender, age, body mass index, waist circumference, education level, employment status, civil status, smoking status, unhealthy drinking, short sleep duration, EDS, depression symptoms, chronic stress, diabetes mellitus, and T90. A sensitivity analysis of the ordinal logistic regression model was conducted replacing T90 with ODI as a measure of OSA severity. Results from the

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

regression model are presented as odds ratios and 95% confidence intervals (OR [95%CI]). A p-value less than 0.05 (two-tailed) was considered statistically significant.

Mediation analyses were conducted, as described previously [17], using the PROCESS procedure for SPSS version 4.2 to determine whether there was a mediator relationship between sleep disorder status (predictor), T90 (mediator), and hypertensive status (outcome). Bootstrapping methods with 5000 samples were used to obtain confidence limits.

Results

3832 participants (54.2% female, 57.5 ± 4.3 years) were included in the final analysis after excluding participants with missing or incomplete sleep recording, ISI, or covariates (Figure 1). 10.5% of this population had insomnia only, 18.1% had OSA only, and 3.1% had COMISA. 14.5% of the participants with OSA had insomnia, and 22.6% of the participants with insomnia had OSA. The insomnia group was predominantly female (69.3%), while the OSA group was predominantly male (66%). The gender distribution in COMISA is more even than in the groups with only one of the sleep disorders (42.4% female). AHI, ODI, and T90 were highest in the OSA and COMISA groups. While AHI and ODI did not differ between these two groups (p=0.86 and p=0.08, respectively), T90 was significantly higher in the COMISA group (p=0.01).

COMISA and uncontrolled hypertension

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Hypertensive status differed significantly across the groups in a univariate analysis, where rates of both controlled and uncontrolled hypertension increased in a dose-dependent manner from the control group to the insomnia-only group, to the OSA-only group, and finally to the COMISA group (Table 1, Figure 2, p<0.001). This relationship remained after controlling for confounders in an ordinal logistic regression model, where the OSA and COMISA groups had a significantly greater odds of controlled and uncontrolled hypertension than the control group (OR 1.31[1.05-1.64], p=0.02 & OR 1.88[1.23-2.89], p=0.004, respectively; Table 2). Age, BMI, previous smoking, diabetes mellitus, and T90 were other factors that significantly affected hypertension in this model.

Furthermore, T90 was found to be a significant mediator in the relationship between OSA-only (17%), COMISA (11%) and hypertensive status independent of confounders (Table S1, Figure S1).

In a sensitivity analysis, we replaced T90 with ODI as a measure of nocturnal hypoxic exposure in the regression model and obtained similar results (Table S2).

In an additional sensitivity analysis we investigated the relationship between sleep health status and hypertensive status utilizing a more stringent cutoff for OSA of AHI ≥ 15. In a univariate analysis, we found a similar relationship between this and the main analysis (Figure S2). COMISA defined by this more stringent cutoff was related to hypertensive status independent of confounders among females (OR 2.96[1.14 – 7.70], p=0.03) (Table S3).

OSA and EDS

We also investigated the relationship between combined OSA and EDS and hypertension. Here, there is a dose-dependent increase in uncontrolled hypertension

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

from the control group (4.2%), to EDS only (5.4%), to OSA only (8.0%) to combined OSA and EDS (9.3%, Figure S2), significant in a univariate analysis (ANOVA, $p<0.001$). However, in an ordinal logistic regression model controlling for confounders, the only group with significantly higher rates of hypertension than the control was the OSA-only group (OR 1.41[1.13-1.78], p=0.003). The OSA and EDS group did not have a significantly increased risk of hypertension (OR 1.30 [0.86-1.97], p=0.22, Table S4, Figure S3).

Discussion

In this study we have demonstrated an independent association between OSA and COMISA and uncontrolled hypertension, with a dose-dependent relationship between the rate of controlled and uncontrolled hypertension and sleep disorder status. We have also found that nocturnal hypoxic exposure plays a key role in this relationship. This is the first study to identify the relationship between COMISA and uncontrolled hypertension in a large population-based cohort. Our results highlight the importance of phenotyping and precision medicine in OSA management.

We found that the odds of classifying as controlled hypertensive and/or uncontrolled hypertensive were 31% higher in participants with OSA alone and 88% higher in those with COMISA compared to participants with neither disorder. Our results regarding controlled hypertension and COMISA are largely coherent with the literature. Lechat and colleagues reported a two-fold increase in the odds of hypertension after controlling for age, sex and BMI among participants with COMISA in addition to increased CVD and mortality compared to a healthy reference group in the Sleep Heart Health Study, USA [14]. Wu and colleagues report an increased incidence of hypertension among COMISA participants compared to those without

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

OSA in the Hispanic Community Health Study/Study of Latinos, USA [26]. Wang and colleagues report that while both self-reported insomnia and OSA were associated with increased prevalence of hypertension, COMISA was associated with the greatest risk of hypertension (OR 1.95) in the Suzhou Food Consumption and Health Survey, China [27]. Liu and colleagues have found in a meta-analysis that COMISA is associated with an increased risk of hypertension compared to insomnia alone but not in comparison to OSA alone [28]. The mechanism behind this observed increased risk of hypertension in COMISA is likely multifactorial, with a synergic effect between OSA and insomnia. Intermittent hypoxemia in OSA, as well as hyperarousal with sleep fragmentation which are features of both disorders may accentuate each other, with accompanied alterations in sleep architecture and circadian rhythm resulting in disruptions in autonomic, endocrine, and inflammatory responses. This can have a downstream effect on blood pressure and ultimately manifest CVD [13, 29].

Interestingly, AHI and ODI were similar between OSA and COMISA in our cohort, while T90 was significantly higher in the COMISA group (3.29% vs 5.17%), suggesting that nocturnal hypoxic exposure may be a more relevant measure of OSA severity in this group rather than frequency of respiratory events alone. Furthermore, we found that T90 was a mediator in the relationship between sleep disorder status and risk of hypertension. As T90 can reflect both intermittent hypoxemia as well as total nocturnal hypoxemic burden, both of these mechanisms with resulting sympathetic activation, inflammatory response, and endothelial dysfunction are likely to be involved in the development of hypertension, accentuated by co-occurring insomnia [30-34].

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

There is a need for precision medicine in OSA management as it is becoming increasingly clear in the field that OSA patients are not a homogeneous group. Cluster analyses have indicated that OSA can be separated into several distinct phenotypes with differences in cardiovascular risk and responses to treatment [26, 35-37]. Many of these studies have found distinct clusters based on daytime symptoms as well as sleep disturbances such as insomnia, although their association with hypertension and CVD is not yet fully elucidated. Ye et. al. found that risk of hypertension and CVD was highest among asymptomatic OSA patients, followed by those with disturbed sleep and finally those who were sleepy [37]. Mazzotti et. al., on the other hand, found that excessive sleepiness was associated with incident CVD [35]. Other studies have shown that OSA combined with high night-to-night variability [38] as well as EDS [39] is associated with hypertension. In our cohort, EDS in combination with OSA was not associated with increased risk of hypertension compared to the reference group, while OSA without EDS was (Table S3). This is in line with Ulander et. al. and Ye et. al. who found that EDS was associated with reduced risk of hypertension [40], possibly due to differences in sympathetic activation compared to other groups, with an increased activation among non-sleepy individuals, or perhaps due to delayed OSA diagnosis among non-sleepy individuals. Although the evidence surrounding OSA, EDS, and hypertension is not entirely clear, our results suggest that comorbid insomnia entails a cardiovascular health risk beyond other OSA groups. Screening for insomnia among OSA patients and vice versa may be of value to identify this at-risk group who may especially benefit from additional support.

The present study is the first to identify an association between insomnia, OSA, and uncontrolled hypertension. It was performed on a large population-based cohort,

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

accounting for many relevant confounders. OSA was determined objectively by sleep polygraphy, and according to the established diagnostic cut-off value [20]. Insomnia was determined by ISI, which is a widely used and accepted diagnostic instrument. Solely the Gothenburg cohort of SCAPIS was included in this study as ISI was only available at this center. Despite the rigorous standards of this study, there are a few limitations. The SCAPIS population has a narrow age-range, which can limit the generalizability of our results, as well as our ability to make conclusions about the age-related differences we have found in our analysis. The age-range of SCAPIS is, however, relevant for the purposes of our analysis as both OSA and insomnia are prevalent in middle-age. Although our analysis included a wide range of potential confounders, it did not include physical activity, diet, or treatment adherence, which can influence hypertension, OSA, and insomnia[10, 41-45]. These lifestyle factors can also influence BMI, which is associated with OSA and COMISA, and was shown to be an independent predictor of hypertensive status, opening potential new, non-PAP related treatment avenues[46]. As sleep was not recorded with polysomnography, we also did not have the possibility to measure cortical arousal and arousal index could not be analyzed as a mediator. Additionally, blood pressure data was based on an office measurement which did not allow for detection of 24-hour blood pressure patterns and possible non-dipping patterns, a concern in both OSA and insomnia [10, 47]. Nighttime blood pressure recording may thus have revealed an even greater discrepancy in blood pressure between the groups. 24-hour blood pressure recording may also have reduced the risk of recording “white coat hypertension,” Finally, due to the cross-sectional design of this study, we cannot make conclusions about causal relationships. Longitudinal studies assessing the development and evolution of OSA, insomnia, and hypertension over time as well as

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

randomized controlled trials with focused treatment of OSA, insomnia, and hypertension among COMISA patients would help to elucidate causation.

OSA is a well-established cause of secondary hypertension [10]. However, our study suggests that it is essential to consider other sleep disorders as well to combat hypertension and CVD. COMISA is an illustrative example of the relevance of considering sleep health as a multidimensional construct. Indeed, the American Heart Association has recently added sleep duration to its list of eight most influential health and lifestyle factors for cardiovascular health [48]. Meanwhile, other fundamental components of sleep, such as sleep regularity, timing, efficiency, quality, daytime alertness and snoring have also been associated with hypertension and CVD [49, 50]. This highlights the importance of broadened diagnostic screening and tailored care to manage a diverse sleep health landscape, with heterogeneity even among individuals with the same sleep disorder. (See data supplement for summary of key findings and discussion)

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

References

1. Roth, G.A., et al., *Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study.* J Am Coll Cardiol, 2020. **76**(25): p. 2982-3021.
2. Fifth Joint Task Force of the European Society of, C., et al., *European Guidelines on cardiovascular disease prevention in clinical practice (version 2012): the Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts).* Eur J Prev Cardiol, 2012. **19**(4): p. 585-667.
3. Collaborators, G.B.D.R.F., *Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019.* Lancet, 2020. **396**(10258): p. 1223-1249.
4. Lewington, S., et al., *Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies.* Lancet, 2002. **360**(9349): p. 1903-13.
5. Pengo, M.F., et al., *The role of sleep and sleep disorders in the new 2024 European Society of Cardiology guidelines.* Eur J Prev Cardiol, 2024.
6. Chervin, R.D., *Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea.* Chest, 2000. **118**(2): p. 372-9.
7. Gottlieb, D.J. and N.M. Punjabi, *Diagnosis and Management of Obstructive Sleep Apnea: A Review.* JAMA, 2020. **323**(14): p. 1389-1400.

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

8. Benjafield, A.V., et al., *Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis.* Lancet Respir Med, 2019. **7**(8): p. 687-698.

9. Cowie, M.R., et al., *Sleep Disordered Breathing and Cardiovascular Disease: JACC State-of-the-Art Review.* J Am Coll Cardiol, 2021. **78**(6): p. 608-624.

10. McEvoy, J.W., et al., *2024 ESC Guidelines for the management of elevated blood pressure and hypertension.* Eur Heart J, 2024. **45**(38): p. 3912-4018.

11. Marco Hafner, R.J.R., Erez Yerushalmi, Wendy M. Troxel, *The societal and economic burden of insomnia in adults: an international study*. 2023.

12. Javaheri, S. and S. Redline, *Insomnia and Risk of Cardiovascular Disease.* Chest, 2017. **152**(2): p. 435-444.

13. Sweetman, A., et al., *Bi-directional relationships between co-morbid insomnia and sleep apnea (COMISA).* Sleep Med Rev, 2021. **60**: p. 101519.

14. Lechat, B., et al., *Comorbid insomnia and sleep apnoea is associated with all-cause mortality.* Eur Respir J, 2022. **60**(1).

15. Lechat, B., et al., *All-Cause Mortality in People with Co-Occurring Insomnia Symptoms and Sleep Apnea: Analysis of the Wisconsin Sleep Cohort.* Nat Sci Sleep, 2022. **14**: p. 1817-1828.

16. Bergstrom, G., et al., *The Swedish CArdioPulmonary BioImage Study: objectives and design.* Journal of Internal Medicine, 2015. **278**(6): p. 645-659.

17. Kobayashi Frisk, M., et al., *Eveningness is associated with sedentary behavior and increased 10-year risk of cardiovascular disease: the SCAPIS pilot cohort.* Sci Rep, 2022. **12**(1): p. 8203.

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

18. Sommermeyer, D., et al., *Detection of sleep disordered breathing and its central/obstructive character using nasal cannula and finger pulse oximeter.* J Clin Sleep Med, 2012. **8**(5): p. 527-33.

19. Bailer, M., et al., *Portable polygraphic device (Somnocheck micro CARDIO((R))) provides accurate diagnostic information in psychiatric patients at risk for obstructive sleep apnoea: an observational cohort study.* BMC Psychiatry, 2024. **24**(1): p. 607.

20. Riha, R.L., et al., *ERS technical standards for using type III devices (limited channel studies) in the diagnosis of sleep disordered breathing in adults and children.* Eur Respir J, 2023. **61**(1).

21. Bastien, C.H., A. Vallieres, and C.M. Morin, *Validation of the Insomnia Severity Index as an outcome measure for insomnia research.* Sleep Med, 2001. **2**(4): p. 297-307.

22. Johns, M.W., *A new method for measuring daytime sleepiness: the Epworth sleepiness scale.* Sleep, 1991. **14**(6): p. 540-5.

23. Bush, K., et al., *The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test.* Arch Intern Med, 1998. **158**(16): p. 1789-95.

24. Lundin, A., et al., *The use of alcohol use disorders identification test (AUDIT) in detecting alcohol use disorder and risk drinking in the general population: validation of AUDIT using schedules for clinical assessment in neuropsychiatry.* Alcohol Clin Exp Res, 2015. **39**(1): p. 158-65.

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

25. Kobayashi Frisk, M., et al., *Eveningness is associated with coronary artery calcification in a middle-aged Swedish population.* Sleep Med, 2024. **113**: p. 370-377.

26. Wu, B., et al., *Cardiovascular correlates of sleep apnea phenotypes: Results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL).* PLoS One, 2022. **17**(4): p. e0265151.

27. Wang, C., et al., *Self-reported sleep-disordered breathing and insomnia in association with hypertension: a community-based study in Eastern China.* Blood Press Monit, 2022. **27**(5): p. 320-326.

28. Liu, J., et al., *Clinical Characteristics and Treatment Efficacy for Co-Morbid Insomnia and Sleep Apnea (COMISA): Evidence from Qualitative and Quantitative Analysis.* Behav Sleep Med, 2024. **22**(5): p. 611-635.

29. Buckley, T.M. and A.F. Schatzberg, *On the interactions of the hypothalamic-pituitary-adrenal (HPA) axis and sleep: normal HPA axis activity and circadian rhythm, exemplary sleep disorders.* J Clin Endocrinol Metab, 2005. **90**(5): p. 3106-14.

30. Calbet, J.A., *Chronic hypoxia increases blood pressure and noradrenaline spillover in healthy humans.* J Physiol, 2003. **551**(Pt 1): p. 379-86.

31. Tamisier, R., et al., *14 nights of intermittent hypoxia elevate daytime blood pressure and sympathetic activity in healthy humans.* Eur Respir J, 2011. **37**(1): p. 119-28.

32. Redline, S., A. Azarbarzin, and Y. Peker, *Obstructive sleep apnoea heterogeneity and cardiovascular disease.* Nat Rev Cardiol, 2023. **20**(8): p. 560-573.

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

33. Bartels, K., A. Grenz, and H.K. Eltzschig, *Hypoxia and inflammation are two sides of the same coin.* Proc Natl Acad Sci U S A, 2013. **110**(46): p. 18351-2.

34. Janaszak-Jasiecka, A., et al., *Endothelial Dysfunction Driven by Hypoxia-The Influence of Oxygen Deficiency on NO Bioavailability.* Biomolecules, 2021. **11**(7).

35. Mazzotti, D.R., et al., *Symptom Subtypes of Obstructive Sleep Apnea Predict Incidence of Cardiovascular Outcomes.* Am J Respir Crit Care Med, 2019. **200**(4): p. 493-506.

36. Pien, G.W., et al., *Changing Faces of Obstructive Sleep Apnea: Treatment Effects by Cluster Designation in the Icelandic Sleep Apnea Cohort.* Sleep, 2018. **41**(3).

37. Ye, L., et al., *The different clinical faces of obstructive sleep apnoea: a cluster analysis.* Eur Respir J, 2014. **44**(6): p. 1600-7.

38. Lechat, B., et al., *High night-to-night variability in sleep apnea severity is associated with uncontrolled hypertension.* NPJ Digit Med, 2023. **6**(1): p. 57.

39. Kapur, V.K., H.E. Resnick, and D.J. Gottlieb, *Sleep disordered breathing and hypertension: Does self-reported sleepiness modify the association?* Sleep, 2008. **31**(8): p. 1127-1132.

40. Ulander, M., et al., *Correlates of excessive daytime sleepiness in obstructive sleep apnea: Results from the nationwide SESAR cohort including 34,684 patients.* J Sleep Res, 2022. **31**(6): p. e13690.

41. Dobrosielski, D.A., et al., *Diet and exercise in the management of obstructive sleep apnoea and cardiovascular disease risk.* Eur Respir Rev, 2017. **26**(144).

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

42. Hartescu, I. and K. Morgan, *Regular physical activity and insomnia: An international perspective.* J Sleep Res, 2019. **28**(2): p. e12745.

43. Zhao, M., et al., *The Effects of Dietary Nutrition on Sleep and Sleep Disorders.* Mediators Inflamm, 2020. **2020**: p. 3142874.

44. Lettieri, M.J., et al., *Correlation between positive airway pressure and medication adherence: the healthy user effect.* J Clin Sleep Med, 2024. **20**(7): p. 1087-1092.

45. Wallace, D.M., et al., *Determinants of continuous positive airway pressure adherence in a sleep clinic cohort of South Florida Hispanic veterans.* Sleep Breath, 2013. **17**(1): p. 351-63.

46. Lisik, D. and D. Zou, *Breaking Ground: From CPAP Treatment to the First Medicine for OSA Patients with Obesity.* Current Pulmonology Reports, 2025. **14**(1): p. 3.

47. Lyu, B., et al., *Blood pressure dipping and sleep quality in the Wisconsin Sleep Cohort.* J Hypertens, 2020. **38**(3): p. 448-455.

48. Lloyd-Jones, D.M., et al., *Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health: A Presidential Advisory From the American Heart Association.* Circulation, 2022. **146**(5): p. e18-e43.

49. Buysse, D.J., *Sleep health: can we define it? Does it matter?* Sleep, 2014. **37**(1): p. 9-17.

50. Lechat, B., et al., *Regular snoring is associated with uncontrolled hypertension.* NPJ Digit Med, 2024. **7**(1): p. 38.

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Tables

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Table 1: Demographics and characteristics of participants by sleep disorder status

		Total (n=3832)	Control group (n=2616)	Insomnia only (n=404)	OSA only (n=694)	COMISA (n=118)
Female sex		54.2	57.7	69.3	34.0	42.4
Age (years)		57.5 ± 4.3	57.2 ± 4.3	57.1 ± 4.2	58.7 ± 4.2	57.6 ± 4.1
BMI (kg/m^2)		26.6 ± 4.3	26.0 ± 4.0	26.4 ± 4.1	28.4 ± 4.4	30.1 ± 5.1
Waist Circumference (cm)		92.9 ± 12.4	90.9 ± 11.7	91.3 ± 11.3	99.7 ± 12.2	103.9 ± 12.6
Education	No secondary school	9.0	7.7	12.6	10.8	13.6
	Secondary school	43.2	42.5	41.3	46	48.3
	University degree	47.8	49.8	46	43.2	38.1
No income-related work		11.6	9.4	25.5	10.2	22.9
Married / Living with partner		71.6	73.6	58.4	73.1	64.4
Smoking	Never	48.2	50.1	39.6	47.1	42.4
	Ex-smoker	38.8	37.9	40.6	39.9	44.1

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

	Current smoker	13.0	12	19.8	13	13.6
Unhealthy alcohol consumption		32.4	32.3	31.2	33.7	32.2
Self-reported sleep duration <6 hours		38.6	32.5	70.3	37.8	71.2
EDS (ESS ≥ 11)		15.3	13	26.2	15.3	28.8
Depression symptoms in the past year		29.1	24.9	62.1	21.5	53.4
Self-reported chronic stress		21.7	17.5	54.2	15	43.2
HT status	Normotensive	83.0	86.2	83.2	74.1	62.7
	Controlled HT	11.8	9.4	12.4	18	27.1
	Uncontrolled HT	5.2	4.4	4.5	7.9	10.2
Diabetes mellitus		5.6	4.5	6.7	7.6	11.9
ISI (total score)		7.9 ± 5.5	6.4 ± 4.1	17.8 ± 2.7	6.2 ± 4.0	17.4 ± 3.0
AHI (events/hour)		7.3 ± 7.5	4.3 ± 2.5	4.6 ± 2.5	18.4 ± 9.4	18.6 ± 9.1
ODI (events/hour)		2.8 ± 4.8	1.4 ± 1.7	1.7 ± 1.8	7.8 ± 7.7	9.2 ± 9.9

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

T90 (% of time, n=3744)	1.5 ± 4.8	0.9 ± 3.8	1.0 ± 3.7	3.3 ± 6.6	5.2 ± 9.1

Definition of abbreviations: BMI=body mass index, EDS=excessive daytime sleepiness, ESS=Epworth Sleepiness Scale, HT=hypertensive, ISI=Insomnia Severity Index, AHI=apnea hypopnea index, ODI=oxygen desaturation index 4%, T90=oxygen saturation ≤ 90%

Data are expressed as mean ± SD or %

p-values reflect chi-square tests for categorical variables and analysis of variance (ANOVA) for continuous variables

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Table 2: The association between hypertension status, sleep disorder status, and confounders in an ordinal logistic regression model (N=3744)

		Uncontrolled Hypertension	
		OR (95% CI)	p-value
Sleep disorder status	Control group	Reference	
	Insomnia only	1.11 (0.80 – 1.53)	0.54
	OSA only	1.31 (1.05 – 1.64)	**0.02**
	COMISA	1.88 (1.23 – 2.89)	**0.004**
Sex		1.00 (0.79 – 1.26)	0.99
Age (years)		1.11 (1.09 – 1.14)	**< 0.001**
BMI (kg/m^2)		1.09 (1.04 – 1.14)	**< 0.001**
Waist circumference (cm)		1.01 (0.99 – 1.03)	0.21
Education	No secondary school	Reference	
	Secondary school	1.04 (0.77 – 1.40)	0.82
	University degree	0.86 (0.63 – 1.18)	0.34
No income-related work		1.05 (0.80 – 1.38)	0.70
Married / Living with partner		1.10 (0.90 – 1.35)	0.36
Smoking	Never	Reference	
	Ex-smoker	1.27 (1.04 – 1.55)	**0.02**

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

	Current smoker	1.08 (0.81 – 1.45)	0.60
Unhealthy alcohol consumption		1.14 (0.94 – 1.38)	0.19
Self-reported sleep duration <6 Hours		0.91 (0.75 – 1.12)	0.35
EDS (ESS ≥ 11)		1.05 (0.82 – 1.34)	0.70
Depression symptoms in the past year		1.03 (0.83 – 1.29)	0.79
Self-reported chronic stress		1.26 (1.00 – 1.59)	0.05
Diabetes mellitus		2.15 (1.58 – 2.92)	**< 0.001**
T90 (% of time)		1.02 (1.00 – 1.03)	**0.048**

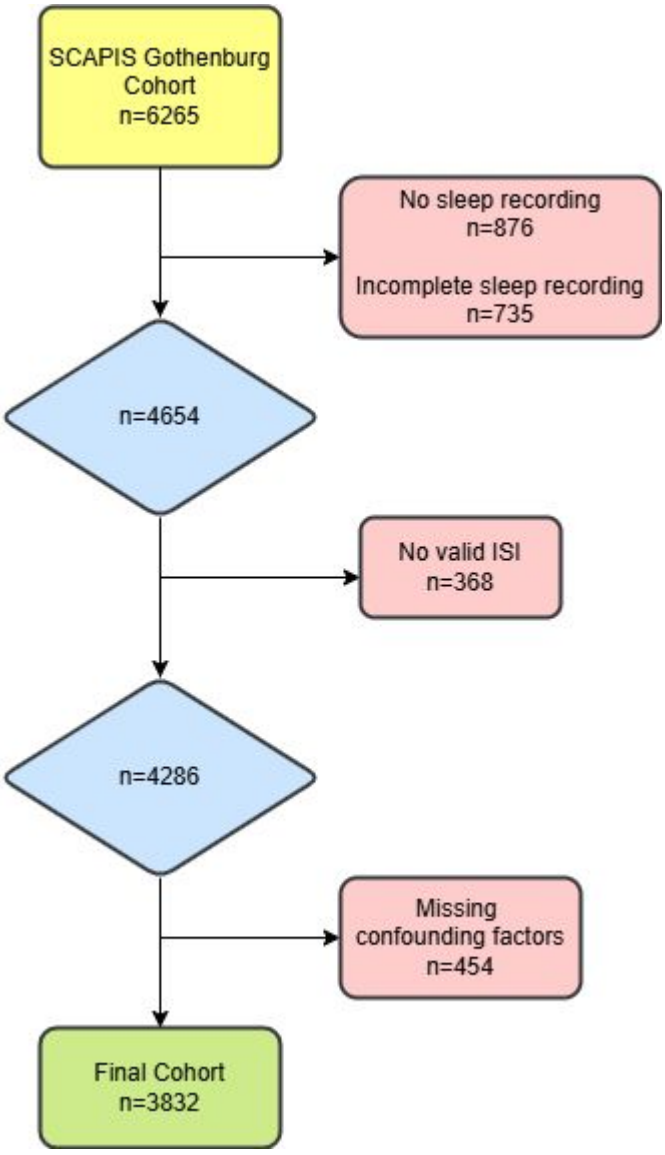
Definition of abbreviations: BMI=body mass index, EDS=excessive daytime sleepiness, ESS=Epworth Sleepiness Scale, T90=oxygen saturation ≤ 90%

Data are expressed as odds ratios (OR) with 95% confidence intervals (CI)

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

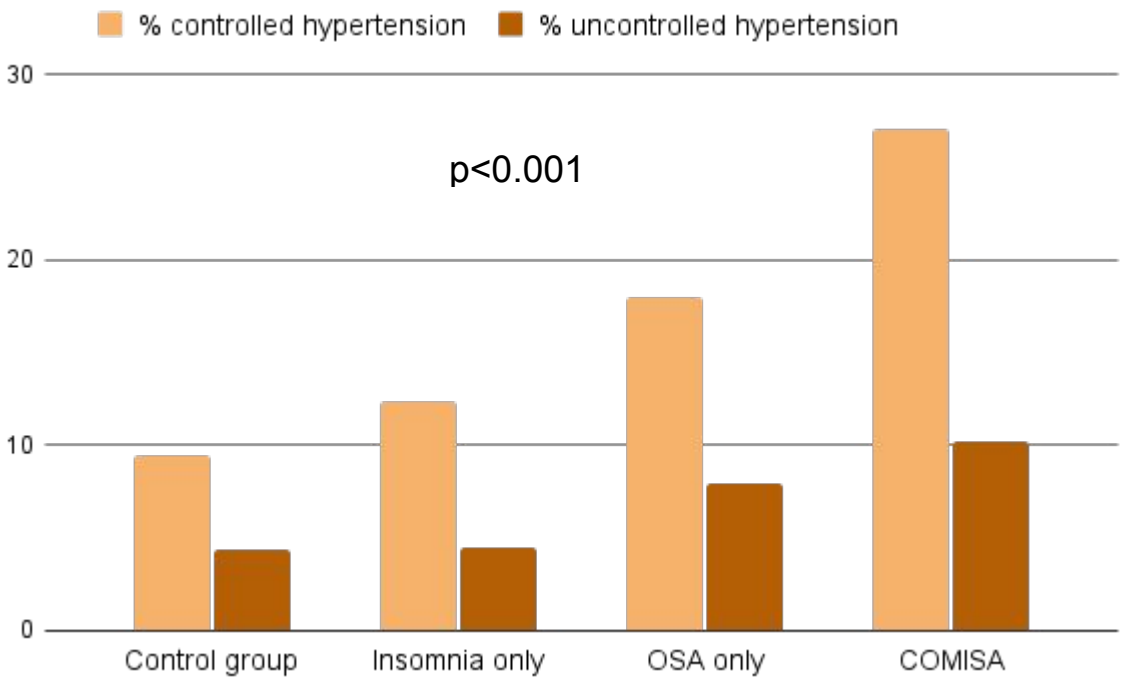
Figures

Figure 1: Study Flow Chart



ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Figure 2: Blood pressure by sleep disorder status



Rates of both controlled and uncontrolled hypertension increased in a dose-dependent manner from the control group to the insomnia-only group, to the OSA-only group, and finally to the COMISA group. ANOVA, p<0.001

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Co-morbid Insomnia and Sleep apnea Is Associated with Uncontrolled Hypertension in a Middle-aged Population

Mio Kobayashi Frisk[1], Joel Bergqvist[1,2], Sven Svedmyr[1,2], Philippe Diamantis[1], Göran Bergström[3,4], Ding Zou[1]

[1]Center for Sleep and Vigilance Disorders, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

[2]Department of Sleep Medicine, Respiratory Medicine and Allergology, Sahlgrenska University Hospital, Gothenburg, Sweden

[3]Department of Molecular and Clinical Medicine, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden

[4]Department of Clinical Physiology, Sahlgrenska University Hospital, Gothenburg, Sweden

Supplementary Materials

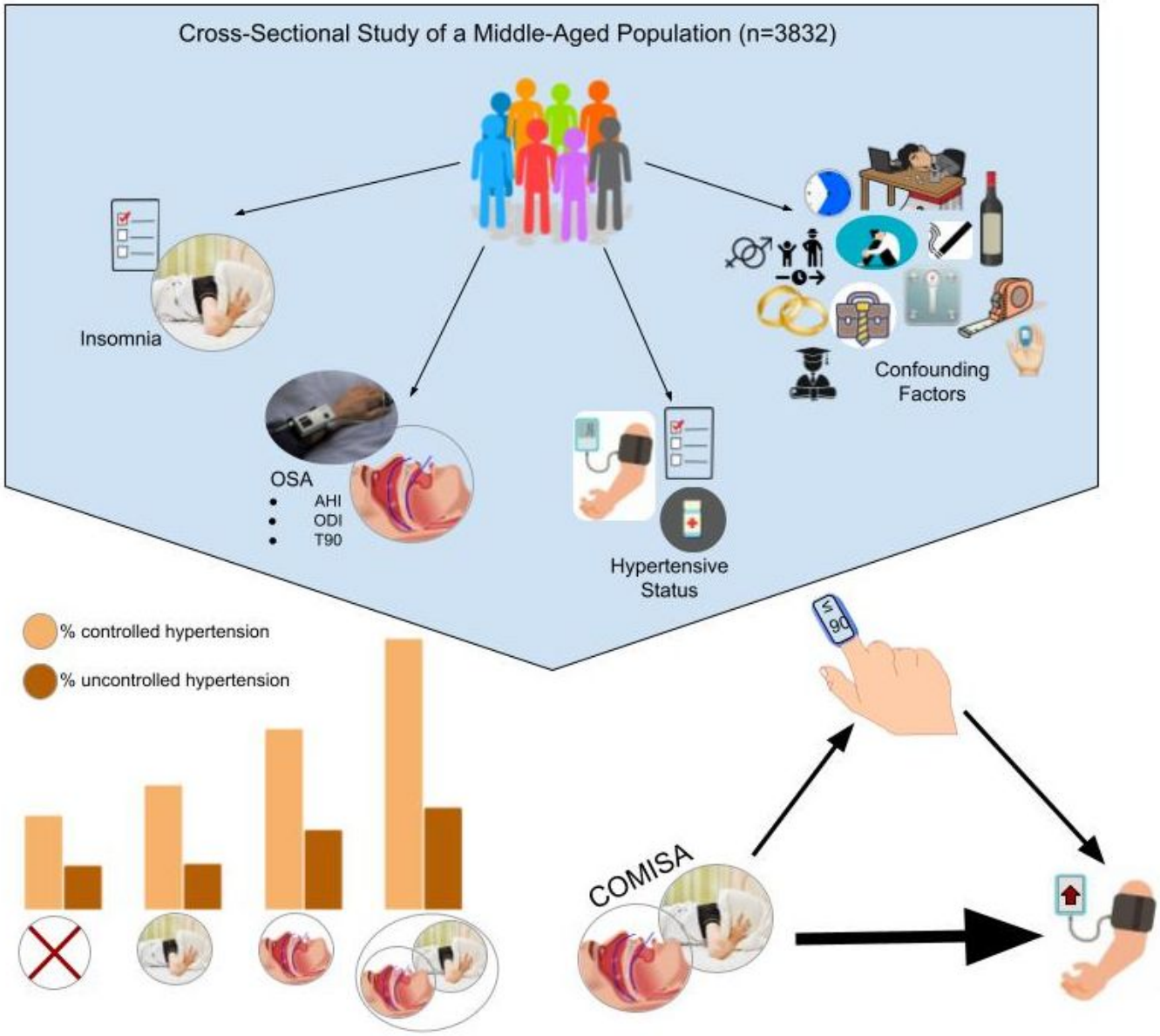
Correspondence:

Mio Kobayashi Frisk, MD

Center for Sleep and Vigilance Disorders
Department of Internal Medicine and Clinical Nutrition
University of Gothenburg
Medicinaregatan 8b Box 421
SE-40530, Gothenburg
Sweden
E-mail: mio.kobayashi.frisk@vgregion.se

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Graphical Abstract



ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

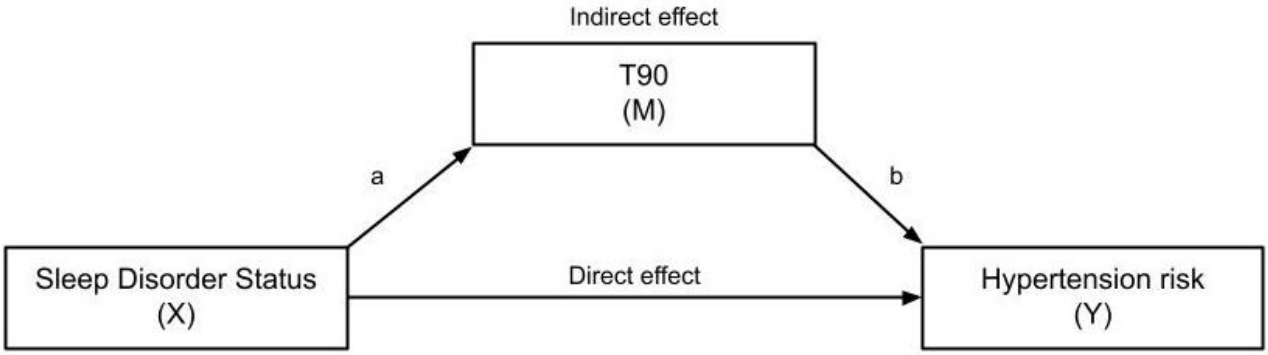
Table S1. Summary of mediation analysis of T90 in an adjusted model

	Coefficients	t	P value	Bootstrapping [95%CI]
Model a				
Control vs. Insomnia only	-0.0500	-0.1849	0.85	
OSA only	1.6496	7.9960	**<0.001**	
COMISA	3.1295	6.9711	**<0.001**	
Model b				
T90	0.0057	3.1937	**0.001**	
	Relative total effect			
Total effect model				
Control vs. Insomnia only	-0.0006	-0.0217	0.98	
OSA only	0.0565	2.4959	**0.01**	
COMISA	0.1602	3.2526	**0.001**	
	Relative direct effect			
Direct effect of X on Y				
Control vs. Insomnia only	-0.0004	-0.0121	0.99	
OSA only	0.0470	2.0630	**0.04**	
COMISA	0.1423	2.8732	**0.004**	
	Relative indirect effect			
Indirect effect of X on Y				
Control vs. Insomnia only	-0.0003			[-0.0033 - 0.0027]
OSA only	0.0095			**[0.0016 - 0.0186]**
COMISA	0.0179			**[0.0027 - 0.0395]**

Significant results marked in bold. X=sleep disorder status, Y=hypertensive status, M=T90. Model a represents the association between X and M. Model b represents the association between M and Y (see figure S1). 17% of the relationship between increased risk of poorer hypertensive status among the OSA-only group and 11% among the COMISA group compared to the control group was mediated by T90 in an adjusted model. The model is adjusted for age, sex, BMI, waist circumference, education level, income-related work, civil status, smoking status, unhealthy alcohol consumption, short sleep duration, excessive daytime sleepiness, depression symptoms, chronic stress, and diabetes mellitus.

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Figure S1: Illustration of mediation analysis of COMISA, T90 and hypertension risk



Bootstrapping methods were applied to obtain confidence limits of the indirect effect (number of samples=500)

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Table S2: The association between hypertension status, sleep disorder status, and confounders including ODI instead of T90 in an ordinal logistic regression model

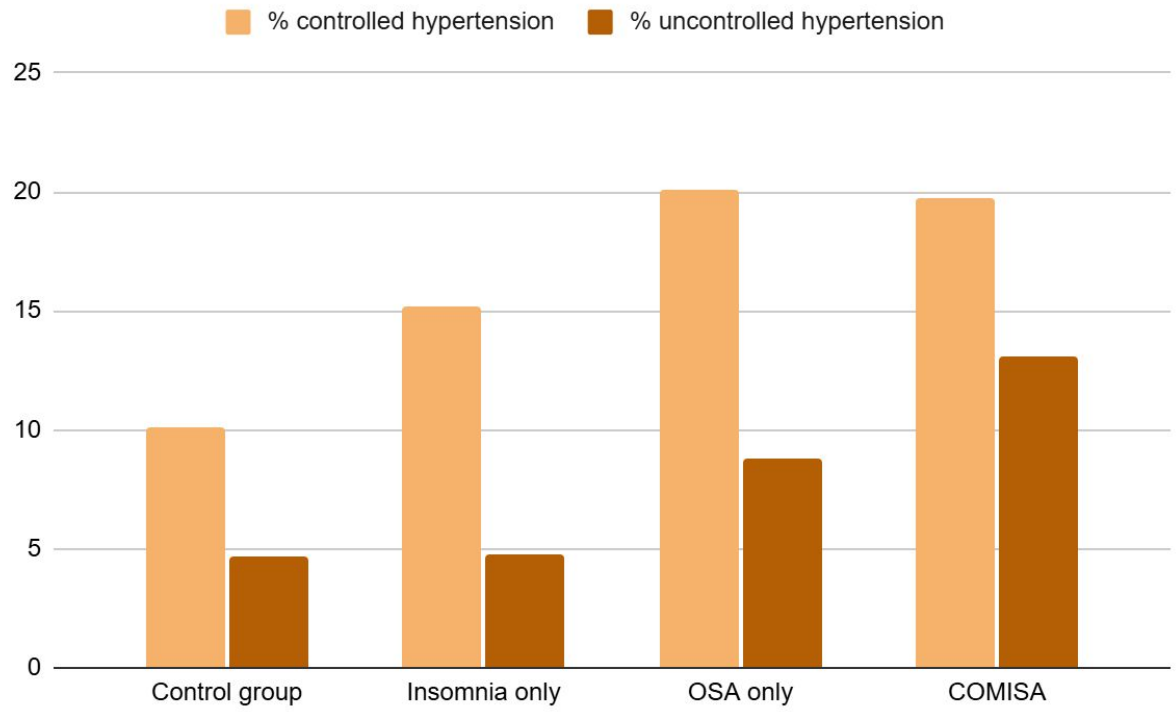
		Uncontrolled Hypertension	
		OR (95% CI)	p-value
Sleep disorder status	Control group	Reference	
	Insomnia only	1.13 (0.82 - 1.55)	0.45
	OSA only	1.35 (1.06 - 1.73)	**0.02**
	COMISA	1.90 (1.22 - 2.96)	**0.004**
Sex		1.00 (0.80 - 1.26)	0.98
Age (years)		1.11 (1.09 - 1.14)	**< 0.001**
BMI (kg/m^2)		1.09 (1.05 - 1.14)	**< 0.001**
Waist circumference (cm)		1.01 (0.99 - 1.03)	0.22
Education	No secondary school	Reference	
	Secondary school	1.01 (0.75 - 1.35)	0.97
	University degree	0.85 (0.63 - 1.16)	0.30
No income-related work		0.98 (0.75 - 1.28)	0.89
Married / Living with partner		1.08 (0.88 - 1.32)	0.45
Smoking	Never	Reference	
	Ex-smoker	1.28 (1.05 - 1.55)	**0.01**
	Current smoker	1.05 (0.79 - 1.40)	0.73
Unhealthy alcohol consumption		1.14 (0.94 - 1.38)	0.18
Self-reported sleep duration <6 Hours		0.93 (0.77 - 1.13)	0.47
EDS (ESS > 10)		1.03 (0.81 - 1.31)	0.82
Depression symptoms in the past year		1.01 (0.81 - 1.25)	0.95
Self-reported chronic stress		1.27 (1.01 - 1.60)	**0.04**
Diabetes mellitus		2.21 (1.63 - 2.99)	**< 0.001**
ODI (events/hour)		1.00 (0.98 - 1.02)	0.75

Definition of abbreviations: BMI=body mass index, ODI=oxygen desaturation index 4%, EDS=excessive daytime sleepiness, ESS=Epworth Sleepiness Scale

Data are expressed as odds ratios (OR) with 95% confidence intervals (CI)

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Figure S2: Blood pressure by sleep disorder status with AHI ≥ 15 as OSA cutoff



Rates of uncontrolled hypertension increased in a dose-dependent manner from the control group to the insomnia-only group, to the OSA-only group, and finally to the COMISA group. OSA is defined as AHI ≥ 15 and insomnia is defined as ISI ≥ 15. Participants meeting criteria for both OSA and insomnia have COMISA. ANOVA, $p<0.001$

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Table S3: The association between hypertension status, sleep disorder status with a cutoff of AHI ≥ 15 to define OSA, and confounders among females in an ordinal logistic regression model (N= 2026)

		Uncontrolled Hypertension	
		OR (95% CI)	p-value
Sleep disorder status	Control group	Reference	
	Insomnia only	1.28 (0.88 – 1.85)	0.20
	OSA only	1.22 (0.75 – 1.97)	0.43
	COMISA	2.96 (1.14 – 7.70)	**0.03**
Age (years)		1.12 (1.08 – 1.15)	**< 0.001**
BMI (kg/m^2)		1.09 (1.03 – 1.15)	**0.002**
Waist circumference (cm)		1.01 (0.99 – 1.04)	0.21
Education	No secondary school	Reference	
	Secondary school	1.06 (0.68 – 1.64)	0.81
	University degree	0.76 (0.48 – 1.20)	0.24
No income-related work		1.10 (0.76 – 1.60)	0.60
Married / Living with partner		1.22(0.93 – 1.61)	0.15
Smoking	Never	Reference	
	Ex-smoker	1.30 (0.98 – 1.73)	0.07
	Current smoker	1.11 (0.74 – 1.68)	0.59
Unhealthy alcohol consumption		1.34 (1.01 – 1.77)	**0.04**
Self-reported sleep duration <6 Hours		0.93 (0.71 – 1.23)	0.63
EDS (ESS ≥ 11)		0.95 (0.68 – 1.33)	0.78
Depression symptoms in the past year		0.94 (0.67 – 1.26)	0.66
Self-reported chronic stress		1.25 (0.92 – 1.71)	0.16
Diabetes mellitus		1.70 (1.02 – 2.82)	**0.04**
T90 (% of time)		1.02 (1.00 – 1.04)	0.12

Definition of abbreviations: BMI=body mass index, EDS=excessive daytime sleepiness, ESS=Epworth Sleepiness Scale, T90=oxygen saturation ≤ 90%

Data are expressed as odds ratios (OR) with 95% confidence intervals (CI)

Table S4: Hypertensive status in OSA combined with EDS in an ordinal logistic regression model with confounders (N=3744)

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

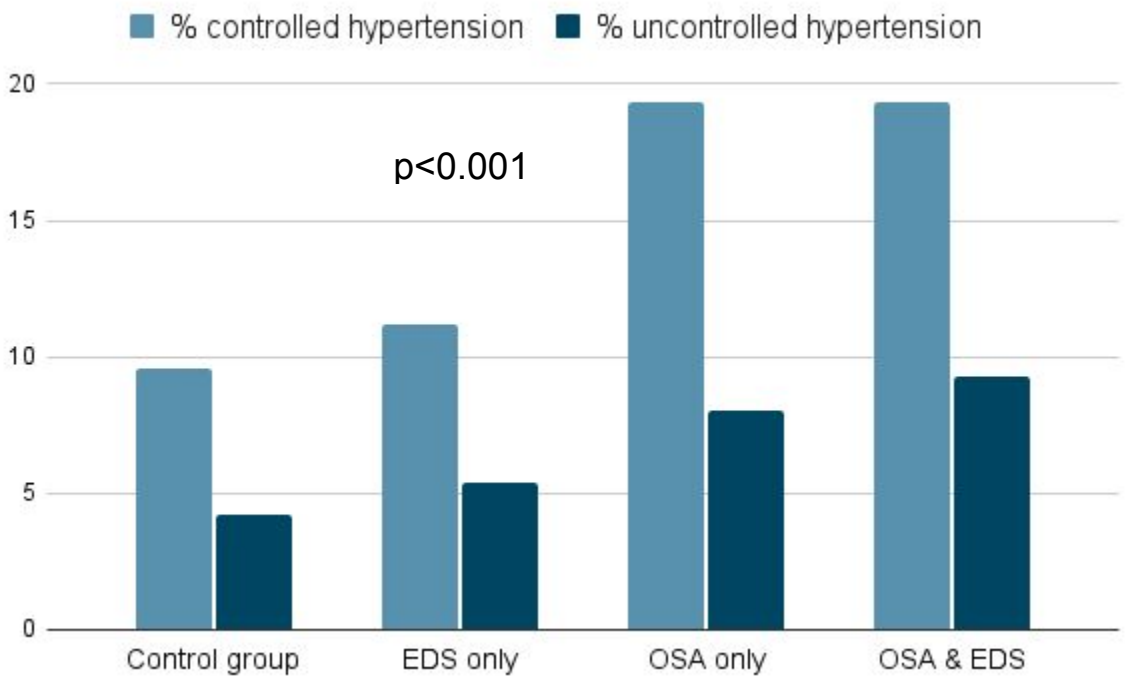
		Uncontrolled Hypertension	
		OR (95% CI)	p-value
Sleep disorder status	Control group	Reference	
	EDS only	1.12 (0.84 - 1.50)	0.45
	OSA only	1.41 (1.13 - 1.78)	**0.003**
	OSA and EDS	1.30 (0.86 - 1.97)	0.22
Sex		1.00 (0.79 - 1.26)	1.0
Age (years)		1.11 (1.09 - 1.14)	**< 0.001**
BMI (kg/m^2)		1.09 (1.04 - 1.14)	**< 0.001**
Waist Circumference (cm)		1.01 (0.99 - 1.03)	0.23
Education	No secondary school	Reference	
	Secondary school	1.04 (0.77 - 1.41)	0.79
	University degree	0.87 (0.63 - 1.18)	0.37
No income-related work		1.06 (0.81 - 1.39)	0.70
Married / Living with partner		1.11 (0.90 - 1.36)	0.34
Smoking	Never	Reference	
	Ex-smoker	1.27 (1.04 - 1.55)	**0.02**
	Current smoker	1.08 (0.81 - 1.44)	0.61
Unhealthy alcohol consumption		1.14 (0.94 - 1.38)	0.19
Self-reported sleep duration <6 Hours		0.91 (0.75 - 1.11)	0.35
Insomnia (ISI ≥ 15)		1.20 (0.92 - 1.58)	0.18
Depression symptoms in the past year		1.03 (0.83 - 1.29)	0.78
Self-reported chronic stress		1.26 (1.00 – 1.59)	0.06
Diabetes mellitus		2.14 (1.57 - 2.91)	**< 0.001**
T90 (% of time)		1.02 (1.00 - 1.03)	**0.04**

Definition of abbreviations: BMI=body mass index, EDS=excessive daytime sleepiness, ISI=Insomnia Severity Index, T90=oxygen saturation ≤ 90%

Data are expressed as odds ratios (OR) with 95% confidence intervals (CI)

Figure S3: Blood pressure by sleep disorder status (OSA and EDS)

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC



There is a dose-dependent increase in risk for uncontrolled hypertension from the control group (4.2%), to EDS only (5.4%), to OSA only (8.0%) to combined OSA and EDS

Summary of Key Findings

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC

Summary of key findings and discussion:

- *We found an independent, dose-dependent relationship between OSA, COMISA, and uncontrolled hypertension. This is largely coherent with the existing literature and there are likely multiple mechanisms behind this relationship, with a likely synergic effect between OSA and insomnia.*
- *Nocturnal hypoxic exposure as measured by T90 was found to be a mediator in the above relationship. This suggests that both intermittent and total nocturnal hypoxemic burden may be involved in the development of hypertension among people with OSA and COMISA.*
- *We found an independent relationship between OSA without EDS and uncontrolled hypertension, but not between OSA with EDS and uncontrolled hypertension. The literature on this topic is conflicting, but possible mechanisms for these findings are an increased sympathetic activation among those who are not sleepy, or delayed OSA diagnosis among participants without EDS.*
- *These findings highlight the importance of considering heterogeneity in OSA with broadened diagnostic screening and personalized care.*

ANNALSATS Articles in Press. Published September 08, 2025 as 10.1513/AnnalsATS.202501-080OC