The Link Between Sleep and Cardiovascular Health: Implications for Narcolepsy and Idiopathic Hypersomnia

In 2022, the American Heart Association declared **sleep is essential for heart health**, adding it as one of its Life's Essential 8™ key measures[1,2]

Poor sleep can contribute to major CVD risk factors including **high blood pressure**, **obesity**, and **diabetes**[3]

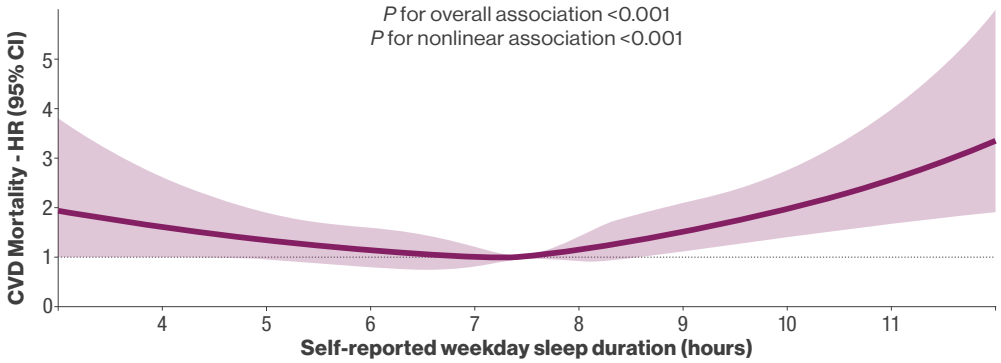
CVD risk factors are common in sleep disorders, such as narcolepsy and idiopathic hypersomnia[3]

Mechanistic Connections Between Sleep and Cardiovascular Health

Sleep Duration[4]

A J-shaped association between self-reported sleep duration and **CVD mortality** has been observed. Both shorter and longer sleep duration is associated with higher CVD mortality

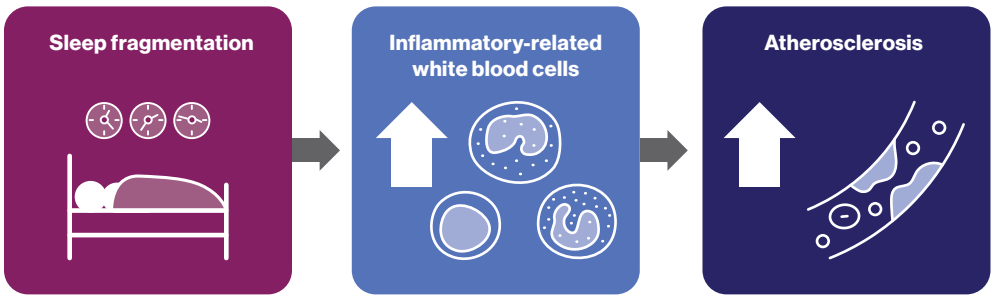
~7 to 8 hours of sleep is considered a normal sleep duration for most adults



Sleep Fragmentation[5]

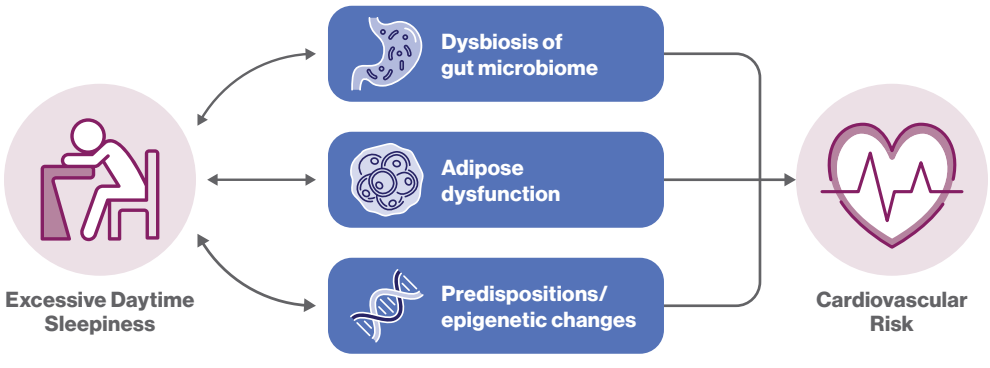
Poor-quality sleep has been associated with elevated counts of inflammatory-related white blood cells, which may confer an increased risk for **atherosclerosis**

Specifically, PSG- and actigraphy-measured sleep fragmentation was associated with increased absolute neutrophil count, which predicted higher coronary artery calcification scores in a population-based sample of adults



Excessive Daytime Sleepiness[6]

Interactive and bidirectional mechanisms may promote EDS while also increasing **CV risk.** For instance, dysbiosis of the gut microbiome stimulates systemic inflammation, which is associated with both EDS and CV risk. Other factors, such as increased stress, are also associated both with EDS and CV risk[6,7]



CV, cardiovascular; CVD, cardiovascular disease; CI, confidence interval; EDS, excessive daytime sleepiness; HR, hazard ratio; PSG, polysomnography.

References: 1. American Heart Association, Inc. Life's Essential 8TM. https://www.heart.org/en/healthy-living/healthy-lifestyle/sleep. **2.** American Heart Association, Inc. Life's Essential 8TM. https://www.heart.org/en/healthy-living/healthy-lifestyle/lifes-essential-8. **3.** American Heart Association, Inc. Sleep Disorders and Heart Health. https://www.heart.org/en/health-topics/sleep-disorders/sleep-and-heart-health. **4.** Khao B, et al. *JAHA*. 2023;12:e027832. **5.** Vallat R, et al. *PLoS Biol*. 2020;18:e3000726. **6.** Bock J, et al. *Heart*. 2022;108:1761-1766. **7.** Kashani M, et al. *Stress*. 2012;15:45-51.

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Abnormal Sleep (eg, Disrupted Nighttime Sleep and Long Sleep Duration) and Excessive Daytime Sleepiness are Clinical Features of Narcolepsy and Idiopathic Hypersomnia[8,9]

Narcolepsy and Cardiovascular/Cardiometabolic Comorbidities

In the CV-BOND study, adults with **narcolepsy** had **more comorbidities** at baseline and a **higher risk** of **new onset CV conditions** compared with matched controls without narcolepsy[8]

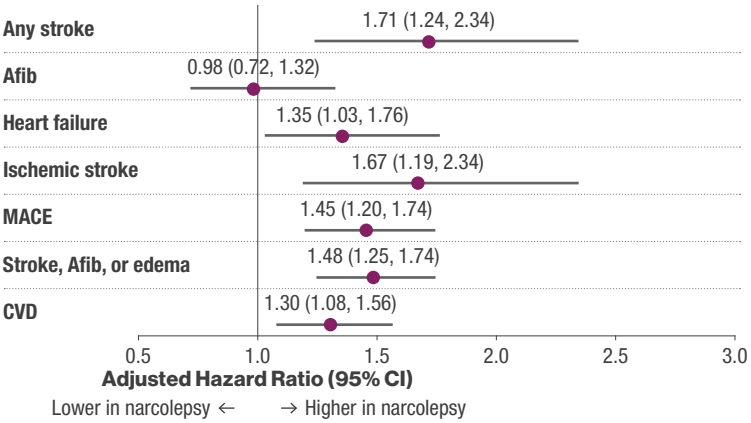
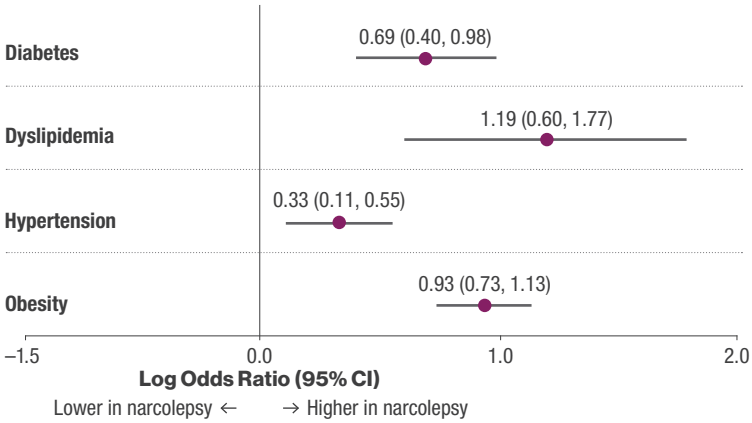


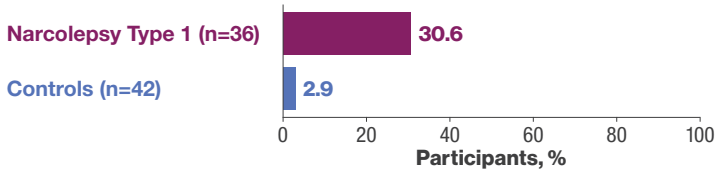
Figure demonstrates adjusted HRs for incidence of new-onset CV conditions. Study used US insurance claims data from adults with narcolepsy (n=12,816) and matched controls (n=38,441).[8] Figure adapted from Ben–Joseph RH, et al. *Sleep*. 2023;46:zsad161. http://creativecommons.org/licenses/by/4.0/.

The results of a meta-analysis showed that **narcolepsy** is associated with a **higher prevalence** of **CV/CM comorbidities** compared with controls without narcolepsy[10]



Meta-analysis of 48 observational studies (studies analyzed: diabetes, n=7; dyslipidemia, n=3; hypertension, n=7; obesity, n=9).[10]

Non-dipping nocturnal BP is **more prevalent** among people with **narcolepsy**[11]

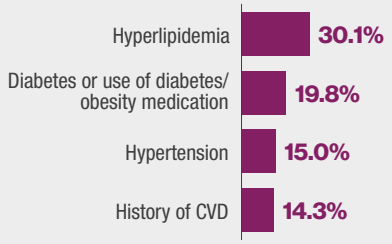


Nighttime and daytime ambulatory BP and their night-to-day ratio were measured in drug-free patients with narcolepsy and controls. Non-dipping defined as a nocturnal diastolic BP dip <10% lower than daytime BP.[11]

Decreased nocturnal BP ("dipping") is a normal feature of sleep in people without narcolepsy.[12] "Non-dipping" nocturnal BP (blunting of typical BP decreases, or "dips," during nighttime sleep) is associated with **higher CV mortality in the general population**, independent of hypertension. Sleep fragmentation may trigger non-dipping nocturnal BP[13]

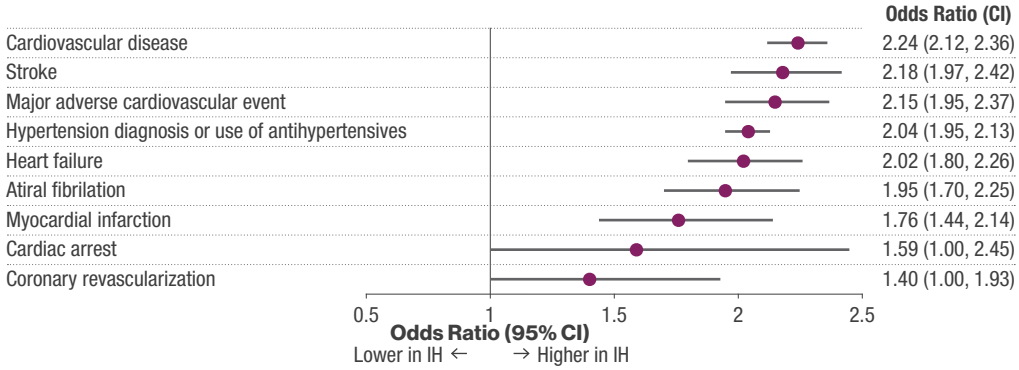
Idiopathic Hypersomnia and Cardiovascular/Cardiometabolic Comorbidities

A retrospective cohort study found that **CV and CM conditions were common in US adults newly diagnosed with IH**[14]



Merative™ MarketScan® administrative claims were analyzed. Patients were excluded from the IH cohort if they had a diagnosis of IH within the baseline period, indicating a history of IH, or a diagnosis of cataplexy within the baseline period.[14]

In the CV-RHYTHM study, adults with **IH** showed **higher prevalence of CV comorbidities** than matched controls without IH[15]



Merative™ MarketScan® administrative claims were analyzed. Patients with a medical claim for IH were matched 1:5 to a control cohort for age, sex, geographic region, insurance type, and cohort entry date.[15]

Afib, atrial fibrillation; BP, blood pressure; CI, confidence interval; CM, cardiometabolic; CV, cardiovascular; CV-BOND, Cardiovascular Burden of Narcolepsy Disease; CV-RHYTHM, Cardiovascular Real-World Idiopathic Hypersomnia Total Health Model; CVD, cardiovascular disease; HR, hazard ratio; IH, idiopathic hypersomnia; MACE, major adverse cardiac event; MI, myocardial infarction; NT1, narcolepsy type 1.

References (continued): 8. Ben-Joseph RH, et al. *Sleep*. 2023;46:zsad161. **9.** American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd ed, Text Revision. Darien, IL: American Academy of Sleep Medicine; 2023. **10.** Mohammadi S, et al. *Sleep Med*. 2021;81:268-284. **11.** Dauvilliers Y, et al. *PLoS One*. 2012;7:e38977. **12.** Ohkubo T, et al. *J Hypertens*. 2002;20:2183-2189. **13.** Cuspidi C, et al. *J Clin Med*. 2019;8:1367. **14.** Saad R, et al. *Sleep Epidemiology*. 2023;3:100059. **15.** Saad R, et al. Proceedings from ISPOR; May 7-10, 2023; Boston, MA; Abstract EPH231.

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