

The Association Between REM Sleep and Risk of Mortality

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Reduced REM sleep predicts increased mortality risk in three cohorts.



The Association Between REM Sleep and Risk of Mortality

Introduction

- Sleep disorders and sleep characteristics (e.g., sleep duration) are linked to higher mortality.
- REM sleep has been associated with multiple aspects of mental and physical health and REM is the first stage to rebound after total sleep deprivation.
- HYPOTHESIS:** Reduced REM sleep is associated with increased risk of mortality.

Methods

- Random forests used to assess relative importance of each sleep stage.
- Percent REM evaluated as a continuous variable with 5% increments to aid interpretation.
- Clinical knowledge used to identify >60 covariates commonly associated with sleep architecture and mortality.
- Cox regression models built using 6-fold cross-validation and a priori feature selection.
- Kaplan-Meier plots to illustrate possible threshold effect.
- Sensitivity analyses:
 - Exclude individuals with AHI > 30 or using antidepressants, benzodiazepines, or sleep medications.
 - Exclude individuals with TST < 5 or > 9 hours on PSG or actigraphy.
 - Exclude individuals with depression.
- Replicate findings using data from the Wisconsin Sleep Cohort (WSC) and Sleep Heart Health Study (SHHS).
- Meta-analysis of three cohorts to improve estimate of effect magnitude

Results

- Random forest classifier found that REM was the most important sleep stage for predicting survival, with a mean decrease in accuracy of 0.058.
- MrOS Cohort: 2,675 older men, mean age of 76.3 ± 5.5 had a 13% higher mortality rate over 12.8 years (IQR 5.4) for every absolute 5% reduction in REM (HR = 1.13, 95% CI 1.08 - 1.19).
- Wisconsin Sleep Cohort: 1,386 middle-aged men and women, mean age of 51.5 ± 8.5 had a 17% higher mortality rate over 20.8 years (IQR 4.5) for every 5% reduction in REM (HR = 1.17, 95% CI 1.03 - 1.34).
- Sleep Heart Health Cohort: 5,550 older men and women, mean age of 63.0 ± 11.2 had a 13% higher mortality rate over 11.9 years (IQR 2.3) for every 5% reduction in REM (HR = 1.13, 95% CI 1.07 - 1.18).
- Meta-analysis of three cohorts resulted in a HR = 1.13, 95% CI of 1.10 - 1.17 for all-cause mortality and HR = 1.13, 95% CI of 1.06 - 1.20 for cardiovascular mortality.

Conclusions

- Less REM sleep was associated with higher rates of all-cause mortality in three independent cohorts.
- Findings were consistent across different causes of death and sensitivity analyses.

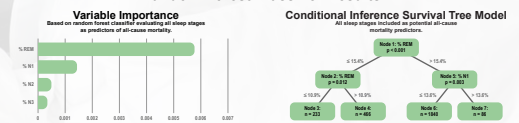
Acknowledgments

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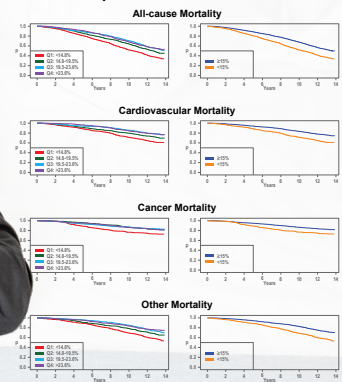
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Random Forest Classifier Results



Kaplan-Meier Plots MrOS

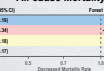


Mortality Risk Ratios

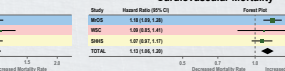
Percent REM as a Continuous Variable, 5% Decrease

	Overall Number Deaths (%)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 4 HR (95% CI)
All-cause Mortality	1,486 (26.2%)	1.13 (1.08 - 1.18)	1.17 (1.09 - 1.26)	1.22 (1.12 - 1.33)
-Females	-	-	1.34 (0.67 - 1.48)	1.16 (1.08 - 1.24)
-Males	-	-	1.04 (0.92)	1.08 (1.03 - 1.17)
Cardiovascular Mortality	460 (31.8%)	1.16 (1.08 - 1.26)	1.22 (1.12 - 1.33)	1.27 (1.14 - 1.41)
Cancer Mortality	319 (22.8%)	1.14 (1.05 - 1.26)	1.19 (1.08 - 1.32)	1.27 (1.14 - 1.41)
Other Mortality (Non-Cardiovascular, Non-Cancer)	696 (22.2%)	1.09 (1.04 - 1.16)	1.13 (1.05 - 1.22)	1.20 (1.11 - 1.30)

All-cause Mortality



Cardiovascular Mortality



Abbreviations: Hatched Rate: HR, Confidence Interval (CI); Smoking Status: Weekly Alcohol, Daily Coffee, Antidepressants, Benzodiazepines, Sleep Medication, Site, Overall Ancestry Index, Sleep Time with Computer, Chronic Disease (COPD, Heart Failure, Stroke, Hypertension, Diabetes, Chronic Kidney Disease, Coronary Artery Disease, Peripheral Vascular Disease, Type 2 Diabetes, Heart Failure, and Stroke); Physical Activity Scale for the Study Site; Depression, Cognitive Function Scale, Chronic Obstructive Pulmonary Disease, Type 2 Diabetes, Heart Failure, and Stroke; WSC Model 2: Age, Sex, Race (with respect to ancestry), Education, Body Mass Index (BMI), Smoking Status, Weekly Alcohol, Daily Coffee, Antidepressants, Benzodiazepines, Sleep Medication, Percent Sleep No. Sleep, Sleep Stage, Sleep Architecture Scale Score, Employment, Type 2 Diabetes, Heart Failure, and Stroke; SHHS Model 2: Age, Sex, Race (with respect to ancestry), Education, Body Mass Index (BMI), Smoking Status, Weekly Alcohol, Daily Coffee, Antidepressants, Benzodiazepines, Sleep Time with Actigraph, Bedtime 95%, Percent Sleep No. Sleep, Research Diagnostic Scale Score, SP-36 Mental Component Scale Standardized Score, SP-36 Marital Health Index Standardized Score, SP-36 Physical Component Scale Standardized Score, Cognitive Function Scale, Chronic Obstructive Pulmonary Disease, Type 2 Diabetes, Heart Failure, and Stroke