1a. Title: Effect of gender on REM vs NREM OSA and the association with daytime sleepiness.

b. Abbreviated Title: Effect of Gender and REM-related OSA

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3. Timeline: Start of analysis on approval; preliminary draft to P&P 9/02

4. Rationale: Prior studies in clinical samples have suggested that while men have higher NREM RDI, the RDI during REM sleep is similar in men and women. Women thus have disproportionately more REM-only OSA than men. (1) Fragmentation of REM sleep has been associated with daytime sleepiness in some studies (2), although the restorative effects of REM sleep remain controversial. (3) This study aims to confirm any gender differences in the prevalence of REM OSA vs NREM OSA in a large community dwelling cohort and compare the effect of REM OSA vs NREM OSA on daytime sleepiness. This study may help to elucidate male-female differences in OSA symptoms.

5. Hypothesis: REM-only OSA is more often identified in women than in men and is associated with different effects on sleepiness and other daytime symptoms than NREM OSA.

6. Data: The data to be used in this analysis include PSG variables (RDI4P and arousal index [total, REM, NREM], time in REM and NREM sleep, quality grades, and PSG notes), Sleep Habits Questionnaire data (ESS score, total sleep time, snoring), age, gender, BMI and SF-36 scores. The source of data will be the Coordinating Center. The analysis will include all subjects with PSG studies during SHHS1 with overall PSG score of fair or better, who also have complete SHQ data.

7. Type of Study: Secondary Study

8. Type of Publication: Journal Article
   Target Journal: Sleep

9. Analysis Responsibility: Local

10. Introduction:
Previous investigators have reported on gender differences in the polysomnographic features of OSA. O’Conner et al (1) demonstrated that in a clinical sample REM OSA was disproportionately more common in women than in men and that OSA was less
severe in women because of milder OSA during NREM sleep. These gender differences did not appear to be age- or weight-related. Other studies (4) have demonstrated that in patients with RDI<10, daytime sleepiness correlates with AHI during REM sleep and that an AHI_{REM} >15 events/h is predictive of reduced sleep latency on MSL testing. Interestingly, using survey data from the Wisconsin Sleep Cohort Study, Young et al (5) demonstrated that women with sleep apnea do not report symptoms that differ significantly from men with the same level of sleep apnea, regardless of the severity of sleep apnea. Polysomnographic data with respect to RDI_{REM} vs RDI_{NREM} was not evaluated. It is possible that REM OSA is unique in its clinical presentation and may be associated with a higher incidence in women and a greater association with daytime sleepiness or other daytime symptoms, such as depressed mood, anxiety, or irritability.

The proposed study will evaluate the relation of gender with REM vs NREM OSA and the relation of REM vs NREM OSA with daytime sleepiness and quality of life in a large population-based cohort.

11. Brief Analysis Plan:
For analysis of gender differences in REM vs NREM OSA, we will use both categorical and continuous measures of RDI. For categorical analysis, OSA will be categorized as absent (RDI_{REM}<5 and RDI_{NREM}<5), OSA_{REM} (RDI_{REM}>5 and RDI_{NREM}<5), OSA_{NREM} (RDI_{REM}<5 and RDI_{NREM}>5), and OSA BOTH (RDI_{REM}>5 and RDI_{NREM}>5). Contingency table analysis will be used to compare the prevalence of OSA types between males and females, both in crude analysis and adjusting for age and BMI quartiles using the Mantel-Haenszel chi-square. Analyses will also be conducted using a threshold of 15 to classify OSA as present or absent. For analysis of continuous RDI variables, the mean RDI_{REM} and RDI_{NREM} and the ratio RDI_{REM}/RDI_{NREM} in men and women will be compared, adjusting for age and BMI in multiple linear regression.

For analysis of the relation of REM-OSA to sleepiness, the mean ESS will be compared among OSA categories by ANOVA, adjusting for age, sex, BMI, and usual total sleep time, for the entire group and stratified by gender. The models will be performed for the entire group, and also by sex-specific strata. Multiple regression analysis will be used to assess the relation of ESS (dependent variable) to RDI_{TOTAL}, RDI_{REM}, and RDI_{NREM} in separate models, adjusting for age, sex and BMI as well as stratified by sex. If RDI_{REM} and RDI_{NREM} are not too highly correlated, both will then be included in the same model to assess their relative contribution to ESS score.

A similar analysis will be performed to examine the association of RDI_{REM} and RDI_{NREM} with SF-36 social functioning, role emotional, mental health, and vitality scores.

12. Summary Section:
The proposed study will analyze the relation of gender to REM vs NREM OSA and then determine whether REM vs NREM OSA differ with respect to daytime symptoms.

13. References:


