SHHS Manuscript Proposal

1. **Full Title:** Polysomnographic predictors of blood pressure
   Abbreviated Title: same

2. **Lead Author:** Susan Redline, MD, MPH

3. **Timeline:**
   Target Start: January 1, 1998
   Target Finish: April 1, 1998

4. **Rationale:**

There is a variety of data that suggests, chronically, that sleep disordered breathing (SDB) increases risk of the development of daytime hypertension, cardiovascular and cerebrovascular diseases, and neurocognitive dysfunction. Compard to data from the National Center for Health Statistics on the general US population, patients with sleep apnea hyponea syndrome (SAHS) may have twice as much hypertension, 3 times as much ischemic heart disease and 4 times as much cerebrovascular disease (1). The types of data that address the relationship of SDB to hypertension include cross-sectional epidemiological studies that have shown associations between snoring or measured apneic activity with reported hypertension or measured blood pressure (2-5); reports from specialty clinics of hypertension prevalence in SAHS patients (3, 6-8) and of SDB prevalence in hypertensive samples (9, 10); studies that have related severity of SDB and level of blood pressure elevation (3, 11); studies of SAHS patients that have reported changes in blood pressure and/or sympathetic excitation following SDB treatment (11, 12): and an animal study that has demonstrated the induction of chronic hypertension in dogs after experimental upper airway occlusion (13). Examinations of end organ effects of hypertension (e.g., left ventricular hypertrophy assessed by echocardiography) also have supported an association of chronic effects of hypertension on SDB (14). However, it has been argued that these relationships may have been confounded with obesity, age or medications (15, 16). The failure of several studies to demonstrate a dose-response relationship between severity of OSA and HTN, after adjusting for body mass index (BMI) (17-19), has been interpreted as evidence against a causal relationship.

One source for discrepancies relating hypertension to OSA may relate to the use of different methodologies for quantifying SDB as an adverse cardiovascular "exposure." Patients with SAHS may experience a number of potentially adverse physiological exposures during sleep. These include as exchange abnormalities and increased sympathetic nervous system activity (20). The latter is probably a response to intermittent hypoxemia and hyporoapnia,

chemoreflex activation and to the increased central nervous system arousal that occurs with obstructed breathing (21). Additionally, large fluctuations in intrathoraic pressure that occur with obstructed breathing may influence venous return, right ventricular filling (left ventricular filling by interdependence), baroreflexes and vagal tone and release of volume regulatory peptides (e.g., rennin, aldosterone and atrial natriuretic factor). The acute cardiovascular responses to these complex influences may include: pulmonary and systemic vasoconstriction and hypertension, reduced cardiac output and arrhythmias. There is currently much controversy regarding the which of these exposures contribute most to the development of hypertension and cardiovascular diseases. Results of experimental work have provided somewhat conflicting data regarding the relative impact of hypoxemia, an obstruction of the upper airway, intrathoraic muscle swings, sympathetic activation and CNS arousal on hemodynamic resonses (22-24). Epidemiological studies suggest stronger relationships between blood pressure and OSA when OSA is defined when using desaturation criteria (25) as compared to respitory effort changes (26); however, more recent work suggests that it is the changes in intrathoraic pressure that are the strongest OSA-associated risk factors for nocturnal blood pressure.

The unique SHHS software will allow a comprehensive assessment of the extent to which blood pressure is predicted by various polysomnographic indices. It is the purpose of this study to identify which polysomnographic marker (characterizing hypoxemia, respitory disturbance frequency, time in apnea, arousal index) best identifies subjects with elevated blood pressure.

5. **Hypotheses:**
Time spent in apnea and hyponea will be more strongly associated with blood pressure than time spent in desaturation, frequency of respiratory disturbances (RDI), and measures of sleep fragmentation (arousal index and percentage stage I).

6. **Data Analysis**
Dependent Variables (as continuous measures): mean systolic blood pressure, mean diastolic blood pressure and mean blood pressure; (as binary outcomes): Hypertension, defined as a doctor diagnosed HTN and prescribed anti-HTN medication or a measured BP > 140/90.

Independent Variables: percent time in apnea; percent time in apnea plus hyponea; percent time in desaturation < 85%; RDI (based on 3% desaturation or arousal and based on 4% desaturation); arousal index; percent time in stage I; number of upward sleep stages).

Adjusting Variables (potential confounders): age, BMI, sex, race, smoking exposure, alcohol.

Analysis: Multiple regression and logistic regression. We also will examine how differences in the goodness of fit of the model changes with incorporation of different measures "hypoxic" versus "ventilatory" stress. For binary outcomes, differences in the C statistic will be examined for different madels.

Time window, source, inclusions/exclusions: All polysomnographic data that have been fully scored by January 1 with "no problems with staging" noted.

7. **Type of Study:** Primary

8. **Type of Publication:** Journal Article

9. **Analysis Responsibilty:** Coordinating Center