1. Title: Cross-Sectional study of sleep apnea and hypertension
   Abbreviated: Sleep apnea and hypertension

2. Writing Group (list individual with lead responsibility first):
   Lead: F. Javier Nieto, MD, PhD
   Address: Johns Hopkins University, School of Hygiene & Public Health
            615 N. Wolfe St., Room 6027
            Baltimore, MD 21205
   Phone: (410) 955-4380; FAX: (410) 955-8086
   Email: jnieto@phnet.sph.jhu.edu
   Dr. Ralph D’Agostino
   Dr. Michael Lebowitz
   Dr. Thomas Pickering
   Dr. Jonathan Samet
   Dr. Eyal Shahar
   Dr. Terry Young
   To be determined, Coordinating Center

3. Timeline:
   Immediately

4. Rationale:
   As many as 80% of patients with sleep apnea (SA) have hypertension, and 30% or more of the hypertensives have SA (Kales et al, 1984; Lavie et al, 1984; Fletcher et al, 1985; Williams et al, 1985). Epidemiologic studies have consistently shown an association between snoring and hypertension, although some studies suggest that the association is due to the confounding effect of age or obesity (Gislason et al, 1987; Schmidt-Nowara et al, 1990). The lack of an independent effect in some studies may be due to misclassification errors resulting from the questionable validity of the snoring information based on self-report (Wiggins et al, 1990; Stradling and Crosby, 1991). A study based on the spouses’ report showed an independent association, even after controlling for age and weight (Norton and Dunn, 1985). Furthermore, a relation between PSG-assessed SA and hypertension has been found in healthy populations in which obesity is practically absent (Lavie, 1983), and even after careful control of BMI and other confounding factors (Young et al, 1997). Clinical studies have shown that treatment of SA leads to improvement in hypertension (Wilcox et al, 1993; Suzuki et al, 1993).
Despite recent criticisms (Wright et al, 1997), the epidemiologic evidence linking snoring and SA with hypertension seems to be fairly consistent, although important questions remain unanswered, particularly the pathophysiologic mechanisms underlying the association between SA and hypertension (Jeong andDimsdale, 1989; Hoffstein et al, 1991). Although arousal is widely considered the dominant factor mediating an alleged SA-hypertension association, recent data obtained in canine models suggest that SA is associated with increase blood pressure independent of arousals (O’Donnel et al, 1996; Brooks et al, 1997). Finally, the large sample size available to explore the association between snoring and hypertension in the SHHS offers a unique opportunity to corroborate a recent report from the Wisconsin Sleep Cohort Study suggesting that snoring is part of the continuum of the SRBD syndrome in its association with hypertension (Young et al, 1996).

5. Main Hypothesis:
   1) SA (measured by RDI/arousal index) and its symptoms (snoring, sleepiness) are cross-sectionally associated with hypertension.
   2) These associations are independent of body weight.
   3) Higher RDI is associated with increased blood pressure independently of arousals.

6. Data (variables, time window, source, inclusions/exclusions):
The main independent variables will be RDI (e.g., RDI, 4%), arousal index, snoring history, and sleepiness index (Epworth scale).

The main dependent variables will be blood pressure (as a continuous outcome in linear regression analyses) and prevalent hypertension (categorically defined in logistic regression analyses).

The potential confounding effect of overweight and other possible confounders (age, gender, SES, alcohol intake) will be assessed by means of stratified analyses and multivariate regression models.

The independent effect of RDI and arousal index will be assessed by stratification and multivariate adjustment (if appropriate).