1.a. Full Title: The association between sleep apnea and cancer mortality: pooled results from the Wisconsin Sleep Cohort and the Sleep Heart Health Study.

b. Abbreviated Title (Length 26 characters): Sleep apnea and cancer mortality


I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _FJN_ [please confirm with your initials electronically or in writing]

First author: F. Javier Nieto
Address: University of Wisconsin School of Medicine and Public Health
         Population Health Sciences
         707c Warf Office Building
         610 Walnut St.
         Madison, WI 53726

Phone: (608) 265-5242       Fax: (608) 263-2820
E-mail: fnieto@wisc.edu

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
Name: Moyses Szklo
Address: Johns Hopkins Bloomberg School of Public Health
         615 North Wolfe Street; Room W6009
         Baltimore, MD 21205
Phone: (410) 955-346    Fax: (410) 955-8086
Email: mszklo@jhsph.edu

3. Timeline:

4. Rationale:
Intermittent hypoxia, a common pathophysiological insult in sleep apnea, has been associated with cancer progression (accelerated tumor growth) in animal models (1). Increased angiogenesis mediated by increased VEGF production might be the mechanism explaining this association (1-4).

In a longitudinal study from the Wisconsin Sleep Cohort, sleep apnea was associated with increased cancer mortality, although the results were not statistically significant due to insufficient sample size (5).
Pooling data from the Wisconsin cohort and the SHHS cohort offers the opportunity to assess the existence of an association between sleep apnea and cancer mortality in a larger sample.

5. Main Hypothesis/Study Questions:
Baseline sleep apnea is associated with increased cancer mortality.

Data:
Inclusions: ARIC participants in the SHHS (Minneapolis, Washington County)

Data needed:
- Date of ARIC baseline exam
- History of cancer at baseline
- Cancer death during follow-up
- Censoring indicator (lost to follow-up or death from other causes)
- Date of event (cancer or censoring).
- ARIC ID (for linkage with SHHS data)

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

Data from the ARIC subcohorts will be pooled with that from other SHHS subcohorts (CHS, Framingham, Strong Heart, Arizona) and from the Wisconsin Sleep Cohort to conduct a survival analyses on the relation between sleep apnea (in categories of severity) and cancer mortality. Cox proportional hazards regression analysis will be used to control for potential confounders such as age, sex, BMI, and smoking (these data will be obtained from the SHHS dataset).

Summary/conclusion:
Animal models and preliminary epidemiologic evidence suggest that sleep apnea and associated intermittent hypoxia might increase the risk of cancer growth and mortality. Pooling data from SHHS and the Wisconsin cohort offers a unique opportunity to verify this hypothesis in a large population-based cohort.

7.a. Will the data be used for non-CVD analysis in this manuscript?  _X_ Yes  ____ No

b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used?  _X_ Yes  ____ No
(This file ICTDER03 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?  ____ Yes  _X_ No
8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = “No use/storage DNA”?  

____ Yes  ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at:  

http://www.csc.unc.edu/ARIC/search.php

____X___ Yes  _______ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

N/A

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  

____X__ Yes  ____ No

11.b. If yes, is the proposal

_____ A. primarily the result of an ancillary study (list number* _1995.12_)

_____ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* __________ __________ __________)

*ancillary studies are listed by number at  

http://www.csc.unc.edu/ARIC/forms/

12. Manuscript preparation is expected to be completed in one to three years. If a Manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.
References:


