ARIC Manuscript Proposal #767S

PC Reviewed: 01/16/01 **Status: A** **Priority: _____**
SC Reviewed: 01/30/01 **Status: A** **Priority: _____**

1.a. Full Title: Relationship of prevalent diabetes to sleep disordered breathing in those at risk for CVD

1.b. Abbreviated Title: Diabetes and SDB

2. Lead Author: Helaine Resnick, Barbara Howard, Strong Heart Study, Susan Redline PSG Reading Center

3. Timeline:

Target Start: Immediately upon approval and availability of analysis staff at coordinating center

Target Finish: Manuscript to be completed by Summer/Fall, 2001

4. Rationale: Sleep disordered breathing (SDB) may be causally associated with cardiovascular disease (CVD), and this association may be modified by diabetes, or by diabetic complications.[1,2,3] One mechanism through which diabetes may modify the SDB—CVD association is through the effects cardiovascular autonomic neuropathy (CAN) in an affected sub-set of diabetic individuals. A recent study showed that one in four diabetic individuals with autonomic neuropathy had obstructive sleep apnea.[4] The relatively high prevalence of sleep disturbance in the presence of diabetic neuropathy raises the possibility that impaired central control of respiration may link diabetes and SDB; diabetes may therefore modify an SDB—CVD association, should one exist.[5] Reports of increased prevalence of sleep apnea and nocturnal oxygen desaturation in diabetic patients with CAN support a diabetes—SDB link.[6,7,8] Diabetes and SDB may also be linked in the opposite direction: a recent study showed decrements in carbohydrate metabolism following sleep deprivation similar to those observed in normal aging.[9] In small, cross-sectional studies, the confounding effects of obesity make analysis of the independent effect and direction of these factors difficult to isolate, and power is often limited. Moreover, individuals with a history of CVD or its risk factors may adopt lifestyle modifications that can influence interpretation of cross-sectional risk factor data related to diabetes and SDB.

To begin evaluating the potential role of diabetes in the SDB-CVD relationship, it is first necessary to clarify the cross-sectional association between diabetes and SDB, independently of obesity and prevalent CVD. The purpose of this paper is to report baseline characteristics of Sleep Heart Health Study participants with and without diabetes, focusing on sleep parameters such as RDI and CVD risk factors, within strata of BMI among individuals who are at risk for CVD. The intended target audience of this paper includes individuals with an interest in diabetes and CVD epidemiology, and health care providers who see diabetic patients.

General Null Hypothesis:
There will be no difference in CVD risk factors, RDI and other PSG-based sleep parameters across diabetes—BMI strata among those at risk for CVD.

Data: *Use data from baseline exam; need history of reported diabetes*

Selection criteria: 1. Baseline SHHS sample, excluding ppts. with reported history of CVD.
2. Ppts. must have non-missing data for reported diabetes
3. Ppts. must have non-missing data for baseline BMI
4. Ppts. must have non-missing data for RDI

Type of Publication: Manuscript to *Diabetes Care* or *Diabetes.*

Analysis Responsibility: Coordinating Center

Introduction: Elucidating mechanisms linking diabetes to CVD are critical for identifying risk-factor specific interventions aimed at reducing the occurrence and consequences of CVD. It is known that obesity is common in diabetes, and there are data to suggest that SDB is common in people with diabetes, although the direction of causality remains unclear. Further, obesity and diabetes are both common CVD risk factors. Clarifying the cross-sectional, obesity-independent relationship between diabetes and SDB is an important first step in understanding potential pathways by which diabetes may be involved in a potential relationship between SDB and CVD.

Preliminary Analysis Plan:

1. Classify subjects according to diabetes status at baseline
2. Classify subjects according to recent NHLBI obesity guideline: <18.5 kg/m^2, 18.5 to <25 kg/m^2, 25 to <30 kg/m^2 and >=30 kg/m^2.
3. Show age-adjusted CVD risk factors, RDI by diabetes (2 groups); ttest for differences in age-adjusted means between diabetic and non-diabetic groups.
4. Show age-adjusted CVD risk factors, RDI by diabetes and BMI (8 groups); ttest for differences in age-adjusted means between diabetic and non-diabetic groups within BMI strata.

Selected Demographic and CVD risk factors, by baseline diabetes status

Variable	Reported diabetes	No reported diabetes	p [chisq or ttest]*
Ethnicity			
White			
Black			
Mex-Am			
Am. Indian			
Gender (% female)			
LDL-c			
HDL-c			
TG			
BMI			
<18.5			
18.5 to <25			
25 to <30			
>=30			
Smoking (% current or former vs. never)			
Hypertension (%)			
Waist circumference			
Males			
Females			

* For continuous variables, p value is for difference in age-adjusted means between the diabetes groups; for categorical variables, p value is for the chi-square test of proportions.

Histogram to show distribution of RDI according to diabetes status, within BMI strata
Plot Y-axis=RDI, X-axis= duration of diabetes among those with diabetes- group data by BMI and have several OLS lines overlying one another on the same plot→ would expect worse measures in people with longer duration of diabetes, and measures should be worse in heavier people; possible synergy between these two factors?
Multivariate analysis can be used to assess the association of diabetes and SDB, adjusted for potential confounders including BMI; can test interaction of diabetes and BMI on RDI.

Summary: I expect that the data will show that within strata of BMI, people with diabetes have worse CVD risk factors and worse measures collected in PSG I.

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[2] Nielsen FS, et al.: Increased sympathetic activity during sleep and nocturnal hypertension in type 2 diabetic patients with diabetic nephropathy. *Diabet Med* 16:555-62, 1999.
[3] Foley DJ et al.: Associations of symptoms of sleep apnea with cardiovascular disease, cognitive impairment, and mortality among older Japanese American men. *J Am Geriatr Soc* 47:524-8, 1999.
[4] Ficker JH et al.: Obstructive sleep apnoea and diabetes mellitus: the role of cardiovascular autonomic neuropathy. *Eur Respir J* 11:14-9, 1998.
[5] Page MMcB et al.: Cardiorespiratory arrest in diabetic autonomic neuropathy *Lancet* i:14-16, 1978
[6] Rees PJ et al.: Sleep apnea in diabetic patients with autonomic neuropathy. *J R Soci Med* 74:192-95, 1981
[7] Neuman C et al.: Nocturnal oxygen desaturation in diabetic patients with severe autonomic neuropathy. *Diabetes Res Clin Pract* 28:97-102, 1995.
[8] Sobotka PA et al.: Impaired hypoxic ventilatory drive in diabetic patients with autonomic neuropathy. *J Clin Endocrinol Metab* 62:658-63, 1986.
[9] Spiegel K, Leproult R, Van Cauter E: Impact of sleep debt on metabolic and endocrine function. *Lancet* 354: 1435-9, 1999.