ARIC Manuscript Proposal #770

PC Reviewed: 02/15/01 Status: A Priority: 2 SC Reviewed: 03/01/01 Status: A Priority: 2

1.a. Full Title: Identification of psychological attributes associated with the risk of incident diabetes

b. Abbreviated Title (Length 26 characters): Psychological traits and diabetes

2. Writing Group (list individual with lead responsibility first):

Lead: Sherita Hill Golden, MD, MHS

Address: Division of Endocrinology and Metabolism

1830 E. Monument Street

Suite 333

Baltimore, MD 21287

Phone: 410-955-3921 Fax: 410-955-8172

E-mail: sahill@welch.jhu.edu

Writing group members: Frederick Brancati, MD, MHS, Daniel Ford, MD, MPH, Janice Williams, PhD, MPH, F. Javier Nieto, MD, PhD, Kay Sanford, PhD (others welcomed)

3. Timeline: Analysis to begin immediately

4. Rationale:

Identification of modifiable risk factors for diabetes is important for its prevention. There has been a growing interest in psychological traits as novel risk factors for diabetes. Possible mechanisms include the influence of these traits on behaviors, such as activity and diet, or their influence on the activity of the hypothalamic-pituitary-adrenal (HPA) axis.

The prevalence of depression in diabetic individuals is increased compared to the general population (1;2) and several studies have demonstrated that the presence of depressive symptoms is predictive of incident diabetes (3-6). Disordered carbohydrate metabolism has been demonstrated in non-diabetic individuals with depression/mood disorders (7;8). Individuals with depression are also known to have hypercortisolism (7). Thus, a possible mechanism by which depression may lead to the development of diabetes is via neuroendocrine activation of the hypothalamic-pituitary-adrenal (HPA) axis or the sympathetic nervous system. Both cortisol and catecholamines are counterregulatory hormones that can lead to a state of insulin resistance.

Depressive symptoms have also been shown to be predictive of cardiovascular disease (9-12), as have other psychological traits, including trait anger (13) and vital exhaustion, which is characterized by a state of fatigue, lack of energy, feelings of hopelessness, loss of libido, and increased irritability (14;15).

Cardiovascular disease and diabetes share common metabolic precursors (16), so they may also share antecedent psychological risk factors. Previous epidemiological studies of psychological risk factors in diabetes have been limited by small sample sizes and limited physiological data. Vital exhaustion and trait anger have not been evaluated in relation to incident diabetes. ARIC is an attractive study in which to evaluate this relationship because data are available on the above psychological factors in a large cohort of individuals. While ARIC does not have direct assessment of depressive symptoms, data is available on anti-depressant medication use at baseline, which can serve as a proxy for the presence of depression. Previous associations of trait anger and vital exhaustion with incident CHD suggest a potential common soil.

5. Main Hypothesis/Study Questions:

- 1.) Independent predictors of incident type 2 diabetes will include:
 - a.) Vital exhaustion
 - b.) Trait anger
 - c.) Anti-depressant medication use
- 2.) These relationships will be mediated by obesity, insulin resistance (as indicated by hyperinsulinemia), physical inactivity, and/or high dietary energy intake.

6. Data (variables, time window, source, inclusions/exclusions):

Visit 1 variables: anti-depressant medication use, prevalent diabetes, fasting insulin, smoking status

Visit 2 variables: age, race, gender, body-mass index, waist-to-hip ratio, presence of hypertension, fasting glucose, prevalent diabetes, prevalent CHD, HDL-cholesterol, total triglycerides, systolic blood pressure, diastolic blood pressure, anti-hypertensive medication use, anti-depressant medication use, physical activity score, caloric intake, white blood cell count, heart rate variability (R-R interval), responses to part B of Health and Life Profile Questionnaire, responses to part C of Health and Life Profile Questionnaire

Visits 3 and 4 variables: incident diabetes

Individuals with prevalent diabetes at visits 1 and 2 and individuals missing data on response to parts B and C of the Health and Life Profile Questionnaire will be excluded from analysis.

Analysis Plan: Logistic regression and Cox Proportional Hazards modeling

7.0	a. Will the data be used for non-CVD	analysis in this manuscrint?	Vac		No	
/ .a.	i. Will the data be used for non-CVD	analysis in this manuscript:	1 es	X	_ 110	
b. If Yes, is the author aware that the file ICTDER02 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? Yes No (This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)						
8.a.	a. Will the DNA data be used in this n	nanuscript?	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 ICTDER02 must be used to exclude those with value RES_DNA = "No use/storage DNA"? Yes No						
Reference List						
(Talbot F, Nouwen A. A review of the relationship between depression and diabetes in adults: is there a link? Diabetes Care 2000; 23(10):1556-1562.				
(2	· / · · · · · · · · · · · · · · · · · ·	Gary TL, Crum RM, Cooper-Patrick L, Ford D, Brancati FL. Depressive symptoms and metabolic control in African-Americans with type 2 diabetes. Diabetes Care 2000; 23(1):23-29.				
(.		Lustman PJ, Griffith LS, Clouse RE. Depression in adults with diabetes. Results of 5-yr follow-up study. Diabetes Care 1988; 11(8):605-612.				
(4		Eaton WW, Armenian H, Gallo J, Pratt L, Ford DE. Depression and risk for onset of type II diabetes. A prospective population-based study. Diabetes Care 1996; 19(10):1097-1102.				
(:		Kawakami N, Takatsuka N, Shimizu H, Ishibashi H. Depressive symptoms and occurrence of type 2 diabetes among Japanese men. Diabetes Care 1999; 22(7):1071-1076.				
((between depressive symptoms and	Grandinetti A, Kaholokula JK, Crabbe KM, Kenui CK, Chen R, Chang HK. Relationship between depressive symptoms and diabetes among native Hawaiians. Psychoneuroendocrinology 2000; 25(3):239-246.				
((7) Nathan RS, Sachar EJ, Asnis GM,	Halbreich U, Halpern FS. Relativ	ve insulin in	sensit	ivity	

- and cortisol secretion in depressed patients. Psychiatry Res 1981; 4(3):291-300.

 (8) Winokur A, Maislin G, Phillips JL, Amsterdam JD. Insulin resistance after oral glucose
- tolerance testing in patients with major depression. Am J Psychiatry 1988; 145(3):325-330.
- (9) Hippisley-Cox J, Fielding K, Pringle M. Depression as a risk factor for ischaemic heart disease in men: population based case-control study. BMJ 1998; 316(7146):1714-1719.

- (10) Ariyo AA, Haan M, Tangen CM, Rutledge JC, Cushman M, Dobs A et al. Depressive symptoms and risks of coronary heart disease and mortality in elderly Americans. Circulation 2000; 102(15):1773-1779.
- (11) Jonas BS, Mussolino ME. Symptoms of depression as a prospective risk factor for stroke. Psychosom Med 2000; 62(4):463-471.
- (12) Everson SA, Roberts RE, Goldberg DE, Kaplan GA. Depressive symptoms and increased risk of stroke mortality over a 29- year period. Arch Intern Med 1998; 158(10):1133-1138.
- (13) Williams JE, Paton CC, Siegler IC, Eigenbrodt ML, Nieto FJ, Tyroler HA. Anger proneness predicts coronary heart disease risk: prospective analysis from the atherosclerosis risk in communities (ARIC) study. Circulation 2000; 101(17):2034-2039.
- (14) Appels A, Mulder P. Excess fatigue as a precursor of myocardial infarction. Eur Heart J 1988; 9(7):758-764.
- (15) Cole SR, Kawachi I, Sesso HD, Paffenbarger RS, Lee IM. Sense of exhaustion and coronary heart disease among college alumni. Am J Cardiol 1999; 84(12):1401-1405.
- (16) Stern MP. Diabetes and cardiovascular disease. The "common soil" hypothesis. Diabetes 1995; 44(4):369-374.