ARIC Manuscript Proposal # 923r

PC Reviewed: 06/09/04	**Status: __A__**	**Priority: __2__**
SC Reviewed: _07/01/04___	**Status: _____**	**Priority: _____**

1.a. Full Title: Differences in Cardiovascular Risk Factor Profiles, Subclinical Atherosclerosis, and Incident CHD Between Impaired Fasting Glucose and Impaired Glucose Tolerance.

b. Abbreviated Title (Length 26 characters): IGT vs. IFG and CVD Risk

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

Lead: David Kwan

Writing group members: James Pankow
Bruce Duncan
Maria Ines Schmidt
David Couper
Sherita Golden
Christie Ballantyne

3. Timeline:

Begin analysis: March 2003
Manuscript: July 2004

4. Rationale:

Recent changes in the diagnosis of diabetes have initiated substantial debate over the appropriate criteria for type 2 diabetes. In 1997 the American Diabetes Association recommended the criteria for diabetes as a fasting serum glucose > 7.0 mmol/l (126 mg/dl). The recommendations also introduced a new category of diagnosis, referred to as impaired fasting glucose (IFG), determined as a fasting glucose ≥ 6.1 mmol/l (110 mg/dl) and < 7.0 mmol/l. The recommended cutpoint for IFG was recently lowered to 5.6 mmol/l (100 mg/dl). In contrast, the World Health Organization (WHO) released their criteria in 1999 to consist of both a fasting serum glucose > 7.0 mmol/l and a postload glucose level of > 11.1 mmol/l (200 mg/dl) after a 75 g oral glucose load. Similar to the impaired fasting glucose category, a category of impaired glucose tolerance (IGT) – a serum glucose post-load of ≥ 7.8 mmol/l (140 mg/dl) and < 11.1 mmol/l – has been identified as a group at increased risk of becoming diabetic.

Several studies have indicated considerable differences in the persons identified impaired by the oral glucose tolerance test (OGTT) and the fasting plasma glucose (FPG). The DECODE-study group indicated that 31% of the population from 17 European studies would not be identified as diabetic according to FPG alone. Eschwège et al. found higher all-cause mortality among men with isolated IGT (with normal FPG) than men with normal fasting glucose (NFG) and IFG in

the Paris Prospective Study cohort. Men with IGT were found to be significantly heavier, had higher systolic blood pressure, and higher fasting as well as 2-hour insulin level.

The populations characterized with isolated IFG or isolated IGT are considered to have very different traits and risk of development of atherosclerosis and other subclinical cardiovascular diseases, macrovascular as well as microvascular. The development of type 2 diabetes is also believed to be different between IFG and IGT, where IFG is considered by some to result from impaired beta cell function while IGT arises from insulin resistance. This study intends to characterize the differences between individuals with isolated IFG, isolated IGT, and with both IFG and IGT, in the ARIC cohort. In view of past investigations, we anticipate individuals with both IFG and IGT to have the poorest cardiovascular risk profile – higher waist circumference, BMI, triglycerides, blood pressure, insulin, and lower HDL – followed by individuals with isolated IGT and those with isolated IFG, in such order. We believe these subgroup populations have considerably different cardiovascular profiles, in atherosclerosis development and associated risk factors, and incident CHD.

Note: With the availability of cohort incidence data through 2001, there are 264 post-visit 4 incident CHD events over an average of 4.3 years of follow-up (cumulative incidence = 4%) among subjects who completed the OGTT at visit 4 and did not have diabetes or a history of cardiovascular disease at the time of the visit 4 exam.

References:

Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 23 Suppl 1:S4-19, 2000 Jan.

World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Geneva, Switzerland: World Health Organization; 1999. Publication WHO/NCD/NCS/99.2

[No authors listed]. Is fasting glucose sufficient to define diabetes? Epidemiological data from 20 European studies. The DECODE-study group. European Diabetes Epidemiology Group. Diabetes Epidemiology: Collaborative analysis of Diagnostic Criteria in Europe. Diabetologia. 42(6):647-54, 1999 Jun.

Eschwege E. Charles MA. Simon D. Thibult N. Balkau B. From policemen to policies: what is the future for 2-h glucose? The Kelly West Lecture, 2000. Diabetes Care. 24(11):1945-50, 2001 Nov.

Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care. 26(11): 3160-3167.

5. Main Hypothesis/Study Questions:

Fasting serum glucose and the 2-hour glucose from the oral glucose tolerance test are associated with different risk factor profiles for atherosclerosis,subclinical cardiovascular disease, and incident CHD.

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

Both fasting glucose and oral glucose tolerance test were measured during visit 4, which confines this study to cross-sectional investigation among participants who have attended visit 4. Individuals with diagnosis of diabetes prior to visit 4 will be excluded. Measurements of cardiovascular profile will cover blood pressure, ankle-brachial index (ABI), carotid artery intimal-medial thickness (IMT) or presence of arterial plaque(s), transient ischemic attacks (TIA)

or strokes, ECG/LVH, and retinal exam. Serum or plasma measurements include white blood cell and platelet count, triglycerides, total cholesterol, HDL, LDL, creatinine, and insulin. Apolipoprotein B, which was measure at the baseline visit, will also be of interest. Other risk factors of interest include alcohol consumption, smoking status, menopause, hormone replacement therapy (HRT), body-mass index, waist circumference, and socioeconomic status (SES). Outcome data will also include incident CHD status and follow-up time as of 2001 from the cohort surveillance dataset.

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

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. 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 ICTDER02 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://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html

___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)?

Manuscript Proposal #545: Duncan B. Baseline characteristics and clinical course of cardio-vascular disease in individuals with impaired fasting glucose.