1.a. Full Title: The Modifiable Effect of Diabetes on the Female Advantage in Coronary Heart Disease.

b. Abbreviated Title (Length 26 characters): Diabetes & the Female Advantage

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

   Lead: Hui Han, MD.
   Address: Jackson Heart Study
            350 West Woodrow Wilson Drive, Suite 701
            Jackson, MS 39213

   Phone: 601-368-4650
   Fax: 601-368-4651
   E-mail: hhan2@medicine.umsmed.edu

   Writing group members: Bobby Clark, Herman Taylor, Jr., Evelyn Walker, Jun Pan, Gail Hughes.

3. Timeline:

   Submit proposal to Publications Committee          Dec 2003
   Statistical analysis                               August 2004
   Submit first draft of manuscript to Publications Committee    August 2005

4. Rationale:

   A distinctive male disadvantage for coronary heart disease incidence has been observed in affluent countries. A number of prospective studies have demonstrated that male gender is a strong risk factor for developing coronary heart disease. Several studies have investigated the cause of this disparity, and what factors contribute to this female advantage. Diabetes is one of the widely accepted risk factors that reduces this female advantage, that is, diabetic women tend to have similar risk to diabetic men. However, there is conflicting results from different studies on what contributes to it. Other factors, however, remains being argued, which include low-estrogen, dyslipidemia, smoking, and hypertension.
The ARIC population provides chances to evaluate the relationship between diabetes and female advantage in incident CHD events. There are 850 CHD events during the 13 year follow up, 236 from diabetic and 609 from non-diabetic population. This made it possible to investigate to what extent does the diabetes influence the gender difference in incident CHD events, also the interaction of this influence and other risk factors.

5. **Main Hypothesis/Study Questions:**

1) Firstly, this study will describe the gender difference in the onset of first cardiovascular events in diabetic and non-diabetic population. It is hypothesized that in the non-diabetic population, women outlive men and experience fewer cardiovascular events. By middle age, women generally lag 20 years behind men in the incidence of myocardial infarction. But in diabetic population, this gap is much closer.

2) Secondly, this study will document the relationship between the diabetes and female advantage in the cumulative incidence of cardiovascular events. It is hypothesized that diabetic status attenuates or even reverses the female advantage. In the diabetic population, the relative risk of male to female in coronary heart disease event is significantly reduced compared to the relative risk in non-diabetic population. Diabetes has a bigger impact in women than in men for the risk of experiencing coronary heart disease events.

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

Baseline data (1986-1989) and the 15-year cumulative surveillance data (1986-2000) will be used. Variables of interest include incident coronary heart disease till 2000 (myocardial infarction, fatal CHD), gender, diabetic status, covariates that are associated with CHD risks including age, body mass index, waist-to-hip ratio, hypertension, triglycerol, LDL, HDL, physical activity, female menopause status, hormone replacement therapy.

Cox proportional hazard model will be used for the analysis. The population will be divided into diabetics (defined by fasting plasma glucose ≥ 126 mg/dl) and non-diabetics. The male to female relative risk of developing coronary heart disease will be examined in both populations and compared.

**Key words: diabetics, incident CHD events, female advantage**

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  x 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)?

There are some existing proposals covering the topic of diabetes, but so far no proposals have
mentioned about the effect of diabetes and female advantage on cardiovascular risks yet.
Therefore, there is no direct overlap between this proposal and the existing ARIC proposals.

Here are the most related proposals for diabetes:
MS # 252  Correlates of prevalent diabetes by race
MS #545  Baseline clinical characteristics and clinical course of cardiovascular disease in
individuals with impaired fasting glucose.
MS #528  Is diabetes an independent risk factor for mortality after MI?
MS # 607  Risk factors for CHD incidence among diabetes.
MS #217  Risk advancement : examples from ARIC

11. 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:

1. Barrett-Connor E et al. Why is diabetes mellitus a stronger risk factor for fatal ischemic heart

2. Barrett-Connor E et al. Sex differential in ischemic heart disease mortality in diabetics: a

3. Orchard TJ et al. The impact of gender and general risk factors on the occurrence of
atherosclerotic vascular disease in non-insulin-dependent diabetes mellitus. Annals of


