Manuscript #607

1. Title: Risk Factors for CHD Incidence Among Diabetics
   Abbreviated Title: CHD Risk Factors: Diabetes

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3 Timeline:

4. Rationale:
   Few population-based studies have examined nontraditional risk factors for CHD among people with diabetes. Using the new definition of diabetes (fasting glucose > 126 mg/dL) we have determined there are over 1,600 diabetics at baseline, in whom 176 have developed CHD (MI, fatal CHD, silent MI or procedures) by 1995. With 1996 closure, we believe we can address our hypotheses. (Note that this does not overlap with ARIC Ms. #546, on subclinical disease predictors and CHD in diabetes, which was deferred apparently because of sample size.)

1. Estimates of intake at baseline from foods and supplements (est 1987-89 intake using supplement type and duration variables gathered at visit 3.
   A. minerals: magnesium
   B. vitamins: vitamin C, Vitamin E
   C. servings of: fruit, vegs, nuts & whole grain
2. Estimates (above of food and nutrient intake at Visit 3 (to assess diet stability)
3. Years of supplement use: A. multivitamins, any supplement providing Vit C, Vit E (these variables are derived by the research team of J Mares-Perlman from supplement data collected at V 1-3).
4. Blood values at baseline and follow-up visits: magnesium
5. Other variables to evaluate as explanatory variables, confounders or effect modifiers:
   A. Serum values form Visit 1: glucose, insulin, triglycerides, HDL, and LDL cholesterol, ultrasonographically determined carotid wall thickness, history of cigarette smoking (never, past, current), numbers of cigarettes/day, avg weekly intake of alcoholic beverages (beer, wine, hard liquor), history of past
heavy drinking, education, income, race, gender, height, weight, body mass index, waist to hip ratio, physical activity, systolic and diastolic blood pressure measurements, history of hypertension, history of diabetes with insulin use, history of diabetes without insulin use, use of diabetic diet and years on diabetic diet.

Analyses and Statistical Power: Logistic regression will be used to evaluate relationships of nutritional variables to early renal disease. The main outcome measure to reflect early renal disease will be a change in serum creatinine of 0.4 mg/dL between Visit 1 and 4 (after correcting for any analytic drift in creatinine values and excluding persons with baseline serum creatinine values of over 1.5 mg/L). Based on incidence of serum creatinine between visit one and two, we estimate 180 people to have developed an increase in serum creatinine of this magnitude between visits one and four. This will result in the ability to detect odds ratios of 1.5 among people in high or low quintiles versus all other quintiles for dietary macronutrients and micronutrients at 80% power. The power to detect statistically significant odds ratios between high and low quintiles is somewhat less (1.75). If values for microalbuminuria become available, relationships of diet to this separate indicator of early diabetic nephropathy may be explored, as well.

5. Main Hypothesis:
Main: new risk factors contribute additionally beyond major risk factors in predicting CHD among diabetics. (Note: New definition is arbitrary and probably will not be used in the paper.)
Ancillary: Observed associations between new risk factors and CHD are different for diabetics and nondiabetics. This inter-action analysis will be underpowered, but will be examined qualitative for completeness.

6. Data:
Includes ARIC V1 participants stratified by diabetes status.
Major risk factors: hypertension, smoking, LDL cholesterol, MBI, physical activity, TG, HDL-C (HDL2, HDL3).
New risk factors: hemostasis variables, Lp(a), apoproteins AI and B, Mg, Cr, albumin, WBC, WHR.
Special considerations: serum glucose and insulin.
Covariates: Sex, age, center, race, diabetes med use, duration of diabetes, consideration will be given to possible race and sex differences, although power will be low.

Analysis, as Woody suggested, could consider diabetes as a time-dependent variable, instead of diabetes at base line. However, covariates are not all available at all visits.