

ARIC MANUSCRIPT PROPOSAL # 686

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1.a Full Title:

The association between weight at birth and risk factors in middle-age associated with the multiple metabolic syndrome: the ARIC Study

1.b Abbreviated Title:

Birthweight and MMS

2. Writing Group (List individuals with lead responsibility first):

Kathryn Rose, Al Tyroler, Catherine Paton, Joe Coresh, Aaron Folsom, Marion Wofford

Contact Information for Lead Author.

Kathryn Rose, Ph.D.
Cardiovascular Disease Group
University of North Carolina at Chapel Hill
137 E. Franklin Street
NationsBank Plaza, Suite 306
Chapel Hill, NC 27514

Phone: (919) 966-1933 Fax: (919) 966-9800

Email: kathy.rose@sph.unc.edu

3. Timeline

Analysis would begin as soon as the proposal is approved. It is anticipated that an abstract would be submitted to a national meeting in the fall and that an initial draft of this manuscript would be ready for review by co-authors by January, 2000.

4. Rationale

The Barker Hypothesis purports that unfavorable fetal exposures in utero (e.g., inadequate fetal nutrition) lead to higher rates of development of chronic diseases in

adulthood (1). In support of this hypothesis, he cites a large number of studies demonstrating inverse associations between infant birth weight and CVD-related outcomes (e.g., 2-5). However, there is considerable debate in the literature as to the plausibility of the Barker hypothesis (e.g., 6,7), and data that supports his hypothesis is often criticized because it comes from ecological studies or has not adequately addressed issues of confounding. Nevertheless, there is a growing body of epidemiologic evidence consistent with this hypothesis. Investigators from the Nurses Health Study reported an independent, inverse association of birth weight, ascertained in adulthood, with nonfatal cardiovascular disease (8), while Swedish investigators recently reported an inverse association of birthweight with fatal CVD (9). Additionally, associations have been demonstrated with type 2 diabetes (10,11) hypertension (12,13), and with the multiple metabolic syndrome (MMS) (14). Moreover, there is some suggestion that associations of birth weight with CVD-related outcomes may be modified by adult obesity status and a familial predisposition to these conditions, with inverse associations being stronger among those who are obese (14) and for diabetes, weaker among those with a positive family history of the condition (15).

Thus, the purpose of the current study will be to examine the association between birth weight, ascertained at visit 4, and the prevalence of hypertension, diabetes, and dyslipidemia, individually, as well as with the clustering of these conditions in the multiple metabolic syndrome (MMS). A unique contribution of using data from the ARIC study is that it includes African-Americans as well as whites and more socioeconomically diverse population than most of the other studies reviewed. The inclusion of African-Americans is of particular interest given consistent reports in the literature of lower birth weights among African-Americans compared to whites.

We recognize that there may be concerns about the validity of retrospectively obtained, self-reported birth weight data. However, several epidemiologic studies (e.g., Nurse's Health Study, Rancho Bernardo Study) have demonstrated an association with similarly obtained retrospective, self-reported birth weight data. Also, in the Nurses Health Study a validation study was conducted and found that self-reported birth weight correlated highly with both maternal report and birth records (16).

5. Main Hypothesis:

There will be an inverse association of low birth weight with levels of SBP, DBP, fasting and challenged glucose levels, LDL cholesterol and triglycerides and a positive association of birth weight with serum HDL cholesterol.

Those with low birth weight will have a higher prevalence of diabetes, hypertension, and dyslipidemia, and a greater occurrence of the MMS.

Inverse associations will be attenuated after controlling for childhood SES.

Inverse associations will be stronger among those with higher levels of indices of (adult) obesity.

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

All analyses will be restricted to the subset of baseline participants who attended the Visit 4 exam, as participants' birth weight was queried only at this exam. Outcome (diabetes, hypertension, dyslipidemia, MMS) and most covariate (BMI, WHR, early childhood education, parental history of CVD-related conditions) data will also be obtained from the Visit 4 examination. Additional covariate data (age, adult level of education and income) will be ascertained from the Visit 1 examination.

Multiple linear regression analysis will be used to examine the association between birth weight and continuous outcomes (SBP, DBP, LDL, HDL, triglycerides, and fasting and challenged glucose). Logistic regression analyses will be used to analyze the association between birth weight and dichotomous outcomes (hypertension, diabetes, dyslipidemia, MMS). Variables considered as potential effect modifiers/ confounders include BMI, waist-hip ratio, age, ethnicity, gender, current and early childhood socioeconomic status, parental history of CVD-related conditions (e.g., diabetes, hypertension, and myocardial infarction).

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