ARIC Manuscript Proposal #2196

PC Reviewed: 8/13/13	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: BMI change and trajectories over 25 years: the relationship between spouse pairs, in the Atherosclerosis in Communities Study

b. Abbreviated Title (Length 26 characters): BMI Trajectories and Spouse Pairs

2. Writing Group:
Writing group members: Laura K. Cobb, Mara McAdams DeMarco, Cheryl Anderson, Mark Woodward, Elizabeth Selvin, Josef Coresh; others welcome [invited Ellen Demerath]

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. LKC **[please confirm with your initials electronically or in writing]**

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3. Timeline: All data for the proposed analyses are currently available. We aim to complete this manuscript within a year of approval

4. Rationale:

The vast majority of epidemiologic studies that have examined the consequences of obesity have measured body mass index (BMI) and, occasionally, other measures of adiposity at a single point in time. However, the trajectory of adiposity over time can have important effects on mortality. For instance, in the elderly, both weight loss and weight gain are associated with higher levels of mortality than weight maintenance. [1,2] While the rise of the obesity epidemic means that younger cohorts are heavier than their older counterparts at every age, on average all cohorts exhibit an age-related rise in weight over time [3,4] until old age, when weight decreases. [5]

Changes in the human environment are the key drivers behind the dramatic rise in obesity over the last thirty years. [6] Spouses by definition share the same home environment and therefore are likely exposed to many of the same obesogenic influences. A recent study looking at the predictors of adult weight gain identified unhealthy diet, low levels of physical activity, quitting smoking, insufficient or too much sleep, and television watching as the key drivers, [7] all of which could plausibly be shared between spouses. Understanding the association of changes in BMI over time between spouses may help to determine the extent of the influence of the home environment on obesity. Further, the effect of even successful lifestyle interventions to reduce weight has been limited and diminishes over time. [8] For married couples, the natural unit of intervention may be the pair rather than the individual.

A number of studies have found an association between the BMI of one spouse and that of the other. [9] However, most studies that explore this spousal relationship are cross-sectional in nature [10,11], making it difficult to know whether similarities are due to assortative mating (where people marry those with similar characteristics) or the shared environment. A few longitudinal studies have begun to tease this apart. Ajslev et al. use BMI at age 13 to show that assortative mating plays a small but increasing role in the similarity of BMI across spouses. [12] Other studies find significant correlations in changes in BMI over time across spouses, suggesting a role for environmental factors. [13] [14] Finally, one study found that spouses of participants randomized to a life-style intervention lose more weight than spouses of participants randomized to the control group. [15]

Only one study [14] has a length of follow-up comparable to that available in ARIC and none look at whether the association between spousal obesity varies by age. As noted above, weight often drops in old age after rising steadily before. More importantly, the relationship between BMI and mortality also varies by age. Unlike at older ages, weight loss in middle age is not associated with mortality.[16] Further, few of the longitudinal studies assess whether sharing behaviors such as diet, physical activity and smoking status would impact the association between spouse's BMI change over time.

The ARIC study enrolled 4,500 spouse pairs ranging in age from 45-64 at baseline (1987- 1989) and followed participants for 25 years. The combination of the long follow up time and the specific part of the life-span captured make this a unique opportunity to understand how spouses' BMI trajectories are related.

5. Main Hypothesis/Study Questions:

The primary aim of this study is to understand whether changes in BMI over time in an individual are associated with changes in BMI over time in their spouse. We plan to include the ~4,500 spouse pairs enrolled in ARIC at baseline, using data from visits 1-5. We hypothesize that there will be a modest association between the change in BMI from one visit to the next in one spouse and the change in BMI in the other spouse, and that this association will attenuate when confounders such as diet, physical activity and socioeconomic status are considered. Further, we hypothesize that the membership of one spouse in a specific BMI trajectory will be associated with the other spouse's membership in that trajectory.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

Study design and population: The primary analysis will be a longitudinal analysis across all five study visits of spouse pairs enrolled in ARIC. Spouse pairs were identified based on their responses at the household enumeration survey prior to enrollment. If participants who were members of the same household both identified themselves as married during enumeration, they were considered to be spouse pairs.

Inclusion and exclusion criteria: This analysis is limited to the ~4,500 spouse pairs with measured height and weight data at baseline. At each subsequent visit, the population included will be those where both members of the spouse pair survived, where measured weight data is available on both, and where the spouses have not subsequently divorced or separated. Spouse pairs where one or both members reports being divorced, separated or widowed after baseline will be considered to be no longer married and will be re-categorized for subsequent visits. Marital status is reported in some of the annual follow up phone calls.

Outcome: We will look at three outcomes of interest. The first two are assessed at each visit: (1) change in BMI since the last visit (based on changing weight since height measured only at visit 1) and (2) change in waist circumference since the last visit. The third, membership in a BMI trajectory latent class, summarizes information from all visit to create a single classification.

Exposure: We will have three primary exposures of interest: (1) change in spouse's BMI since the last visit, (2) change in spouse's waist circumference since the last visit, and (3) spouse's membership in a BMI trajectory latent class.

Other potential variables of interest: We hypothesize that certain attributes of the spouse pair may impact the change in BMI of both spouses, thus confounding the association. The primary analysis will incorporate the characteristics of the person of interest, while sensitivity analyses will use the characteristics of their spouse

- Socioeconomic characteristics: race, education, income, center, occupational status, health insurance

- Physiological characteristics: age, baseline BMI, cancer or other illness that could cause weight loss, CVD, diabetes or other illness that might prompt intentional weight loss
- Behavioral: time varying physical activity, caloric intake, dietary quality, alcohol intake, smoking status, frequency of routine physicals. We will also construct indicator variables to mark pairs as concordant or discordant on these key behavioral characteristics

Potential effect modifiers: We will formally test for effect-modification with age, socio-economic status and indicator of whether spouses were concordant on behavioral characteristics, particularly diet, physical activity and smoking status.

Statistical analysis: To understand the overall pattern of BMI change over time in the population, we will use group based trajectory modeling to break up the study participants into clusters who follow similar patterns of BMI change over time. [17] We will do this both overall and also separately for the men and women to determine whether patterns differ by sex. The next step will assess the cross-sectional association between spouse pairs' BMI at each visit, using linear regression to determine the association between the BMI of the husband and that of the wife.

The primary analysis will use linear mixed effects models to characterize the association of changes in husband's BMI with changes in a wife's BMI and vice versa. The secondary analysis will use dual trajectory modeling to calculate the likelihood of a husband belonging to a specific weight trajectory given the trajectory membership of their wife and vice versa. [17] A sensitivity analysis will assess whether the relationship between trajectories changes when self-reported weight at age 25 is used as the baseline. We will also look at both cross sectional and longitudinal analyses of weight status (normal, overweight, obese). Finally to address the potential that mortality during follow up may bias the results, we propose to conduct a sensitivity analysis where we use inverse probability weighting to weight the sample at each visit so that it resembles the baseline sample.

Limitations: This analysis has a number of limitations, particularly the large time lag between visits four and five and the likelihood that many of the spouse pairs will either have dropped out or have had at least one member die in the interim (we have not yet assessed the number of spouse pairs included in visit 5). However, assuming that the resulting missing data is missing at random, the maximum likelihood approach specified above will be valid. We will also consider sensitivity analyses using the spouse pairs included in the carotid MRI sub-sample, assuming enough pairs were sampled. A further limitation is that the dietary intake data in ARIC is not collected at every visit and only assesses a limited number of foods. Finally, the meaning of BMI in an older population is not as clear.

Potential expansions: To most accurately determine whether spouse pairs remain intact across visits, comparing the addresses of participants at each visit would be needed. In this case, spouse pairs whose addresses no longer match will be considered divorced.

References:

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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 ICTDER03 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 ICTDER 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 ICTDER03 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://www.cscc.unc.edu/ARIC/search.php

___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)?

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____ Yes __X__ No

11.b. If yes, is the proposal
___ A. primarily the result of an ancillary study (list number* _____)
___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12a. 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.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PUBMED Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to Pubmed central.