ARIC Manuscript Proposal #2044

PC Reviewed: 12/11/12	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title:
Does dietary pattern modify the asthma-obesity association? Evaluation of the ARIC Cohort

b. Abbreviated Title (Length 26 characters):
Diet & Asthma-Obesity Link

2. Writing Group:
Writing group members:

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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. Initials: EB

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3. **Timeline**: Begin immediately.

4. **Rationale**:

While there is strong data to suggest that obesity is a risk factor for asthma (asthma prevalence is higher in obese individuals (Ford, 2005), obesity has been shown in some studies to precede asthma onset (Beuther et al, 2007), and treatment of obesity through restricted caloric intake or bariatric surgery has been shown to alleviate asthma (Juel et al, 2012)), the mechanism of this relationship remains unclear (as reviewed in Dixon, 2012). Proposed mechanisms include a derangement in respiratory mechanics, increased inflammation due to cytokine or adipokine release from fat tissue, and dietary differences.

The most recent American Thoracic Society workshop on obesity and asthma concluded that the role of acute and chronic macronutrient intake in the pathophysiology of asthma remains unknown and may be a significant source of oxidative stress in the obese (Dixon et al, 2010). Cross-sectional and longitudinal studies relating individual vitamins (A,C, D, E), minerals (copper, selenium, zinc, magnesium) and dietary components (fatty acids, sodium) to asthma have yielded some mixed results (as reviewed in McKeever and Britton, 2004). Many of these studies focused on individual components of diet rather than dietary patterns or whole foods, which could fail to identify synergistic effects between factors. A recent meta-analysis demonstrated supportive evidence for some of these factors, including fruits and vegetables and a Mediterranean diet, in the prevention of asthma in children (Nurmatov et al, 2010). An additional study of Mediterranean diet and fresh fruit intake demonstrated a positive correlation with improved asthmatic control in adults (Barros et al, 2008). While not all studies show positive results, these correlations bear further investigation as well as careful evaluation of confounders.

Diet is an important, modifiable risk factor that may influence the relationship between asthma and obesity, and would inform design of future interventions aimed at improving asthma prevalence and morbidity. No study that we are aware of has been designed to examine dietary patterns as a modifying or predictive factor in the asthma-obesity relationship as a primary outcome. A study identifying a role for diet in the asthma-obesity link would add a significant piece to the understanding of this association, and prompt further research into the direct mechanisms of this interaction.

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

We hypothesize that less-favorable dietary pattern, independent of obesity, is a predictor of asthma prevalence and morbidity.

To test this hypothesis, we propose to conduct analyses to answer the following questions:

1. What is the cross-sectional relationship between (a) adverse dietary patterns and asthma prevalence and (b) obesity and asthma prevalence? Do these relationships differ by demographic factors such as age, sex, and race?
2. Do adverse dietary patterns modify the relationship between asthma and obesity?
3. What is the cross-sectional relationship between (a) adverse dietary patterns and asthma morbidity and (b) obesity and asthma morbidity. Do these relationships differ by demographic factors such as age, sex, and race?
4. Do adverse dietary patterns modify the relationship between asthma morbidity and obesity?

5. What is the influence of adverse dietary pattern on lung function in asthmatics over time?

If our hypothesis is correct, then this paper should stimulate further research on dietary interventions in asthma and the mechanisms underlying the relationships between asthma, obesity, and diet. It may also inform clinicians on the need for nutritional counseling of asthmatics irrespective of anthropometric measures.

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).

We propose to analyze data on all ARIC participants with complete data on asthma status, pulmonary function, anthropometric measures, and dietary questionnaires.

Regarding measures of asthma/asthma control, we will investigate: (1) asthma prevalence assessed by current, former, never asthma status, assessed at baseline and yearly and (2): asthma morbidity assessed by inhaled corticosteroid use (visits 1-4), hospitalizations (annual followup), and lung function as FEV1, FVC (visits 1, 2, and any available data from visit 5). Measures of obesity will include: BMI (at visits 1,2,3,4), WHR (at visits 1,2,3,4), subscapular and tricep skinfolds (visits 1,2). Dietary data (visits 1 and 3) will be analyzed for intake of nutrients (i.e. vitamins A, C, D, E, fatty acids), food groups, and dietary patterns. Diet patterns such as the Western diet pattern will be derived using principal components analysis or a food score (Steffen et al, 2005; Lutsey et al, 2008). We will consider use of the Mediterranean diet score when data becomes available, and whether may be applied to this population's dietary intake. Other variables of interest include: race, age, sex, smoking status (never, former, current), level of education, family income. These data points can be found at baseline exam and smoking status in yearly follow-up.

We will evaluate data using bivariate and multivariate models. We will include interaction terms to explore effect modification.

7.a. Will the data be used for non-CVD analysis in this manuscript? __x__ Yes ____ 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? __x__ 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)?**

Schanen JG, Iribarren C, Shahar E, Punjabi NM, Rich SS, Sorlie PD, Folsom AR. Asthma and incident cardiovascular disease: the Atherosclerosis Risk in Communities Study. Thorax. 2005 Aug;60(8):633-8.

Steffen LM, Jacobs DR Jr, Stevens J, Shahar E, Carithers T, Folsom AR. Associations of whole-grain, refined-grain, and fruit and vegetable consumption with risks of all-cause mortality and incident coronary artery disease and ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Clin Nutr. 2003 Sep;78(3):383-90.

Nettleton JA, Steffen LM, Loehr LR, Rosamond WD, Folsom AR. Incident heart failure in associated with lower whole-grain intake and greater high-fat dairy and egg intake in the atherosclerosis risk in communities (ARIC) study. Journal of the American Diabetic Association. 2008. 108(11): 1881-1887.

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.

References:

Barros R, Moreira A, Fonseca J et al. Adherence to the Mediterranean diet and fresh fruit intake are associated with improved data control. Allergy. 2008 Jul;63(7):917-23.

Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. Am J Respir Crit Care Med. 2007 Apr 1;175(7):661-6.

Dixon AE. The treatment of asthma in obesity. Expert Rev Respir Med. 2012. 6(3):331-340.

Dixon AE, Holguin F, Sood A, Salome CM, Pratley RE, Beuther DA, Celedón JC, Shore SA; American Thoracic Society Ad Hoc Subcommittee on Obesity and Lung Disease. An official American Thoracic Society Workshop report: obesity and asthma. Proc Am Thorac Soc. 2010 Sep;7(5):325-35.

Ford ES. The epidemiology of obesity and asthma. J All Clin Immunol. 2005.115:897-909.

Juel CT, Ali Z, Nilas L, Ulrik CS. Asthma and obesity: does weight loss improve asthma control? a systematic review. Journal of Asthma and Allergy.2012. 5:21-26.

McKeever TM and Britton J. Diet and Asthma. American Jounal of Respiratory and Critical Care Medicine. 2004. 170: 725-729.

Lutsey PL, Steffen LM, Stevens J. Dietary intake and the development of the metabolic syndrome: the atherosclerosis risk in communities study. Circulation. 2008. 117;754-761.

Nurmatov U, Devereux G, Sheikh A. Nutrients and foods for the primary prevention of asthma and allergy: Systematic review and meta-analysis. J Allergy Clin Immunol. 2010. 127(3):724-733.

Steffen LM, Kroenke CH, Yu X, Pereira MA et al. Associations of plant food, dairy product, and meat intakes with 15-y incidence of elevated blood pressure in young black and white adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Am J Clin Nutr. 2005 Dec;82(6):1169-77.