ARIC Manuscript Proposal # 1698

PC Reviewed: 10/12/10	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Occupation and the prevalence and incidence of respiratory health conditions: the ARIC Study

b. Abbreviated Title (Length 26 characters): Occupation and respiratory health

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

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3. Timeline:
This is an analysis of existing data. We expect to complete the manuscript <18 months after approval.

4. Rationale:

The American Thoracic Society reports that up to 15% of asthma among adults may be due to exposures that occur at work (Balmes et al. 2003). Occupational exposures to respiratory irritants (e.g., ammonia, chlorine, diesel particulates) and sensitizing agents (e.g., isocyanates, flour, latex, plant and animal proteins) can exacerbate symptoms in individuals with pre-existing respiratory health conditions or initiate new symptoms among previously asymptomatic individuals. Cleaning, farming, and painting are among the traditional occupations previously identified in population-based epidemiologic research as having elevated prevalences of asthma (Kogevinas et al. 1999). Recent studies have shown increased risks among men and women working in laboratories and in the health care industry (Delclos et al. 2007; Mirabelli et al. 2007), where the use of disinfecting and cleaning agents is nearly ubiquitous.

Data from the ARIC study provide a unique opportunity to assess associations of these and other occupations with respiratory health in a large, population-based cohort. Information about the prevalence and incidence of respiratory symptoms and conditions across a wide range of occupations will form the basis for longitudinal analyses of ARIC data to evaluate occupational risk of new-onset symptoms among previously asymptomatic individuals, exacerbations of existing symptoms, and progression of lung disease.

5. Main Hypothesis/Study Questions:

There are three main objectives of this proposed paper:
(1) To describe the prevalence of respiratory symptoms (e.g., cough, phlegm, wheeze) and conditions (e.g., asthma, chronic bronchitis, emphysema) within major occupational categories
(2) To assess the incidence of respiratory symptoms and conditions among previously asymptomatic individuals within each of the major occupational categories
(3) To assess changes in lung function among symptomatic and asymptomatic individuals within each of the major occupational categories.

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

The first proposed analysis is a cross-sectional analysis of data collected during visit 1. The proposed analyses of new-onset of symptoms and conditions among previously asymptomatic individuals and of changes in lung function will use data collected during visits 1 and 2.

Inclusion/Exclusion Criteria

Participants with RES_OTH="CVD Research" will be excluded.

Independent Variable (Occupation)

Occupational categories will be created based on baseline self-reported occupation information. Each participant reported his/her current employment status (HOM55), most recent occupation (HOM57), and self-employment status (HOM58). The three variables will be used to construct occupational categories. The primary categorization of occupation will be based on existing categorization of respondents' current/most recent occupations (HOM57) into the 15 broad

occupational groups, which are based on the 1977 Standard Occupational Classification (SOC) coding system and shown in ARIC Manual 2 Visit 1 Appendix III (pp. A18-A24). A list of the full occupational classification system and the broad groupings (p. A25) are included at the end of this proposal. The existing categorization will be modified to include a category of homemakers (HOM55=A) and to ungroup occupations for which there is previous literature suggesting an elevated risk of respiratory disease (Kogevinas et al. 1999; Olivieri et al. 2010). Such occupations include jobs in agriculture and forestry, baking, caretaking, chemical processing, cleaning, electrical processing, healthcare, hairdressing, metalworking, plastics or rubber industries, printing, spray painting, and welding.

A secondary categorization will be considered if the data in job title categories are sufficiently sparse to limit our ability to conduct rigorous analysis. The secondary categorization will be based on the application of an asthma-specific job exposure matrix (asthma JEM) to the data in order to estimate exposure to known respiratory irritants, allergens, and settings (Kennedy et al. 2000). Exposures estimated by the asthma JEM include: high molecular weight agents (antigens from animals, fish, flour, plants, mites, enzymes, latex, bioaerosols, drugs), low molecular weight agents (reactive chemicals, isocyanates, cleaning/disinfecting products, wood, metals), environments with mixed exposures (metalworking, textile, agriculture), high risk of irritant peak exposures, and other respiratory hazards (vehicle exhaust, environmental tobacco smoke, irritant gases or fumes).

Dependent Variables (Respiratory health)
Variables to describe respiratory health will be created using responses to questions from the ARIC Respiratory and Physical Activity (RPA) questionnaire (visit 1) and the ARIC Respiratory Symptoms (RPA) questionnaire (visit 2). Respiratory health outcomes and the questionnaire items on which they are based are shown below; questionnaire items are shown in parentheses as '(visit 1 question/visit 2 question, where applicable).' Questions about physician confirmation of conditions (marked with asterisks) will not be used to create main outcome variables, but may be used in subsequent sensitivity analyses if results generated using the unconfirmed conditions are unexpectedly common. Data about chronic cough, chronic phlegm, and current wheezing will also be combined to assess a 'current symptoms' summary variable.

Additional variables to describe respiratory health will be created using measures of lung function collected using spirometry conducted during the physical examinations at ARIC visits 1 and 2. The measures will be used to assess changes in lung function between visit 1 and 2. The measures are described below.

Chronic cough
"Do you usually cough as much as 4 to 6 times a day, 4 or more days out of the week?" (RPA2/RPA2)

Chronic phlegm
"Do you usually bring up phlegm [from your chest] as much as twice a day, 4 or more days out of the week?" (RPA8/RPA5)

Current wheezing

"Does your chest ever sound wheeze or whistling apart from colds?" (RPA14/RPA8)

Asthma attack
"Have you ever had an attack of wheezing that has made you feel short of breath?" (RPA17/RPA10)

Current chronic bronchitis
"Have you ever had chronic bronchitis?" (RPA27)
"Do you still have it?" (RPA28)
"Was it confirmed by a doctor?" (RPA29)*

Current emphysema
"Have you ever had emphysema?" (RPA31)
"Do you still have it?"(RPA32)
"Was it confirmed by a doctor?" (RPA33)*

Current asthma
"Have you ever had asthma?" (RPA35)
"Was it confirmed by a doctor?" (RPA36)*
"At what age did it start?" (RPA37)
"Do you still have it?" (RPA38)
"At what age did it stop?" (RPA39)

Spirometric measurements
Forced Expiratory Volume in 1 second (FEV_1)
Percent of predicted FEV_1
Forced Vital Capacity (FVC)
Percent of predicted FVC
FEV_1/FVC
Percent of predicted FEV1/FVC

Covariates
Age, childhood asthma, educational attainment, race, sex, smoking status, and ARIC site will be considered as covariates. Childhood asthma will be defined as asthma before the age of 16. Smoking status will be defined as current smoker, former smoker, and lifetime non smoker. Age, ethnicity, height, race, and sex will be used to calculate predicted spirometric values.

Statistical Methods
Using data from ARIC visit 1, the prevalences of each of the respiratory health outcomes will be presented overall and within categories of current employment status and broad occupational grouping (or asthma JEM exposure categories). Binomial regression, specified with a log link, will be used to assess associations between employment status and occupational groupings and respiratory health outcomes. Associations will be presented as prevalence ratios (PRs) with 95% confidence intervals (CIs). The referent category for all models will be the population (N=3,960) with a most recent occupation classified as executive, administrative, and managerial (SOC codes 003-037) or clerical and administrative support (SOC codes 303-389).

Data from ARIC visits 1 and 2 will be combined to assess the incidence of chronic cough, chronic phlegm, wheezing, and attacks of asthma among individuals who did not report these symptoms at ARIC visit 1. The incidence will be presented as a cumulative incidence of symptoms that arose between visits 1 and 2, and were reported at visit 2. Binomial regression will be used to assess associations between employment status and occupational groupings and new-onset of respiratory health outcomes. Associations will be presented as relative risks (RRs) with 95% CIs. In the case that binomial regression models do not fit the data, Poisson regression models, specified with robust error variance, will be considered.

Data from ARIC visits 1 and 2 will also be combined to assess changes in lung function among individuals in each of the occupational categories and among individuals with and without symptoms reported at visit 1. Changes in lung function will be presented as mean (with standard deviation) changes in % predicted FEV_1, % predicted FVC, and % predicted FEV1/FVC.

Limitations

The main limitation to this analysis will be misclassification of exposure, which will be based on occupation, and the resulting error in the attribution of risk based on responses about "most recent occupation." If individuals with respiratory symptoms exited occupations that are at high risk for inhalation exposures at a higher rate than individuals without respiratory symptoms, then occupations that are truly high-risk may incorrectly appear to be lower-risk because of the apparently healthy workforce (i.e., the healthy worker effect). This effect is expected to be less than what would occur in a workforce-based study, therefore while it is a limitation of this analysis, it is also a strength of using a general population-based cohort to assess respiratory health effects of occupational exposures.

A second limitation of the analysis is the absence of a measure of atopic status. Individuals with atopy may be more likely to have asthma-like symptoms following exposures to allergens such as those that occur among people who work with animals, foods, latex, mites, plants, or other similar agents. Without information about atopic status, the results will not be used to draw conclusions about allergic versus irritant asthma-like symptoms.

A third limitation of this analysis is that a long list of other factors affecting respiratory health will not be considered here. The potential for family history, medication use, pets and other household exposures, and ambient air quality to affect respiratory health will be acknowledged.

References

Balmes J, Becklake M, Blanc P, et al. American Thoracic Society Statement: Occupational contribution to the burden of airway disease. Am J Respir Crit Care Med 2003;167 (5):787-97.

Delclos GL, Gimeno D, Arif AA, et al. Occupational risk factors and asthma among health care professionals. Am J Respir Crit Care Med 2007;175 (7):667-75.

Kennedy SM, Le Moual N, Choudat D, Kauffmann F. Development of an asthma –specific job exposure matrix and its application in the French epidemiological study of the genetics and environment of asthma (EGEA). Occupational and Environmental Medicine 2000; 57: 635-41.

Kogevinas M, Anto JM, Sunyer J, et al. Occupational asthma in Europe and other industrialised areas: a population-based study. Lancet 1999;353 (9166):1750-4.

Mirabelli MC, Zock JP, Plana E, et al. Occupational risk factors for asthma among nurses and related healthcare professionals in an international study. Occup Environ Med 2007;64:474-9.

Olivieri M, Mirabelli MC, Plana E, et al. The healthy hire effect, job selection and inhalation exposure among young adults with asthma. Eur Resp J 2010; 36(3):517-23.

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 ICTDER03 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)?**

There are currently no related manuscript proposals in ARIC.

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/

12. 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.