1.a. Full title: Low lung function, lung function decline, and hospitalizations in the Atherosclerosis Risk in Communities Study

1.b. Abbreviated title: Lung function decline and outcomes

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3. Time line:
The data to do this basic analysis has already been collected. A draft manuscript will be distributed for internal circulation by May 2003. A secondary goal of this analysis would be to provide the basis for a separate proposal that would look at genetic factors that may predict both low lung function and rapid decline in lung function.

4. Rationale:
The diagnosis of obstructive lung disease has traditionally depended on the presence of symptoms, such as chronic cough or chronic sputum production. (1) New international guidelines for the diagnosis of obstructive lung disease, however, use spirometrically determined measurements of lung function to define mild, moderate and severe obstructive lung disease. (2) COPD has been long recognized as a heterogenous disorder or group
of disorders, with the components of asthma, chronic bronchitis, emphysema, and airflow obstruction all being important parts of the final disease process. Different components of disease heterogeneity in COPD include different mechanisms in development, presentation, and course.

Smoking is the primary risk factor for the development and progression of COPD; however, fewer than 25% of smokers develop COPD, and about 15% of COPD related mortality occurs in never-smokers, suggesting that other factors are important. Smoking cessation is the single most important intervention in COPD management, although the best reported cessation rates are still less than 30%, indicating that better treatments for smoking cessation are needed. Alpha 1-antitrypsin deficiency is an important cause of COPD in a very small percentage of cases. Other undefined genetic factors certainly play an important role in COPD development. The role of infections in both the development and progression of COPD is receiving increased attention, including the role of adenoviral infections in emphysema and the role of intracellular infections in asthma. Occupation and environmental exposures to various pollutants are also important factors in the development of COPD.

We propose a study which would apply the current criteria for COPD diagnosis to data collected at visits 1 and 2 in the ARIC study to define a cohort of subjects with normal lung function and varying levels of COPD, along with subjects who experienced rapid decline in lung function between visit 1 and visit 2. If there are questions as to the quality of the pulmonary function testing for some individuals, we may have to modify this approach not to look at changes in pulmonary function for those individuals. We would then follow these cohorts through the follow-up period, looking for all subsequent hospitalizations, especially those for lung disease, cardiovascular disease, and looking for mortality. The analysis will use Cox proportional Hazards models. Because the primary focus of this proposal is on hospitalizations, it does not overlap with manuscript proposals 433 or 629.

5. Main Issues/Hypotheses to be addressed:

The extent to which low levels of lung function and rapid decline in lung function predict morbidity related to both COPD and other factors. If we find increased utilization, we would propose a separate up study to determine what genetic factors are associated with lower levels of lung function and rapid decline of lung function in both blacks and whites and among smokers and non-smokers.

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

Baseline demographics, smoking history.
Lung function at visits 1 and 2
Hospitalization screening data for the follow-up period (data base where diagnoses
Mortality data. Any data to document when the subject was last known alive for use in the survival analyses.

The main analytic approach will be to look at hospitalizations (both all cause and focusing on cardiorespiratory causes), controlling for covariates related to lung function and hospitalizations (age, sex, smoking duration and intensity, race, etc.) We may also do a survival analysis with time to hospitalization for any cause or cardiorespiratory disease as our end point. The database is big enough that we may also be able to do stratified analysis (limiting to current/former smokers with > 60 pack years of tobacco use, etc.) We acknowledge that there may be some residual confounding, but also note that this dataset offers a unique opportunity because of its size, with the resulting ability to stratify by some of these potential confounding factors.

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 ICTDER02 must be used to exclude persons with a value RES_OTH = CVD Research for non-DNA analysis, and for DNA analysis RES_DNA = No use/storage DNA would be used?  __X__ Yes  ____ No
(This file ICTDER01 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 ICTDER01 must be used to exclude those with value RES_DNA = No use/storage DNA?  ____ Yes  ____ No
Reference List


