1.a. Full Title:
Symptomatic Chronic Bronchitis and Risk of Diabetes Mellitus: The Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters):
Chronic Bronchitis and DM

2. Writing Group (list individual with lead responsibility first):

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3. Timeline:
   Spring, Summer 2001: Data Analysis
   Summer, Fall 2001: Manuscript Completion

4. Rationale:
   Chronic inflammation has been associated with an increased risk of cardiovascular events in previous research and is thought to play a central role in atherosclerosis (1). Atherosclerosis is more common among persons with diabetes mellitus, which may be partially attributed to the “common soil” hypothesis that has identified similar risk factors for diabetes mellitus and cardiovascular disease (2-3). Accordingly, the identification of an inflammatory role in atherosclerosis has spurred investigation of an inflammatory role in the development of diabetes mellitus. Pro-inflammatory cytokines, such as tumor necrosis factor-α and interleukin-6, have been shown to be elevated in adipose tissue and to play a role in metabolic syndrome X, a predictor of diabetes mellitus (4-5). In addition, other inflammatory markers such as leukocytes, serum albumin, fibrinogen, and factor VIII have been significantly associated with the development of diabetes mellitus (6-7).

   Chronic bronchitis, characterized by inflammation and chronic infection, has been identified as an independent risk factor for coronary disease (8) and chronic productive coughs, characteristic of chronic bronchitis, have been associated with increased risk for myocardial infarction (9). These preliminary associations are intriguing and suggest further research into chronic respiratory infections and risk of cardiovascular disease and diabetes mellitus is warranted. Accordingly, the aim of this proposal is to investigate the relationship of symptoms of chronic bronchitis with risk of diabetes mellitus, which has not been reported in the literature.
5. **Main Hypothesis/Study Questions:**
   1. Is symptomatic chronic bronchitis associated with increased risk of incident diabetes mellitus?
   2. Is symptomatic chronic bronchitis associated with increased risk of incident impaired fasting glucose (IFG) levels?
   3. Is symptomatic chronic bronchitis associated with increased risk of incident impaired glucose tolerance (IGT)?

6. **Data (variables, time window, source, inclusions/exclusions):**
   Persons with diabetes at baseline will be excluded from the analysis. Variables from ARIC visits 1-4 will be used for the analysis. The variables include the following: amha1, bmi01, center, chmb07, chmx07, cigt01, diabts03, diabts23, diabts34, diabts42, drnkr01, elel01, elel02, fev1fvc1, fev3fvc1, gender, hhxb05d, hom62, hom10e, hom15b, hom23b, id, lipa01, lipa02, lipc4a, lipx03, lismr01, mrsra0sf, mrsrb24f, msrc24g, msrc24g, phxb6c, racegrp, rpa07, rpa08, rpa11, rpa12, rpa27, rpa28, rpa29, rpa30, sbpa21, sbpa22, sprt_i02, v1age01, v1date01, v2age22, v2date21, v3age31, v3date31, v4age41, v4date41, work_i02, wsthpr01, baseline insulin, trig, hdl-c, and v4-2h glucose. Additional variables may be added at a later time upon further investigation.

   The primary exposure is symptomatic chronic bronchitis ascertained from responses to the respiratory symptoms/physical activity form at the baseline ARIC examination. Symptomatic chronic bronchitis is defined by ‘yes’ responses to the following criteria: bringing up phlegm from the chest as much as two times a day for four or more days a week, bringing up phlegm on most days for at least three consecutive months during the year, and two or more years of trouble with phlegm.

   The primary outcome is incident diabetes mellitus determined at visits 2, 3, and 4. Diabetes mellitus is defined as a fasting blood glucose level $\geq 126$ mg/dl, a diagnosis by a physician, or use of hypoglycemic medication. An additional outcome is impaired fasting glucose (IFG) level determined at visits 2, 3, and 4. IFG is defined as a fasting blood glucose level $\geq 110$ and $< 126$ mg/dl. Impaired glucose tolerance is defined as non-diabetic but a two-hour glucose level $\geq 140$ mg/dl detected at visit 4. The covariates, collected at the baseline ARIC examination, are center, gender, race, education level, body mass index, waist-to-hip ratio, hypertension status, triglycerides, HDL cholesterol, fasting insulin, smoking status, drinker status, parental history of diabetes mellitus, and physical activity level.
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 ICTDER01 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 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

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://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html

_____ Yes  ________ No

References:


