ARIC Manuscript Proposal # 1541

PC Reviewed: 8/11/09	Status: A	Priority: 2
SC Reviewed: _____	Status: _____	Priority: ____

1.a. **Full Title**: Reliability and validity of self-reported gout in the Campaign Against Cancer and Heart Disease (CLUE II) Cohort and Atherosclerosis Risk in The Community (ARIC)

b. Abbreviated Title (Length 26 characters): Self-reported gout validity

2. **Writing Group**:
Writing group members: Mara McAdams, Janet Maynard, Anna Kottgen, Sandy Clipp, Alan Baer, Allan Gelber, Josef Coresh, Others welcome.

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

First author: Mara McAdams, MS
Address: 615 North Wolfe St, W6017
Baltimore, MD 21205

Phone: (973) 943-1967 Fax: none
E-mail: mmcadams@jhsph.edu

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
Name: Josef Coresh, MD, PhD
Address: Welch Center for Prevention, Epidemiology & Clinical Research
2024 E. Monument St., Suite 2-600
Baltimore, MD 21287

Phone: (410) 245-0495 Fax: (410) 955-0476
E-mail: coresh@jhu.edu

3. **Timeline**: Data analysis to start after approval of this manuscript proposal, first draft available by August, 2009

4. **Rationale**:

Gout is a major cause of arthritis in the United States and the prevalence is increasing worldwide (1). In the United States, 6.1 million adults have a diagnosis of gout (1). Its risk factors have been partially established from large epidemiological studies. However, many of these epidemiologic studies have used self-report to identify gout cases, which may lead to misclassification. An important component of gout research is determining the reliability and validity of self-reported gout from cohort studies. Reliability refers to the ability of participants to consistently self-report their gout status on multiple questionnaires or at multiple visits. Validity refers to the ability of participants to correctly self-report their gout status.

The validity of a diagnosis of gout has been evaluated in a study of administrative claims data (2). However, claims data do not include self-reported medical history and often lack detailed medical information about potential risk factors, such as body mass index. Two population-based studies have evaluated the reliability or agreement of self-reported gout in cohort studies (3,4). One study evaluated the six-month reliability (test-retest reliability) of self-reported gout in the Dutch population aged 25 years and older (3). The authors found that 64% of participants self-reported gout after six months and the kappa value for reliability was 0.64. A second study in the Potsdam component of the European Prospective Study into Cancer and Nutrition (EPIC) cohort evaluated the agreement between self-reported gout obtained in an interview and on a questionnaire approximately 2 years apart (4). The two-year reliability was 45% (kappa=0.61). However, these studies were not performed in the US and did not assess the long-term reliability of self-reported gout.

Both community-based and population-based cohorts are a valuable data source for epidemiologic studies of gout. However, the reliability and validity of self-reported gout over extended follow-up has not been previously published. Understanding the risk factors for the development of gout is critical given its high prevalence. However, in US cohorts the reliability and validity of self-reported gout over long-term follow-up are unclear. The Atherosclerosis Risk in Communities Study (ARIC) provides a valuable sample of participants with self-reported gout. Additionally, this population-based cohort records information on prescription drug use and hospital discharge diagnoses.

We propose to assess the reliability and validity of self-reported gout over long-term follow-up. The reliability of self-reported gout will be estimated using Campaign Against Cancer and Heart Disease (CLUE II) data. This dataset asks participants to self-report gout on three follow-up questionnaires. In contrast, ARIC collects prescription drug use and hospitalization discharge diagnoses, which can be used as a potential "gold standard" to assess the validity of self-reported gout. Together, these two cohorts will be used to estimate the reliability and validity of self-reported gout. This proposal will focus on the study hypothesis, data needs, and analysis for the validity study in ARIC.

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

Primary study questions for the ARIC component of this study:

1. In the ARIC study, what is the validity of self-reported gout?
2. Does the validity of gout vary by race or sex?

Secondary study questions:

1. When a history of gout medication use is considered the gold standard, what is the validity of self-reported gout?
2. When a history of hospitalization for gout is considered the gold standard, what is the validity of self-reported gout?
3. What percentage of patients with self-reported gout have a history of hyperuricemia at either visit 1 or visit 2?

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:

1. Validation study

Inclusion/Exclusion: All study participants must have self-reported their gout status at visit 4.

Outcome: We will be assessing the validity of self-reported gout at visit 4.

Other variables of interest: The gold standard of gout classification will be either: 1) a prescription for a gout drug at any visit, 2) hospitalization with a discharge diagnosis that includes gout. The hospital surveillance definition of gout is defined as a hospital discharge summary revealing an ICD-9 code for gout (ICD-9 codes 274.0, 274.1, 274.8, and 274.9, Table 1). The hospitalization must occur prior to the date of the visit 4 follow-up to be considered in this analysis. Additionally, if a patient was taking a medication used exclusively to treat gout (Table 2), including allopurinol, colchicine, or probenecid at any study visit then they were defined as a prescription identified gout case. If a patient met either the hospitalization or prescription definition of gout, then that participant was considered to be a gold standard case of gout.

Data analysis

Primary analysis: Our study focused on gout cases identified prior to visit 4 with either a hospitalization for gout or a gout medication. The ARIC participants without a hospitalization for gout or prescription for a gout medication may still have gout. Therefore, our study focused on those participants who were identified as having the gold standard definition of gout.

We will calculate the sensitivity of self-reported gout as a measure of validity. The sensitivity is defined as the number of participants with a gold standard definition of gout who self-reported gout at Visit 4 divided by the total number of participants with a gold standard definition of gout who attended Visit 4. Additionally, we will calculate the reliability stratified by sex and race.

Secondary analyses: In sensitivity analyses, we will investigate whether the sensitivity differs by gold standard definition of gout. We will separately calculate the sensitivity for those participants who had a hospitalization for gout prior to visit 4 and for those with a prescription for a gout medication at any visit.

To support the validity of self-reported gout analysis, we will evaluate the number of participants with self-reported gout who were hyperuricemic at either visit 1 or visit 2. All patients with self-reported gout will be included in this analysis. We will define hyperuricemia as mean serum urate greater than 7.0 mg/dL at either visit 1 or 2, for those participants without a prescription for a gout drug at the visit. We will calculate the percentage of all self-reported gout patients who are hyperuricemic at either visit 1 or 2.

Limitations: The gold standard case definition of gout was based on hospitalization and prescription data rather than being defined by aspiration of monosodium urate crystals from affected joint fluid. It is unlikely that aspirations on all participants in a cohort study will ever be performed.

Not all ARIC participants who have gout will be hospitalized or be taking a prescription for gout. Therefore, our gold standard definition of gout will likely exclude milder cases. However, we will be focusing on the sensitivity of self-reported gout. Additionally, we cannot assess the specificity of self-reported gout since we have no gold standard definition for non-gout cases.

The percentage of self-reported gout patients with hyperuricemia at a study visit will support our validity analysis but cannot be used as a measure of validity. Patients with self-reported gout may have had their first gout attack many years prior to either visit 1 or visit 2 and have adequately

managed uric acid. Additionally, not all patients with hyperuricemia will develop gout. Therefore, the percentage of hyperuricemic patients with self-reported gout would be meaningless with respect to the validity of self-reported gout.

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 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)? CANT LOG ON –NEED TO CHECK

1. #759 - Serum uric acid and risk of stroke: the ARIC study; published
2. #1077r - Uric Acid and Hypertension; published
3. #1229 - Uric Acid & Metabolic Syndrome
4. #1311 - Serum uric acid, lung function and chronic obstructive pulmonary disease in adults
5. #525 1. Elevated uric acid as a risk factor for coronary heart disease: the ARIC study; published
6. #313 1. Association between serum uric acid and asymptomatic carotid atherosclerosis: the ARIC study; published

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)* albuminuria, AS#_2002.02_)

*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.

Table 1. Ambulatory diagnostic codes of interest used to identify gout cases

Diagnosis	ICD-9 codes
Gout	274
Gout with other specified manifestations	274.8x
Gouty nephropathy	274.1x
Gout, unspecified	274.9
Gouty arthropathy	274.0
Special screening for Gout	V77.5

Table 2. Prescription drug codes

Drug	Visit	Codes
Gout drugs	1-4	"680000"="GOUT" "681000"="URICOSURICS" "689900"="COMBINATION GOUT DRUGS"

References:

1. Lawrence RC, Felson DT, Helmick CG, Anrold LM, Choi H, Deyo RA, Gabriel S, Hirsch R, Hochberg MC, Hunder GG, Jordan JM, Katz JN, Kremers HM, Wolfe F. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: Part II. Arthritis Rheum 2008; 58:26-35.
2. Harrold LR, Saag KG, Yood RA, Mikuls TR, Andrade SE, Fouayzi H, Davis J, Chan KA, Raebel MA, Von Worley A, Platt R. Validity of gout diagnosis in administrative claims. Arthritis Care & Res 2007; 57: 103-108.
3. Picavet HSJ, Hazes JMW. Prevalence of self-reported musculoskeletal diseases is high. Ann Rheum Dis 2003; 62: 644-650.
4. Berggman MM, Jacobs EJ, Hoffmann K, Boeing H. Agreement of self-reported medical history: Comparison of an in-person interview with a self-administered questionnaire. Eur J Epi 2004; 19: 411-416.