ARIC Manuscript Proposal # 1479

PC Reviewed: 03/17/09	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: CRP and Venous Thromboembolism Incidence

b. Abbreviated Title (Length 26 characters): CRP and VTE

2. Writing Group:
Writing group members: Aaron Folsom, Pam Lutsey, Brad Astor, Mary Cushman

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

First author:
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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:
Address:

Phone: Fax:
E-mail:

3. Timeline: finish by July 09

4. Rationale:
Inflammation is generally not believed to be important in the etiology of venous thromboembolism (VTE), and most (2,3,7) but not all studies (5) have found no independent association of VTE with CRP or with CRP polymorphisms (1,4). We also found no association of CRP with VTE in a previous LITE nested case control study (6).

The recent addition of CRP to the ARIC visit 4 measurements allows us to re-test this hypothesis. There are over 260 VTE events in ARIC since visit 4, which will provide adequate power for detecting a moderate association. This likely will be a letter or brief report.

5. Main Hypothesis/Study Questions:

CRP at visit 4 is associated positively with incidence of VTE. We expect any univariate association may be explained by obesity.

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).

Design: cohort
Endpoint: VTE incidence
Exposure: visit 4 CRP
Main covariates: age, race, sex, center, BMI
Analysis: Cox proportional hazards, with CRP modeled as a continuous variable and as quartiles. Also look at high (e.g. >90%) CRP vs. low.

REFERENCES

1: Vormittag R, Funk M, Mannhalter C, Schönauer V, Vukovich T, Minar E, Bialonczyk C, Hirschl M, Pabinger I. C-reactive protein 3' UTR +1444C>T polymorphism in patients with spontaneous venous thromboembolism. Atherosclerosis. 2006 Oct;188(2):406-11

2: Fox EA, Kahn SR. The relationship between inflammation and venous thrombosis. A systematic review of clinical studies. Thromb Haemost. 2005 Aug;94(2):362-5. Review.

3: Vormittag R, Vukovich T, Schönauer V, Lehr S, Minar E, Bialonczyk C, Hirschl M, Pabinger I. Basal high-sensitivity-C-reactive protein levels in patients with Spontaneous venous thromboembolism. Thromb Haemost. 2005 Mar;93(3):488-93.

4: Zee RY, Hegener HH, Cook NR, Ridker PM. C-reactive protein gene polymorphisms and the risk of venous thromboembolism: a haplotype-based analysis. J Thromb Haemost. 2004 Aug;2(8):1240-3.

5: Kamphuisen PW, Eikenboom JC, Vos HL, Pablo R, Sturk A, Bertina RM, Rosendaal FR. Increased levels of factor VIII and fibrinogen in patients with venous Thrombosis are not caused by acute phase reactions. Thromb Haemost. 1999 May;81(5):680-3.

6: Tsai A, et al. Coagulation factors, inflammation markers, and venous thromboembolism. Am J Med 2002;113:636-42.

7. Ridker PM et al. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1997;336:973-9.

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

8.c. If yes, is the author aware that the participants with RES_DNA = 'not for profit' restriction must be excluded if the data are used by a for profit group?
____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

Other than ref 6, cited above.

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)?

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? __x__ Yes ____ No

11.b. If yes, is the proposal

__x_ A. primarily the result of an ancillary study (list number* __1998.03 and 2006.16__)

___ 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.