

**ARIC Manuscript Proposal # 783**

**PC Reviewed:** 04/04/01  
**SC Reviewed:** \_\_\_\_\_

**Status:** A  
**Status:** \_\_\_\_\_

**Priority:** 1  
**Priority:** \_\_\_\_\_

**1.a. Full Title:** Protein C, Antithrombin III, and Venous Thromboembolism

**b. Abbreviated Title (Length 26 characters):** Protein C, ATIII and VTE

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

**Lead:** Aaron Folsom

Address: U MN

Phone: 612-626-8862

Fax: 612-624-0315

E-mail: folsom@epi.umn.edu

Writing group members: Cushman, Wang, Aleksic, Wu

**3. Timeline:** Analysis at once. Draft summer 2001.

**4. Rationale:** Deficiencies of protein C and antithrombin (ATIII) are important contributors to familial thrombophilia, leading to venous thromboembolism (VTE). Hereditary deficiency is rare, and the population attributable risks are on the order of two percent or less. Nevertheless, no population based prospective studies exist to relate levels of these proteins to the incidence of VTE. It is possible that across the range of these proteins there actually is a graded risk, as suggested by the LETS study for protein C.

**5. Main Hypothesis/Study Questions:** Low levels of protein C and ATIII (<1%ile) are associated with increased risk of venous thromboembolism. Dose-response will be examined also. Inter-relations with V Leiden will be explored if numbers are sufficient.

**6. Data (variables, time window, source, inclusions/exclusions):** ARIC measured levels of protein C and ATIII at baseline, and the VTE ancillary study (LITE) remeasured ATIII.

Dependent variable: VTE collected as part of LITE.

Independent: Protein C, ATIII from baseline ARIC. ATIII from LITE.

Covariates: age, race, sex, BMI, diabetes, factor VIII, vWF, V Leiden

Exclusions: baseline VTE hx, anticoagulation, baseline cancer.

Analysis of ARIC data will use proportional hazards regression; LITE data, logistic.

**7.a. Will the data be used for non-CVD analysis in this manuscript?**     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 = "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     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