

ARIC Manuscript Proposal # 1078

PC Reviewed: 05/13/05

Status: A

Priority: 2

SC Reviewed: 05/13/05

Status: A

Priority: 2

1.a. Full Title: Metabolic Syndrome and Prostate Cancer Incidence

b. Abbreviated Title (Length 26 characters): Metab Syndrome-Prostate Ca

2. Writing Group:

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3. Timeline: to be completed in summer 2005

4. Rationale:

Prostate cancer is the most common cancer in men worldwide. Over the past 30 years, the incidence of prostate cancer has changed dramatically, both within the United States and elsewhere. The change in incidence is complicated, with increasing levels from 1970's to 1992 when it peaked. It has declined and leveled off since then. Although latent prostate cancer rates are the same throughout the world, clinical prostate cancer levels vary widely. This indicates that there is likely a geographic and/or environmental influence on the progression or development of clinically significant prostate cancer. In addition, several risk factors have been linked to prostate cancer development, including age, family history, race, dietary fat, obesity, and blood levels of androgens and insulin-like growth factor-1 (IGF-1). However, many aspects of what leads to the development and progression of prostate cancer remain unknown.

A cluster of conditions known as the Metabolic Syndrome has grown increasingly common in the developed world, with a prevalence of 22% in the adult US population. (Ford 2002) The Metabolic Syndrome is defined by the National Cholesterol Education Program Expert Panel as the three or more of the following: obesity, elevated triglycerides, decreased-high density lipoprotein cholesterol level, elevated blood pressure, and elevated glucose level (Ford 2002). While several of the components of the Metabolic Syndrome (namely obesity (Andersson 1997), insulin resistance (Hsing 2003), and hyperglycemia (Augustin 2004)) have been associated with increased incidence of prostate cancer, only one study has examined the risk for prostate cancer in men with the Metabolic Syndrome (Laukkanen 2004). This study found that middle-aged men with the Metabolic Syndrome at baseline were 1.9 times more likely to develop prostate cancer, after adjusting for other prostate cancer risk factors. The authors hypothesized that the Metabolic Syndrome caused disturbances in the metabolisms of IGF-1, androgens, and sex hormone binding proteins, which may have a direct effect on the prostate.

In ARIC, participants have been followed through annual telephone calls, surveillance of community hospitals, and for cancer incidence via linkage to state cancer registers. From 1987 to 2000, 400 of the 7082 men (77% white, 23% African American) in the ARIC study developed prostate cancer.

We hope to answer the question of what the relationship is between the Metabolic Syndrome and prostate cancer. This could have implications in who is at increased risk for prostate cancer and when screening should begin. The first author is a medical student who will work with Dr. Folsom, and he has obtained local money to support this analysis.

Ford, E. S., Giles, W. H., & Dietz, W. H. (2002). Prevalence of the metabolic syndrome among US adults: Findings from the third national health and nutrition examination survey. *JAMA : The Journal of the American Medical Association*, 287(3), 356-359.

Andersson, S. O., Wolk, A., Bergstrom, R., Adami, H. O., Engholm, G., & Englund, A. et al. (1997). Body size and prostate cancer: A 20-year follow-up study among 135006 Swedish construction workers. *Journal of the National Cancer Institute*, 89(5), 385-389.

Hsing, A. W., Gao, Y. T., Chua, S., Jr, Deng, J., & Stanczyk, F. Z. (2003). Insulin resistance and prostate cancer risk. *Journal of the National Cancer Institute*, 95(1), 67-71.

Augustin, L. S., Galeone, C., Dal Maso, L., Pelucchi, C., Ramazzotti, V., & Jenkins, D. J. et al. (2004). Glycemic index, glycemic load and risk of prostate cancer. *International Journal of Cancer. Journal International Du Cancer*, 112(3), 446-450.

Laukkanen, J. A., Laaksonen, D. E., Niskanen, L., Pukkala, E., Hakkarainen, A., & Salonen, J. T. (2004). Metabolic syndrome and the risk of prostate cancer in Finnish men: A population-based study. *Cancer Epidemiology, Biomarkers & Prevention : A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology*, 13(10), 1646-1650.

5. Main Hypothesis/Study Questions:

The primary objective of this project is to use the ARIC cohort to assess the hypothesis that middle aged men with the Metabolic Syndrome have an increased risk of prostate cancer development, compared with the men without the Metabolic Syndrome. In

addition, whether ethnic identity (African American vs white) modifies the association of the Metabolic Syndrome with prostate cancer will be examined.

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

Exclusion: baseline cancer history, missing data on metabolic syndrome

Independent: metabolic syndrome and its components, plasma insulin at ARIC baseline

Dependent: Incident prostate cancer

Covariates: age, race, physical activity, smoking, alcohol, perhaps some dietary factors

Hypothesis will be tested using proportional hazards modeling. Metabolic syndrome will be categorized as yes/no and by number of components present, and relative risks calculated. Individual components will also be examined. Test of race differences will be done with an interaction term; however, caution will be needed because of possible race/center differences in completeness of cancer ascertainment.

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 ICTDER02 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 ICTDER02 must be used to exclude those with value RES_DNA = 'No use/storage DNA'? Yes No

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:

HYPERLINK "<http://www.csc.unc.edu/ARIC/search.php>"
<http://www.csc.unc.edu/ARIC/search.php>

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)?

None

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _xx_ Yes

11.b. If yes, is the proposal

xx A. primarily the result of an ancillary study (list number* 5)

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

HYPERLINK "<http://www.csc.unc.edu/aric/forms/>"

<http://www.csc.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.