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TITLE: Dietary Fat and Vitamin E in Prostate Cancer Risk among African Americans and Africans: A Case-Control Study

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14. ABSTRACT The role of dietary fat and vitamin E in prostate cancer risk among African-Americans, African migrants and Africans is being investigated using a dietary assessment tool and by measuring plasma fatty acids and vitamin E in cases and controls. The FFQ appropriate for all three populations has been developed and continues to be in use for the Nigerian population. The BLOCK FFQ will be used for the Nashville population to allow for micronutrient analysis. Nashville site: Administrative process including grant transfer, IRB approval, research assistant hire, design of souvenirs, posters and brochures has been completed, and purchase of supplies is in progress and community network and outreach has been initiated. Nigeria Site: 52 potential cases have been recruited from urology and surgical clinics of the study hospitals and 42 potential controls have been recruited from the community. Data management: The research assistant has been trained to manage the study data. The demographic section for 94 new, dietary assessment for 600 old and new, fatty acid laboratory report for 162 participants have been entered. One manuscript has been published, a second is being revised, two talks and two abstracts have been presented from this study.					
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INTRODUCTION:

[Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.]

This pilot study is designed to compare African American men in the Nashville area with African men living in Nigeria. It is designed as a second part to the study that accrued African men from Nigeria and African migrants and African Americans who live in the Washington metropolitan area between 2000 and 2002. The main objective of the study is to locate prostate cancer cases and select community based controls matched for age, socio-economic status and country of origin such that both groups will be compared with relation to their dietary risk factors for prostate cancer. The specific nutrients of interest are vitamin E, a protective antioxidant and essential fatty acids some of which have been proposed as risk factors for prostate carcinogenesis. Food items of interest that we hope to investigate include dairy products, dietary supplements, fruits, vegetables, meat and fish.

BODY:

[This section of the report shall describe the research accomplishments associated with each task outlined in the approved Statement Of Work. Data presentation shall be comprehensive in providing a complete record of the research findings for the period of the report. Appended publications and/or presentations may be substituted for detailed descriptions but must be referenced in the body of the report. If applicable, for each task outlined in the Statement of Work, reference appended publications and/or presentations for details of result findings and tables and/or figures. The report shall include negative as well as positive findings. Include problems in accomplishing any of the tasks. Statistical tests of significance shall be applied to all data whenever possible. Figures and graphs referenced in the text may be embedded in the text or appended. Figures and graphs can also be referenced in the text and appended to a publication. Recommended changes or future work to better address the research topic may also be included, although changes to the original Statement of Work must be approved by the Grants Officer. This approval must be obtained prior to initiating any change to the original Statement of Work.]

Statement of Work:

Task 1

Hire research assistant. (1 – 3 months): -- Update

Identify phlebotomist / laboratory assistant in the Metro General Hospital to work on this study part-time.

The first research assistant (Angelica Keng) resigned after 10 months, and Sam Vorpor, MD, was hired temporarily to maintain continuity and avoid a break in recruiting. The position has now been advertised to identify a research assistant that will emphasize community outreach activities to increase the number of participants. Meanwhile a part-time MSPH student, Jennifer Murphy, has been trained to continue with data entry. The department of surgery supported the study with a part-time research associate (Marian Ladipo, MPH) who served as study coordinator up till January 2006, and the department will continue to provide such support for this project until we get a new full-time RA.

The CRC continues to provide phlebotomy services.

Task 2

Start-Up Phase and Plan Development (1 – 3 months) -- Update

-Urologists:

We continue to have the support of Dr. Joseph Smith, and Dr. Michael Cookson of Vanderbilt University, and Meharry Medical College is in the process of hiring a urologist.

-Network:

Close ties have been established with the Interdenominational Misters Forum (IMF) and 6 other churches. We continue to make connection with other churches. The PI has been interviewed by one radio station, and has also been interviewed by News Channel 5, and aired on the URBAN OUTLOOK program 21 times. There has been press release about prostate cancer, and this study was mentioned in 5 local news papers.

-August 19, 2005: Obtained IRB approval from the State of Tennessee Bureau of Health Services (State Cancer Registry). We are now in the process of inviting prostate cancer cases to the study, and letters of invitation to participate in this study has been sent out to the first batch of 20 men.

Task 3

Training: New Research Assistant (2 – 4 months): Update

-All persons involved in this project completed training in the area of research ethics, human subject protection, making professional initial telephone contacts to secure participants cooperation, and scheduling study visits. Marian Ladipo, M.P.H., and Sam Vorpor, M.D., received training in handling, labeling, storage and shipping of research samples.

Task 4.

Subject Recruitment and Data Collection in the US. (4 – 24 months)

Nashville, TN:

85 men have been recruited into the study.

Participants	Number
CASES	4
CONTROLS	66
Elevated PSA (Normal DRE)	1
BPH only	6
Sub-Total	77
Data not yet entered	8
Total	85

Benin-City, Nigeria:

Recruitment: 82 additional potential cases have been recruited. Recruitment of new study participants was halted in October 2005. The current focus is to follow-up patients with elevated PSA by home-visits to hand-deliver the doctor's follow-up report. It is hoped that some of the patients will come to the hospital for their scheduled prostate biopsy. They are also contacting patients who had prostate biopsy 2004/2005, and if they consent, they too will complete the study protocol.

Processing Pathology Samples: Pathologist, Dr. Marcia Wills, at the Vanderbilt University has reviewed 24 pathology slides. She has also received 54 additional slides to be reviewed. Note that some patients have more than one biopsy slides.

Participants	2005
CASES	2
CONTROLS	30
Elevated PSA (Normal DRE)	22
Elevated PSA + BPH	14
BPH only	12
Highly suspicious of Prostate Cancer	2
Total	82

Task 5.

Interim and On-going Data Analysis (3 - 24 months)

Data Base:

A lot of progress has been made in this area since a full-time RA took over the task. The study questionnaire is in three main sections and the data is being entered in sections. There are now a total of 684 participants in the SPSS database, including data from the previous 355 participants from the Nigeria and Washington DC survey prior to and including 2003. The RA has now concentrating on cleaning the database and catching up with data entry. The database is made up of five main sections as shown below:

Sections	Previously Entered	Entered Current Period	Total
Personal Information	684	123	807
Dietary Assessment	450	306	756
Anthropometrics	577	113	690
Food Frequency	435	0	435
Free Fatty Acid	157	0	157

It is important to note that we are recruiting potential study participants and collecting information from 'potential cases', men with elevated PSA, before they go for prostate biopsy, so that information can be collected prior to cancer diagnosis. This is because the patients attention will become diverted by the serious diagnosis of prostate cancer, and they may not consent to participate in a study that does not directly impact their treatment. The 'potential controls' pool is be available to select age/SES-matches for each confirmed case.

1. Oral Presentations to 6 Community Groups

Flora Ukoli. Taking Control of Your Prostate Health: The Importance of Early Detection on Prostate Cancer.

Flora Ukoli. Participating in Prostate Cancer Research.

2. Graduate Students Supervision: Using sections of the data collected in this study.

Emeka Amaefuna, M.D. The pattern of essential fatty acid profile among African-American and Nigerian men.

Esiri Esin, M.D. Tobacco and alcohol use pattern among Nigerians and African migrants living in the United States.

Mariam Abayomi-Cole. Assessing Knowledge, Attitudes, and Practices toward the Prevention of Colorectal Cancer

Task 6.

Report Writing and Presentations (18 - 24 months)

Data analysis and manuscript preparation.

1. Panguluri RC, Long LO, Chen W, Wang S, Coulibaly A, Ukoli F, Jackson A, Weinrich S, Ahaghotu C, Isaacs W, Kittles RA. COX-2 gene promoter haplotypes and prostate cancer risk. Carcinogenesis. 2004 Jan 30.

2. Anthropometric Body Fat Predictors of Elevated Prostate Specific Antigen among Rural and Urban Nigerians: A Population-Based Study.
(Submitted: Archives of Ibadan Medicine, 2006.).

3. Fowke, J.H., Schlundt, D., Signorello, L.B., Ukoli, F.A.M., Blot, W.J. Prostate cancer screening among low-income African-American and Caucasian men. Urologic Oncology: Seminars and Original Investigation. 2005;23:333-340.
(This is a related topic, but not from the data collected in this study)

Abstracts: Submitted to the UICC (International Union Against Cancer) World Cancer Congress. Washington DC. July 2006.

1. Ukoli F.A., Oguike T, Akumabor P.N, Oside P, Iyamu E, Osime U. Response to Prostate Biopsy by Nigerian Men: Community and Hospital Experience
2. Akumabor P.N, Aligbe J .U, Ukoli F.A. Management of Prostate Cancer Among Patients Presenting with Prostatic Disease in a Single Urology Practice in Southern Nigeria
3. Adekanyan A, Onawola K, Obarisiagbon E, Oguike T, Akumabor P, Ukoli F. Onuora V. Digitally Guided Transrectal Biopsy Of The Prostate

KEY RESEARCH ACCOMPLISHMENTS:

[Bulleted list of key research accomplishments emanating from this research.]

Nigerian Site:

1. Men with abnormal prostate cancer screening continue to be contacted and encouraged to visit their urologists and consider a prostate biopsy if indicated.
2. Men diagnosed with prostate cancer are receiving usual medical treatment.
3. Men are receiving information about prostate cancer, the meaning of the PSA test, and the available of treatment options for organ confined prostate cancer detected early.

Nashville Site:

1. Community outreach is active. The team attends health fairs, the PI is invited to give prostate health talks, and has been interviewed on Radio and Television.
2. Recruiting control participants in Nashville has started, and is improving.
3. Provided prostate cancer screening for 85 men.
4. IRB approval and support from TN cancer register has been obtained.
5. Recruiting cases started in January 2006, and we have received calls from at least 3 men.
6. Data entry is ongoing.

REPORTABLE OUTCOMES:

[Provide a list of reportable outcomes that have resulted from this research to include:]

The study continues to improve on the achievements of the first year, and in the second year:

1. Maintained partnership with 6 communities in Nashville. Initiated contact with 4 additional churches.
2. The clinical research center (CRC) at Meharry is actively involved in participant recruitment.
3. Two urologists in Nigeria have become part of the research team, actively involved in this study.
4. Collected demographic and dietary assessment information for additional 171 men, bringing the total in the database to 807.
5. Collected and stored plasma, serum, cell, clot and urine samples for laboratory analysis for 171 men.

CHALLENGES:

Nigerian Site:

- 1 Biopsy in Nigeria:
 - a. Men without symptoms, who have elevated PSA, are still uncomfortable and not accepting to undergo prostate biopsy. The urologists do counsel them and leave them to make up their mind if they will undergo the procedure.
 - b. Urologists (no ultrasound guided biopsy) collect 4 biopsy samples for review by the pathologist. 1 or 2 of these slides are forwarded to the PI. A diagnosis of prostate cancer from either pathologists is accepted.
- 2 Biopsy samples were obtained from some prostate cancer cases who promised to return to complete the study survey after 3 months. Efforts to recruit such men into the study is difficult, probably because it may take some time for the patients to accept their diagnosis and consider participation in a study that does not offer direct medical benefits.
- 3 The cost of mailing diagnostic samples and study materials from Nigeria has tripled. Questionnaires are therefore shipped separately (regular mail) while samples continue to be shipped by FedEx.
- 4 The study did not budget for junior investigators in Nigeria, and the honorarium for the urologists was under budgeted. Maintaining their commitment to collect more data will require increasing the budget for that site.

Nashville Site:

- 1 The study has not secured the support of private physicians or urologists in the community, and this is a process we are still working on. It may be necessary to budget some administrative fee for physician office staff to encourage them to pass out study information to African American patients who are 40 years and older. We therefore identify cases from the cancer register, which is current up to 2003. Recruiting more recently diagnosed prostate cancer cases will depend on the support of local urologists.
- 2 Regarding controls: There is need to pay more attention to outreach, offering more information and hoping that men will realize that research is not just for people who do not have health insurance.
- 3 It appears as if the importance of research such as this is not understood by many, such that they are not willing to make any sacrifice to participate. \$30.00 incentive appears to attract only the unemployed, and those who are on wages cannot miss a day's work for \$30.00. Only the very enthusiastic full-time employed men have managed to respond favorably.
- 4 Research staff: This is a pilot study, but the position of a research coordinator is necessary. The RA therefore combined some responsibilities of coordinating, and outreach. It is very easy for a RA to feel overwhelmed, and this might be one reason for the turn-over of that position.

CONCLUSIONS:

[Summarize the results to include the Importance and/or implications of the completed research and when necessary, recommend changes on future work to better address the problem. A "so what section" which evaluates the knowledge as a scientific or medical product shall also be included in the conclusion of the report.]

The study has not met its 24-month accrual target because active accrual of controls started very late in Nashville (March 2005), and accrual of cases has only just started in late January of 2006. Physicians do not show any interest in supporting the study, and a better way of achieving their support need to be investigated.

In Nigeria, public knowledge about cancer in general is low, and even though many people accept to participate in research, the fear of an unfamiliar procedure, such as prostate biopsy is overwhelming. There is urgent need for public campaign about cancer in general and prostate cancer in particular.

Media exposure in local newspapers, newsletters, radio and television, is important and must continue at both sites. In addition, the distribution of study flyers, brochures, and letters of study introduction need to continue in churches, family physician offices, and offices of local urologists.

A Non-Cost extension for 12 months has been requested to provide enough time to meet the projected accrual number. The plan is to ship a large batch of samples (50 cases and 100 controls) to the research laboratory for fatty-acid assay, followed by data analysis.

REFERENCES: *[List all references pertinent to the report using a standard journal format (i.e. format used in Science, Military Medicine, etc.).]*

APPENDICES: *[Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.]*

BINDING: *[Because all reports are entered into the Department of Defense Technical Reports database collection and are microfiched, it is recommended that all reports be bound by stapling the pages together in the upper left hand corner. All original reports shall be legible and contain original photos/illustrations. Figures shall include figure legends and be clearly marked with figure numbers].*

Appendix:

Three abstracts attached:

1. Ukoli F.A, Oguike T, Akumabor P.N, Oside P, Iyamu E, Osime U.

Response to Prostate Biopsy by Nigerian Men: Community and Hospital Experience

Objective

To describe the pattern of response to prostate biopsy among men screened in Nigeria.

Methods:

Volunteers recruited from the four communities and four surgery clinics were screened by PSA test and digital rectal examination, after informed consent. Digitally guided transrectal prostate biopsy was ordered and performed by the urologist for men with abnormal results.

Result:

Of 800 men contacted, 603(75.4%) consented, 559(69.9%) completed the survey, 355(63.5%) in the community, and 204(36.5%) in the hospital, with response rates of 84.4% and 63.7%, and mean age 56.7 ± 13.4 and 66.8 ± 10.8 , respectively, $p < 0.0001$. Educational and economic profiles were comparable. 165(80.9%) from the clinics and 61(17.2%) from the community reported urinary symptoms, $p < 0.0001$, of which 21(34.4%) from the community sought treatment from a doctor. Elevated PSA (≥ 4 ngs/ml) rate was 10.9% to 63.1%, enlarged prostate rate 35.9% to 67.1%, and abnormal prostate suspicious of cancer was 1.2% to 19.7%, for community and hospital men respectively, $p < 0.0001$. Prostate biopsy acceptance was 8.1% (3/37) and 37.2% (48/129), $p < 0.0001$, respectively, and 35.3% for men with symptoms, and 26.7% for those without symptoms.

Conclusion: Men in the surgical clinics and those with symptoms were more likely to accept prostate biopsy, possibly as a result of symptom severity. Lack of knowledge about early stage asymptomatic cancer, cancer phobia, and concern about financial implication of a hospital visit are possible barriers. The need for public campaign about availability of effective treatment especially for early stage cancer diagnosed by screening, and the safety of prostate biopsy, is advocated.

2. Akumabor P.N, Aligbe J .U, Ukoli F.A.

Management of Prostate Cancer Among Patients Presenting with Prostatic Disease in a Single Urology Practice in Southern Nigeria

Objective: To determine prevalence and pattern of presentation, and to describe the quality of care of prostate cancer patients presenting in a urological out-patient in Southern Nigeria.

Method: The case records of all men with prostatic diseases seen at Zuma Medical Center, Benin-City, Nigeria, between 2001 – 2004, were reviewed. These patients were either referred from a general hospital or walk-in patients. They all received full urological appraisal that included physical examination, digital rectal examination (DRE), ultrasonograph, prostate specific antigen (PSA), and transrectal prostate biopsy. Patient management was based on diagnosis, stage of disease, and patient preference. Treatment for non-localized disease was anti-androgen or LHRH, and bilateral orchidectomy was the second treatment option.

Result: Of the 222 patients seen during this period, 45(20.3%) were diagnosed with prostate cancer on the basis of histological findings. DRE accurately identified 38(17.1%) of the cases. 8(17.8%) were aged 50-60 years, 12(26.7%) 61-70 years and 25(55.6%) were 71 years or older. None of the patients presented with organ confirmed disease. 8(17.8%) received anti- androgen or L.H.R.H treatment, 32(71.1%) opted for bilateral orchidectomy, 5(11.1%) who refused orchidectomy, or who could not afford anti-androgens, were placed on 'watchful waiting' with PSA evaluation every 6 months.

3. Adekanyan A, Onawola K, Obarisiagbon E, Oguike T, Akumabor P, Ukoli F, Onuora V.

Digitally Guided Transrectal Biopsy of the Prostate

Objective: To describe the diagnostic usefulness of digitally guided transrectal biopsy of the prostate. **Methods:** All men suspected of prostate cancer on the basis of abnormal digital rectal examination (DRE) and/or elevated prostate specific antigen (PSA) over a one-year period had transrectal prostate biopsy by a urologist using one finger in the rectum to guide the biopsy needle. This was an out-patient procedure using the Bard Monopty biopsy gun, with the patient lying on the left lateral position with the hips and knees flexed, without anesthesia or bowel preparation. Biopsy specimens were collected from the base, middle, and apex of each lateral lobe and reviewed by a pathologist. Patients received prophylactic antibiotics, and information about the process, benefits and risks of complication, and instructed to present if they developed severe pain, fever, haematuria or blood stained stools. They were scheduled for 2-week follow-up visit to review biopsy results. **Results:** 44(84.6%) had abnormal DRE and elevated PSA, and 8(15.4%) had elevated PSA with normal DRE. PSA ranged from 1.8 – 228.5 ng/ml, mean 40.5ng/ml. All the patients tolerated the biopsy procedure well. Histopathological examination revealed carcinoma in 33(63.4%) men. Mean PSA was higher in patients with positive biopsy (48ngs/ml), compared to men with negative biopsy (21.4ng/ml). 6(11.5%) developed mild hematuria and/or blood stained stool, while 1(1.9%) patient with aplastic anemia presented with severe hematuria requiring admission and blood transfusion.