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Development of Meharry Medical College Prostate Cancer Research Program

PRINCIPAL INVESTIGATOR:

Flora A. M. Ukoli

CONTRACTING ORGANIZATION:

Meharry Medical College

Nashville, TN 37208

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14. ABSTRACT
A prostate cancer (PCa) research program has been established at Meharry Medical College. There is substantial urology, oncology, epidemiology, nutrition and other expertise at Meharry and Vanderbilt addressing issues of PCa disparities, and 4 program investigators have maintained partnerships with VU mentors, and established viable community network ties. Dr. Stewart and Dr. Ogunkua continue to develop their research laboratories with great success. They have independent funding and their laboratory continues to grow to include both graduate and undergraduate mentees. They are actively involved in the Meharry Prostate Cancer Group. Dr. Derrick Beech, Dr. Hargreaves, and Dr. Patel collaborate with Dr. Ukoli to run two PCa education programs in Nashville (CMS funded) and Memphis (R03). Ukoli's lycopene pilot study has completed recruitment of study participants from the Nigerian site, controls from Nashville, and has extended collaborative ties with Matthew Walker Comprehensive Health Center to access potential PCa to meet the recruitment goal, at which time additional samples will be shipped for lycopene analysis. Program funding will end without the benefit of renewal as the Department of Defense no longer provides funding under this mechanism.

15. SUBJECT TERMS
Prostate cancer, Dietary risk factors, Lycopene, Genetic predisposition, African-Americans, Cancer research training, Quality of life, Community outreach, Recruiting study participants, Cell line inhibition, Animal studies, Prostate cancer screening.

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INTRODUCTION:

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

The reason for African-Americans (AA) being disproportionately affected by prostate cancer (PCa) may include biologic tumor differences, genetic predisposition, differential exposures, limited utilization of preventive health care such as prostate specific antigen (PSA) testing, and inadequate access to health care. The paucity of minority PCa investigators and low accrual of AAs in clinical trials also contribute to the lack of progress in reducing this disparity. This proposal includes research initiatives to study the genetics, pathogenesis and epidemiology of PCa disparity among AA men. The genetic similarity between AAs and Africans, disparity in the degree of racial admixture, differences in dietary style and body fat patterns provide the unique opportunity to study genetic and environmental causes of PCa in black men. The PCRP now has 9(75%) members of its initial membership at Meharry, all three collaborators at the University of Benin in Nigeria, and each of the pilot project PIs at Meharry continue to retain there mentors/collaborators at VUMC, working on overlapping PCa topics at the genetic, molecular, clinical and epidemiological levels.

The program received a one year non-cost extension to meet the specific goal of the community-based lycopene and PCa risk pilot project, and has requested another non-cost extension to provide opportunity to assay the samples already collected and to intensive efforts to meet recruitment of PCa cases in Nashville.

The program goals are to:

1). Develop an Outreach Core to sustain communication network with AA communities in Nashville, address PCa needs and facilitate recruitment into PCa early detection programs and research studies.

2). Develop a PCa research training program for junior faculty, new PCa investigators, and graduate students.

3). Conduct pilot projects, accumulate preliminary data, submit independent proposals, and generate new research ideas to sustain the PCRP at the completion of this DOD award.

The scientific aims of the program are to:

1). Conduct research of biomarkers and lifestyle risk factors of PCa development and progression in African-Americans and Africans.

2). Study the role of specific genes, gene-gene interactions, gene-environment interactions in PCa initiation and progression in these populations.

3). Conduct investigator-initiated clinical trials with emphases on nutritional interventions and molecular therapeutics.

4). Use mass spectrometry and proteomic-based approaches to identify predictive factors of PCa aggressiveness, treatment response and metastasis and develop molecular classifications and/or biomarkers of aggressive PCa.

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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.]*

Task 1: **Start-Up Phase: (1-2 month)**

Advertise for and hire a senior research assistant (RA) to recruit, consent and interview study participants. The RA will also manage the study database, enter data, order supplies and handle study biological samples.

Two part-time graduate research assistants from the Meharry MSPH program were hired and trained for data and sample collection, data entry and management.

Ms. Amirah Abdullah
Ms. Mirabel Weriwoh

A post-doctoral fellow, T. Fadiya, MBBS, MPH, was identified and hired and in the process of initial training he left the program unable to submit a career development plan in line with the aims and objectives of this program.

Two graduate students from 2009, Mbeja Lomotey and Angel Moore, completed their MSPH thesis using the project database for secondary analysis.

Six undergraduate interns were also trained (DOD, Collaborative HBCU Research Training program) and mentored by the pilot project PIs in basic, translational, and community-based PCa research.

Products:
Graduate students (Ukoli's lab: 2 previous, 2 current; Stewart's lab: 2 previous, 2 current)
Post-doctoral fellow (Ukoli's lab: 2 previous, None currently)
Undergraduate trainees (Ukoli's lab: 4; Stewart's lab: 1; Ogunkua's lab: 1)

Deliverables:
Regular learning contact between mentees and respective mentors.
Monthly tutorials within each pilot project team.

Task 2. Outreach, Subject Recruitment and Data Collection: (1 – 12 months)

A. Development of Program Outreach Core:

The PI has maintained membership of various community network and continues to implement the PCa education program for low-income African-Americans funded by the Centers for Medicare and Medicaid Services (CMS).

Preliminary report from our PCa research work has been presented at several venues including:

a. Meharry Medical College Department of Surgery Grand Rounds
b. Meharry-Vanderbilt Alliance U-54 Retreat
c. 10th Anniversary HBCU/Hispanic Health Services Research Conference, Tuskegee University, Alabama, April 23, 2009.
d. 137th APHA Annual Meeting and Exposition. November 7 -11, 2009.
e. Have been selected to present at the APHA conference in Denver Colorado in November.

The PI remains an active member of several organizations including Men's Health Network (MHN), Women Against Prostate Cancer (WAPC), Prostate Cancer Support Group (USTOO), Jefferson Street United Merchants Partnership (JUMP)

B. Outreach:

With additional funding provided by the CMS Award # 1I0CMS030208/01, ending October 2010, the PI and other investigators have schedule/organize prostate cancer symposium/screening at local health centers, churches, housing complexes, recreation centers, work places and MMC, and encourage participants to participate in this study. We have distributed study flyers/brochures and strategic community locations and urology offices, and appeared on television to talk about PCa in general and our program in particular.

Products: 514 men screened for prostate cancer
100 attendees at community outreach events.

Deliverables: 4 Community symposiums,
2 Community-based prostate cancer screening activities
2 Television interviews.
1 Newspaper appearance (Tennessean of the Year)
http://www.tennessean.com/article/20091227/OPINION01/91227002/Meharry+researchers+named+Tennesseans+of+the+Year

C. The Lycopene Pilot Study: HSRRB Log No. A-13323.0: Title:

"Lycopene in Prostate Cancer Risk among African-Americans and Nigerians: A Case-Control Study" Plasma lycopene analysis was completed for 177 of the 192 samples. Data entry is now in progress and interim data analysis will follow.

Nashville Site: HSRRB Log No. A-13323.1a (Proposal No. PC041176)

Dr. Rodney Davis (Urologist) runs the urology clinic at Nashville General Hospital. Potential study participants are contacted and only those who are not institutionalized qualify for this study. So far 3 participants have been recruited from this population. The PI continues to be an active member of the following community groups/associations, and disseminates study information through the forums they provide: USTOO Meharry Chapter, Men's Health Network, Interdenominational Ministers Fellowship, Women Against Prostate Cancer (WAPC), TN Prostate Cancer Coalition, Nashville NAACP, United Nashville Partners Against Cancer (UN-PAC): Meharry-Vanderbilt-TSU Cancer Outreach partnership, Jefferson Street United Merchants Partnership (J.U.M.P.), Nashville, and Matthew Walker Comprehensive Health Center, Nashville.

Nigeria Site: HSRRB Log No. A-13323.1b (Proposal No. PC041176)

This site closed in October 2009. Final IRB report was submitted to their Research Ethical Committee. One investigator has left the institution leave 2 investigators (Osime and Akumabor) who are still supportive and interested in collaborating with the PI on related projects. Approval has been received from their allowing recruitment until October 2009. It was very difficult to officially register a PCa support group in Nigeria (USTOO Nigeria chapter) therefore volunteers have worked as 'individuals' rather then a not-for profit organization. Their goal is to increase PCa awareness in that community.

Products:

1. Nigeria: Investigators/Collaborators in Nigeria remain supportive.
   Usifo Osime, MBBS, FRCS
   Philip Akumabor, MBBS, FRCS
2. Nashville: Supportive urologists in Nashville:
   William Hughes, M.D. (Midtown Urology)
   Rodney Davis, M.D. (Vanderbilt/Meharry faculty)
   David F. Penson, MD, MPH (Vanderbilt faculty): Initiated new collaboration.

Deliverables:

1. Stored blood samples from 72 new participants: To be analyzed.

2. Data file: Personal information, Urology history, PSA, Diet assessment (Completed)
   Food frequency (FFQ): (85% completed).

3. Publications:

i). Ukoli F, Fowke J, Akumabor P, Oguike T, Murff HJ, Amaefuna E, Kittles R, Ahaghotu C, Osime U, Beech D. The association of plasma fatty acids with prostate cancer risk in African Americans and Africans. JHCPU. 2010; (21):127-147.

ii). Patel K, Kenerson D, Wang H, Brown B, Pinkerton H, Burress M, Cooper L, Canto M, Ukoli F, Hargreaves M. Factors influencing prostate cancer screening in low-income African Americans in Tennessee. JHCPU. 2010; (21): 114-126.

iii). Flora A. Ukoli, MBBS, Philip N. Akumabor, MBBS, Temple C. Oguike, MBBS,

Lemuel L. Dent, MD, Derrick Beech, MD, Usifo Osime, MBBS. The Association of Plasma Fatty Acids with Prostate Cancer Risk in Nigerians. *Ethnicity & Disease*. 2009; 19:454-461.

iv). Flora Ukoli, Khandaker Taher, Mbeja Lomotey, Temple Oguike, Phillip Akumabor, Usifo Osime, Derrick Beech. The Role of Meat, Fish and Egg Intake in Prostate Cancer Risk among Nigerians. Infectious Agents and Cancer. 2009, 4(S1): 1-5.

4. Grants Submitted:

   i) R03 submitted: Prostate Cancer Education and Screening Pilot Program for African-Americans. Funded by NIH/NCI. 1 R03 CA138136-01A1
   ii) Department of Defense (DOD) Collaborative Undergraduate HBCU Student Summer Training Program Award: "Prostate Cancer Research Training in Health Disparities for Undergraduates (PCaRT)". Funded. Grant # W81XWH-09-1-0161. Entering its second year.
   iii). Challenge Grant 09-CA-101 The Basis for Differences in Cancer Incidence: Title: Gene-Nutrient associations in prostate cancer risk in diverse black populations. Not Funded/Not Scored. To be revised

5. Community prostate cancer outreach, education, and health fairs

   i). Egbe Omo Yoruba Health Fair: Tusculum Baptist Church, Nolensville Road, Nashville, TN. August 22, 2009.
   ii). Schrader Lane Church of Christ annual Health Fair. June 13, 2009.
   iii). Fox17 Television Morning News appearance: Prostate cancer in African-Americans: The importance of screening and early detection. May 8, 2009 and June 17, 2009.
   iv). Fox17 Television Morning News appearance: Prostate cancer in African-Americans: The importance of screening and early detection. June 17, 2009.
   v). American Cancer Society, Mid-South Division, Inc
   Participant, American Cancer Society Rolling Lobby Days for Tennessee House Bill 396, Tennessee General Assembly
   vi). MMC-based prostate cancer screening (available daily by appointment)

6. Parent Study SPSS database: Data entered for 1054 participants.
   1. Previously entered data: Personal information/Urology symptom history, Diet assessment, Fatty acid profile, Lipid profile
   2. Entered this reporting period: Food Frequency (FFQ), Lycopene profile from the BLOCK FFQ analysis and Plasma analysis.

D. <u>Continuing Medical Education in Prostate Cancer Research (Ongoing)</u>

CME is ongoing within and outside the program. Each pilot project PI attends the seminars relevant to their topic and area of study. Seminar Series Attendance:

Vanderbilt University
- Epidemiology Seminar series (Weekly)
- Urological Workshop on Research (Weekly)
- Vanderbilt Ingram Cancer Center Seminar series (Weekly)

Meharry Medical College
- Grand rounds in surgery/Prostate cancer seminar series (Monthly)
- Grand rounds in internal medicine/Family medicine (Monthly)
- Works-In-Progress Seminar, Dept. of Cancer Biology (Weekly)

Tennessee State University
- Center for Health Research TN State University (Weekly)

Presentations at National and International Conferences: 2009/2010

Response to prostate cancer screening intervention in a low-income African-American population. Meharry Medical College/Vanderbilt Ingram Cancer Center U54 Partnership 9th Annual Retreat: Perspectives in prostate cancer. Saturday January 23, 2010. Nashville, TN.

A prostate cancer screening program for low-income African-Americans. 137th APHA Annual meeting and Exposition. Philadelphia, PA. November 7-11, 2009. Abstract # 207422.

A prostate cancer education intervention for low-income African-Americans. Surgical Grand Rounds, Meharry Medical College. September 23, 2009.

CANCER PREVENTION & CONTROL: The Role of Support Groups in Community Awareness Campaigns. Presented at the First Delta Diaspora Direct (D3) Conference in North America. New York, NY. September 1, 2009.

Prostate Cancer Screening in Nigeria Challenges, Policy Implications and Recommendations. Presented at the Association of Nigerian Physicians in the Americas (ANPA) 10th Annual Conference in Abuja, Nigeria, July 15 – 19, 2009.

A Prostate Cancer Screening Program for Low-Income African-Americans. Presented at the 10th Anniversary HBCU/Hispanic Health Services Research Conference, Tuskegee University, Alabama, April 23, 2009.

Other conferences attended:

Tennessee Global Health Forum: Institute of Global Health, Student Life Center, Vanderbilt University. February 12, 2010

Project Blossom: A Blueprint for a Healthy Future. November 5 & 6. Nashville TN.

The 13th Annual National Centers for AIDS Research (CFAR) Scientific Symposium. Hosted by the Vanderbilt Meharry CFAR at Vanderbilt University Medical Center. Langford Auditorium, Vanderbilt University. November 5, 2009.

The 12th Annual Tennessee AIDS Education and Training Center (AETC) / Comprehensive Care Center (CCC) HIV Clinical Symposium. Hosted at "aVenue", Downtown Nashville, TN. November 6, 2009.

Task 3. Interim and Final Data Analysis (9 - 12 months)

Undergraduate student Posters:

i).

ii).

iii).

Undergraduate research report:

iv) Regulation of the Erk signaling pathway by the PPAR gamma ligand troglitazone
Danielle Jones

Ph.D. Graduate student Posters:

v). The role of PPAR gamma ligands in androgen-independent prostate cancer cells.
Patrice Moss

v) Troglitazone regulates c-Myc expression within human prostate cancer cells.
Tunde Akinyeke

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Grant proposals submitted:

i) W81XWH-09-1-0161 (PI: Ukoli): Department of Defense (DOD) Collaborative Undergraduate HBCU Student Summer Training Program Award: "Prostate Cancer Research Training in Health Disparities for Undergraduates (PCaRT)". Second year.

ii) 1 R03 CA138136-01A1 (PI: Ukoli): Prostate Cancer Education and Screening Pilot Program for African-Americans. Funded by NIH/NCI.

iii). 09-CA-101 Challenge Grant (PI: Ukoli) The Basis for Differences in Cancer Incidence: Title: Gene-Nutrient associations in prostate cancer risk in diverse black populations: Not Funded/Not Scored. To be revised

iv). 1 K01 CA114253 (PI: LaMonica Stewart) NCI/NIH Regulation of Prostate Cancer Growth by PPAR gamma Ligands

v). 3 K01 Ca114253-04S1 (PI: LaMonica Stewart) NCI/NIH Regulation of Prostate Cancer Growth by PPAR gamma Ligands (Supplement)

Manuscript development:

1. Fatty acids: a). Two publications listed above
   b). Omega-3 to omega-6 ratio in prostate cancer risk among Africans (Preparation stage)

2. Public education: a). One publication listed above
   b). Tailored prostate cancer education for low-income African-Americans: Impact on knowledge and screening (Preparation stage)

3. Lycopene: a). Lycopene and prostate cancer in African-Americans (Data analysis in Progress).

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KEY RESEARCH ACCOMPLISHMENTS:

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

This is indeed a very ambitious program that succeeded in meeting its goal of establishing prostate cancer research projects at Meharry led by Meharry PIs.

1. The prostate cancer research program (PCRP) has been established at Meharry Medical College.

2. Pilot project PIs are involved in an HBCU summer training program where they will mentor minority undergraduates to conduct basic, translational and clinical research in the area of prostate cancer. This will be the second year of that program.

3. Three research teams are in place in collaboration with investigators from Vanderbilt University. (Cell studies, Mice model, Epidemiology)

4. The international collaboration with the University of Benin, Nigeria, continues to be maintained.

5. The program has full access to four research laboratories at Meharry developed by Dr. Stewart, Dr. Ogunkua, Dr. Das, and Dr. Marshall.

6. In partnership with Derrick Beech, M.D., (Professor and Chair of Surgery), and Margaret Hargreaves, Ph.D. (Professor of Medicine), community trust continues to grow as we offer PCa education and outreach through our Community-Based Participatory Research (CBPR) funded by the Centers for Medicare and Medicaid Services, and now the NIH/NCI.

7. Graduate and Undergraduate student exposure:
   a. Dr. Stewart's laboratory continues to support 2 doctoral students, one MSPH student, and one undergraduate intern.

   b. Dr. Ukoli's project continues to support two MSPH students, and 4 undergraduate interns.

   c. Dr. Ogunkua's project continues to support one undergraduate intern.

8. Publications: The PI had four publications in 2009 and is currently developing two new manuscripts.

REPORTABLE OUTCOMES:

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

1. Partnership established with several organizations and community groups in Nashville including: Interdenominational Ministers Forum (IMF), local church communities, local prostate cancer non-profit organizations, local African-American fraternities, and several community groups and organizations such as 100 Black Men of America, NAACP, World Baptist Center and Academy for Educational Development (AED)

2. Partnership with the clinical research centers at Meharry and Vanderbilt:
    i) CRC at Meharry is actively involved
    ii) GCRC at VU ready to support program with DNA extraction and genotyping.
    iii) Institute of Global Health (IGH) at Vanderbilt

3. Partnership with the Nigerian research collaborators: Usifo Osime (General surgeon), Philip Akumabor (Urologist), Obarisiagbon (Urologist).

4. Partnership with mentors and collaborators at Vanderbilt.

5. The Meharry PCRP has 5 active PIs who are developing PCa research at Meharry: Dr. Flora Ukoli, Dr. LaMonica Stewart, Dr. Ben Ogunkua, Dr. Maureen Sanderson, and Dr. Kushal Patel. Other prostate cancer investigators include Dr. Derrick Beech, Dr. Margaret Hargreaves, Dr. Carlton Adams, Dr. Lemuel Dent, and Dr. Alphonse Pasipanodya.

CHALLENGES:

PCRP Funding:

This grant has ended and the Department of Defense (DOD) has discontinued this funding mechanism making it difficult to renew the proposal and secure full funding for another three-year period.

Post-Doctoral Fellow Retention:

Retaining a post-doctoral fellow in this program has been a challenge. One of the scored criteria for a career development grant is evidence of previous scholarly activities between the mentor and the post-doc. Given the nature of epidemiological studies, it is a challenge to achieve that within a one-year period. Some post-doctoral fellows are therefore likely to seek a position on a new grant with assurance of a position for at least 3 years, or non-grant funded position.

Study Participant Recruitment:

Nashville Site:

Urology practices are not comfortable allowing direct communication with patients to solicit interest in study participation, especially when the practice is not listed on the grant as a collaborating institution. Budget consideration for recruiting participants at other sites other than Meharry may be useful. Secondly the participant incentive was not enough to stimulate interest and

motivation for a person on wages to take a day off work ($80-$100 being an average wage for a day).

Nigerian Site:

Lack of equipment for ultrasound-guided biopsy continues to be a challenge, and so is the cost of biopsy. Men without symptoms who have sustained elevated PSA may not get a prostate biopsy such that their diagnosis remains unresolved. Providing ultrasound biopsy at a subsidized cost in future research projects may be useful.

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 prostate cancer research program (PCRP) at Meharry.

The faculty at Meharry Medical College have successfully developed a prostate cancer research program (PCRP) at Meharry. A DOD grant renewal is essential to strengthen and sustain this program above its current operational level. The Meharry PCRP faculty continue to perform excellent research, sourcing for and securing independent funds to maintain their activities. They are also training the next generation of minority researchers in the area of PCa research through mentoring and internships.

The Lycopene and prostate cancer pilot project.

The lycopene pilot study has met its recruitment goal in Nigeria. The recruitment challenge of cases in Nashville can be overcome by working closely with the Mathew Walker Comprehensive Health Center where up to 80 men with elevated PSA, potential PCa cases, were identified in our PCa education program. These men may volunteer to participate in this study if invited in a culturally appropriate manner. A non-cost extension period has been requested for this purpose.

Data analysis: Trans-lycopene is significantly higher among African-Americans compared to Nigerians, 10.12 ± 5.9 vs 4.99 ± 3.7, $p < 0.001$. While African-American PCa cases have a much lower trans-lycopene level than their controls 7.45 ± 41.1 vs 11.22 ± 6.2, $p < 0.006$, Nigerian PCa cases and controls were similar. However Nigerian cases recorded lower 13-cis-lycoepene and 9-cis lycopene B in comparison with their controls, 3.02 ± 1.8 vs 4.95 ± 3.2, $p < 0.002$, and 1.16 ± 0.9 vs 1.74 ± 1.2 $p < 0.02$, respectively.

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

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Appendices:

List of Content:

Appendix 1: Flora A. Ukoli, MBBS, Philip N. Akumabor, MBBS, Temple C. Oguike, MBBS, Lemuel L. Dent, MD, Derrick Beech, MD, Usifo Osime, MBBS. The Association of Plasma Fatty Acids with Prostate Cancer Risk in Nigerians. *Ethnicity & Disease*. 2009; 19:454-461.

Appendix 2: Ukoli F, Fowke J, Akumabor P, Oguike T, Murff HJ, Amaefuna E, Kittles R, Ahaghotu C, Osime U, Beech D. The association of plasma fatty acids with prostate cancer risk in African Americans and Africans. JHCPU. 2010; (21):127-147.

Appendix 3: Patel K, Kenerson D, Wang H, Brown B, Pinkerton H, Burress M, Cooper L, Canto M, Ukoli F, Hargreaves M. Factors influencing prostate cancer screening in low-income African Americans in Tennessee. JHCPU. 2010; (21): 114-126.

Appendix 4: Flora Ukoli, Khandaker Taher, Mbeja Lomotey, Temple Oguike, Phillip Akumabor, Usifo Osime, Derrick Beech. The Role of Meat, Fish and Egg Intake in Prostate Cancer Risk among Nigerians. Infectious Agents and Cancer. 2009, 4(S1): 1-5.

Appendix 5: Student Posters and Reports:

a. Project 1: (Report by Danielle Jones): Inhibition of PCa Growth by Histone Deacetylase (HDAC) inhibitors. (Mentor: Stewart L)

b. Project 2: (Poster by Charlette Goodin): The Role of lycopene in PCa Risk among African-Americans: A Case-Control Study. (Mentor: Fowke J/Ukoli F)

c. Project 3: (Poster by Liana Geddes): Overcoming barriers to PCa screening among low-income African-Americans in Nashville. (Mentor: Ukoli F/Adams)

d. Project 4: (Poster by Ayodele Osho) Prostate cancer and diet in Jamaican men: A feasibility study. (Mentor: Beech D/Ukoli F)

Appendix 6: Meharry Medical College Institutional Review Board (IRB) continuing review application.

THE ASSOCIATION OF PLASMA FATTY ACIDS WITH PROSTATE CANCER RISK IN NIGERIANS

Flora A. Ukoli, MBBS; Philip N. Akumabor, MBBS; Temple C. Oguike, MBBS; Lemuel L. Dent, MD; Derrick Beech, MD; Usifo Osime, MBBS

Purpose: To investigate the role of fatty acids (FAs) in prostate cancer (PCa) risk in Nigeria, a country in transition to westernized diet high in animal fats, and currently experiencing rising rates of prostate cancer.

Methods: Men ≥40 years were recruited from surgery/urology clinics, University of Benin Teaching Hospital and from 2 rural and 2 urban communities. Personal information, urological symptom history and anthropometrics were recorded, digital rectal examination performed, and 30 mLs of fasting blood collected for prostatic specific antigen and fatty acid (FA) analysis. Odds ratio (OR) of PCa risk was determined by unconditional logistic regression with the plasma FA 1st quartile as reference, controlling for age, education, waist-to-hip ratio, and family history.

Results: Mean ages for 66 (22.6%) cases and 226 (77.4%) controls were 71.9±11.47 and 56.7±12.69 years, $P<.001$, and median (25th, 75th percentile) fasting plasma FA were 2,447 (2,087, 3,024) and 2,373 (2,014, 2,751) μg/mL, respectively. PCa risk trend was observed for total ω-6 FA, adjusted $OR_{Q3vs.Q1}$ 2.33 (95%CI,0.77–7.07), $P<0.05$. Unadjusted $OR_{Q4vs.Q1}$ for behenic and nervonic acids were 2.79 (95%CI,1.27–6.10) and 2.40 (95% CI,1.19–4.85), and unadjusted $OR_{Q2vs.Q1}$ for erucic and arachidonic acids were 4.20 (95%CI,1.79–9.82) and 3.81 (95%CI,1.50–9.70) respectively. Unadjusted $OR_{Q2vs.Q1}$ for ω-3 FAs eicosapentaenoic (EPA) and docosapentaenoic (DPA) were 0.39 (95%CI, 0.18–0.85) and 0.79 (95%CI, 0.35–1.79) respectively.

Conclusions: In this population with high total plasma ω-3, we observed modest positive PCa risk trend with total plasma ω-6 (2.3), inverse risk reduction with EPA (0.4), and strong positive risk associations with behenic (2.8), erucic (4.2), and nervonic (2.4) acids. Total plasma ω-6 is highest in the educated high-income group. These findings should be confirmed in a larger study because of the potential serious implication of dietary transition particularly in a region designated as low-incidence for PCa. (*Ethn Dis.*2009;19:454–461)

Key Words: Prostate Cancer, Fatty Acids, Omega-3, Omega-6, Nigerians, Case-Control

From Department of Surgery, Meharry Medical College, Nashville, Tennessee (FAU, LLD, DB), Department of Surgery (Urology), University of Benin Teaching Hospital, Nigeria (PNA, TCO), Department of Surgery, University of Benin, Benin-City, Nigeria (UO).

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INTRODUCTION

The incidence of prostate cancer (PCa) varies widely across the world. African ancestry, increasing age, and family history are recognized significant risk factors.[1–3] Based on global age-standardized PCa incidence data, Sub-Saharan Africa is designated low-incidence, less than 24.5 per 100,000 inhabitants.[4] Without routine screening in Nigeria, PCa diagnosis is on the rise, becoming the most diagnosed male cancer.[5,6] Comparative studies of African-Americans in Washington, DC and Nigerian men in Ibadan demonstrated similar incidence of latent PCa, although African-Americans recorded 10-fold higher incidence of clinical PCa.[7] Growth and differentiation of the prostate is under androgen control, and differences in estrogen and androgen metabolites and urinary steroid levels observed between healthy Africans and African-Americans were reported to depend on their respective diets, which could explain disparate PCa rates.[8,9] A possible ecological link between PCa and diet was originally based on international differences in PCa mortality rates and national average dietary fat.[10] The role of diet in PCa etiology has been reported in numerous studies including a multicenter study of dietary factors that demonstrated that 10–15% of the ethnical differences in PCa incidence were accounted for by the differences in saturated fat intake,[11] and that diets rich in red meats and fat from animal sources are associated with increased PCa risk.[12–14] Recent increase in PCa incidence among Nigerians has been attributed to improved diagnosis, transition to a more westernized diet high in meat and animal fat, and the increase in the number of older men at risk for PCa resulting from increased longevity.[6,15] Most case-control studies associated high intakes of animal fat and saturated FAs with increased PCa risk based on dietary assessments using food-frequency questionnaires (FFQ), while a few reported objective biomarker information that did not rely on the precision of food composition databases, accuracy of self-reports or the appropriateness of FFQ items.[16,17] The plasma phospholipids sub-fraction better reflects type of dietary fat eat-

We examined PCa risk association of plasma FAs… sub-group totals and individual fasting plasma FA concentrations among Nigerians in a case-control design.

en,[18–20] and fasting plasma concentration reflects usual essential FA intake.[21] We examined PCa risk association of plasma FAs by estimating odds ratio (OR) across quartiles of total, sub-group totals, and individual fasting plasma FA concentrations among Nigerians in a case-control design.

METHODS

Study Population

Apparently healthy men aged ≥40 years were recruited house-to-house in two rural and two urban communities of Edo and Delta states of southern Nigeria. Men presenting with prostate-related symptoms at the surgery/urology clinics, University of Benin Teaching Hospital (UBTH), Benin-City, were also recruited. Participants signed appropriately administered informed consent. Cases were histologically diagnosed with PCa and controls had normal prostate on digital rectal examination (DRE) and serum prostate specific antigen (PSA) <4 ng/mL. Trained and certified research assistants collected demographic and urology history information, FFQ diet assessment by interview, and anthropometric measurements (height, weight, waist, hip, mid-arm circumference, biceps, triceps, and sub-scapular skin-fold thickness) using standard protocols with participants wearing light clothing and without shoes. Participants were instructed to eat dinner before 9:00 pm the previous night, and to fast until their blood was drawn the next morning before 9:00 am by a certified phlebotomist/registered nurse. This was followed by a medical consultation that included a DRE by a general surgeon/urologist. The 30 mL fasting venous blood was drawn into red-, yellow-, and lavender-top vacutainer tubes, centrifuged after standing for 30–60 minutes, sub-fractions were separated into accurately labeled microvials, and samples were stored at −20°C until shipped quarterly, on dry ice, to the United States where they were stored at −40°C. Serum PSA was measured at a reference laboratory in Nashville and the result forwarded to the attending surgeon/urologist within five working days. An aliquot of plasma from each participant was shipped to a specialized research laboratory for FA analyses. The capillary gas chromatography-electron-capture negative-ion mass spectrometry (GC/MS) method was used for the quantitative determination of plasma C8–C26 total FAs.[22]

Table 1. Characteristics of Nigerian study population

Characteristics	Frequency (%)	
	Cases (*n*=66)	Controls (*n*=226)
Recruitment site*		
Community	8(12.1)	165(73.0)
Urology/surgery clinics	58(87.9)	61(27.0)
Age (Years)*		
< 54	2(3.0)	106(46.9)
55–74	40(60.6)	104(46.0)
≥ 75	24(36.4)	16(7.1)
Education status		
< High school	44(66.7)	133(58.8)
High school	6(7.6)	36(15.9)
Some college	8(12.1)	26(11.5)
College/post-grad	8(12.1)	21(9.3)
Not recorded	1(1.5)	10(4.4)
Socioeconomic status		
Low	52(78.8)	157(69.5)
Middle	7(10.6)	16(7.1)
High	4(6.1)	15(6.6)
Not recorded	3(4.5)	38(16.8)
Obesity (BMI)		
Normal weight (<24.9)	45(68.2)	153(67.7)
Overweight (25.0–29.9)	14(21.2)	52(23.0)
Obese I (30–34.9)	2(3.0)	15(6.6)
Obese II (≥35.0)	0(0.0)	1(0.4)
Not recorded	5(7.6)	4(1.8)
Family history of PCa	3(4.5)	4(1.8)
Urology history		
BPH no symptom	4(6.1)	52(23.0)
BPH with symptom	27(40.9)	27(11.9)

BPH - Benign prostatic hyperplasia.
* P<.001.

Statistics

Summary statistics for plasma FA (μg/mL) were reported as mean ± standard deviation (SD) and median (25^{th} percentile, 75^{th} percentile). The Chi-squared and non-parametric tests for independent samples were used to compare cases and controls as appropriate, and unconditional logistic regression was used to estimate OR (95% confidence intervals) of PCa risk across quartiles of plasma FA relative to the lowest quartile (Q1), with P calculated with FA as continuous data in each quartile. ORs were adjusted for age, education, family history of PCa, and waist-hip ratio. Income was appropriately stratified as low, middle, and high, and educational status as low (≤6), middle (6–12), and high (≥13) formal years of education. Data analysis was performed using SPSS, v14.0 (SPSS, 2001, Chicago, Ill.). Study participants with elevated PSA≥4 ng/mL who did not have any prostate biopsy informa-

Table 2. Plasma fatty acids (μg/ml) of Nigerians by educational status

	Mean (SD)				
	Primary or less	Some/complete secondary	Post secondary or college	*P*-value	
Fatty acids	*n*=182	*n*=82	*n*=69	Group*	Linear†
Total	2,486.7(589.4)	2,341.6(612.6)	2,658.4(764.0)	.01	.20
Saturated total	892.6(217.1)	855.5(247.9)	958.1(289.5)	.03	.16
ω-9 total	685.4(218.6)	603.8(179.9)	675.4(234.0)	.02	.31
ω-7 & ω-5 total	115.4(51.9)	102.2(54.0)	116.0(65.0)	.17	.70
ω-6 total	661.6(181.6)	658.1(181.7)	766.9(216.4)	.0001	.001
ω-3 total	116.6(60.6)	107.9(57.7)	127.6(86.3)	.19	.42
Trans total	16.6(6.2)	14.2(6.1)	18.2(8.5)	.004	.46
Lauric	8.0(20.3)	7.1(9.2)	10.1(14.2)	.53	.50
Myristic	28.5((20.8)	27.7(14.9)	34.8(26.6)	.07	.07
Palmitic	615.1(144.2)	582.9(176.1)	647.4(203.5)	.06	.39
Stearic	183.9(44.6)	179.3(51.1)	196.9(53.9)	.07	.13
Behenic	16.2(4.9)	16.5(4.9)	20.8(6.8)	.0001	.0001
Palmitoleic	68.9(38.0)	60.5(39.9)	68.1(46.4)	.28	.60
Vaccenic	45.0(33.6)	38.6(13.9)	43.4(19.6)	.21	.42
Palmitelaidic	2.2(1.4)	1.9(1.1)	2.3(1.5)	.18	.60
Elaidic	9.2(3.7)	7.9(3.7)	10.1(4.9)	.006	.60
Oleic	625.3(213.9)	551.5(170.9)	615.5(221.6)	.03	.32
Mead	4.6(3.5)	3.6(2.6)	3.9(3.1)	.05	.07
Erucic	0.9(2.2)	0.7(0.2)	0.8(0.3)	.46	.40
Nervonic	32.3(9.0)	30.7(9.7)	35.5(11.7)	.01	.08
Linoleic	492.8(134.8)	493.4(128.0)	560.7(162.8)	.002	.002
γ-linolenic	7.9(5.2)	7.8(5.0)	9.3(5.2)	.11	.08
Di-homo-γ-linolenic	28.7(11.5)	27.7(11.5)	33.5(14.2)	.007	.018
Arachidonic	116.5(46.0)	114.2(53.3)	145.6(62.1)	.0001	.001
α-linolenic	6.0(4.0)	5.7(3.2)	6.6(4.8)	.35	.37
Eicosapentaenoic	28.7(20.2)	29.9(24.4)	32.2(31.1)	.58	.31
Docosapentaenoic	3.4(2.1)	3.1(2.1)	4.1(2.8)	.03	.12
Docosahexaenoic	69.0(36.0)	60.1(29.2)	74.8(48.6)	.05	.60

* Between-group difference.
† Linearity across group difference.

tion at the time of data analysis were excluded from the risk analysis.

RESULTS

Of 340 consenting participants, 66 (19.4%) were confirmed PCa cases, 48 (14.1%) with elevated PSA, and 226 (66.5%) were controls, with mean ages of 71.9±11.47, 67.0±11.12, and 56.7±12.69, respectively, $P<.001$. Prostate cancer cases were more likely to report a family history compared to controls, 3 (4.5%) to 4 (1.8%), present with symptoms, 27 (40.9%) to 27 (11.9%), and have enlarged prostate on DRE without symptoms, 4 (6.1) to 52 (23.0), $P<.001$. Cases and controls were similar by marital, educational, socioeconomic, and obesity status (Table 1). Total FA was 2,526±781 μg/mL, 2,236±526 μg/mL, and 2,778±710 μg/mL, $P<.04$, across low, middle, and high income groups, respectively (not displayed). Total, saturated, all ω-6 except γ-linolenic, trans FAs, behenic, trans elaidic, nervonic, docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA), but not total ω-3 FAs, were highest in the more educated men. Total ω-9 FAs, specifically oleic and mead, were higher in men with low education (Table 2).

All saturated FAs were similar for cases and controls except for behenic acid with a median of 18.4 (14.8, 22.6) μg/mL to 15.8 (12.7, 19.8) μg/mL, respectively, $P<.001$. Monounsaturated FAs were similar for cases and controls except for erucic acid with a median of 0.8 (0.7, 0.9) μg/mL to 0.7 (0.5, 0.8) μg/mL, respectively, $P<.001$, and nervonic acid with median 38.0 (32.7, 48.9) μg/mL to 28.8 (24.3, 34.7) μg/mL, respectively, $P<.001$. Arachidonic acid was higher in cases, 132.0 (105.9, 160.6) μg/mL to 104.5 (76.6, 143.4) μg/mLl, $P<.001$. Regarding ω-3 FAs, eicosapentaenoic (EPA) was lower in cases, DPA higher in cases, and DHA was similar for cases and controls. Essential ω-6 linoleic acid and essential ω-3 α-linolenic acid were similar for cases and controls (Table 3). Adjusted OR trend was significant across quartiles of total ω-6 FA with $OR_{Q3vs.Q1}$ 2.33 (95%CI, 0.77–7.07), but not for total saturated nor trans FAs. Unadjusted and adjusted OR trends were not

Table 3. Plasma fatty acids (μg/mL) of Nigerian prostate cancer cases and controls

Fatty acids	Median (25^{th}, 75^{th} percentile)	
	Cases	Controls
Total	2446.8 (2,087.4, 3,024.2)	2,373.5 (2,013.6, 2,750.6)
Saturated	886.5 (728.2, 975.1)	846.2 (728.2, 975.1)
n-9 total	624.6 (532.3, 875.4)	602.7 (517.4, 750.2)
n-7 & n-5 total	95.9 (80.4, 130.0)	101.0 (76.8, 135.3)
n-6 total	694.4 (564.8, 880.1)	654.0 (550.4, 779.5)
n-3 total	97.1 (67.3, 145.0)	104.9 (75.3, 152.4)
Trans total	15.1 (10.6, 20.9)	15.5 (12.2, 20.0)
Lauric	4.4 (2.5, 9.0)	4.2 (2.7, 8.0)
Myristic	21.6 (16.2, 37.2)	24.1 (16.5, 38.3)
Palmitic	603.0 (539.2, 744.1)	572.0 (503.6, 658.5)
Stearic	188.0 (152.0, 229.6)	175.4 (150.0, 209.1)
Behenic	18.4 (14.8, 22.6)	15.8 (12.7, 19.8)†
Palmitoleic	53.0 (42.3, 73.4)	58.8 (40.2, 85.0)
Vaccenic	41.2 (33.0, 52.5)	38.1 (30.3, 48.3)
Palmitelaidic (trans)	1.8 (1.1, 2.7)	2.1 (1.3, 2.9)
Elaidic (trans)	8.7 (5.9, 12.1)	8.6 (6.5, 11.0)
Oleic	568.0 (471.9, 809.0)	550.3 (471.7, 687.7)
Mead	3.5 (2.1, 5.2)	3.5 (1.9, 5.6)
Erucic	0.8 (0.7, 0.9)	0.7 (0.5, 0.8)†
Nervonic	38.0 (32.7, 48.9)	28.8 (24.3, 34.7)†
Linoleic	513.4 (436.3, 658.7)	491.8 (417.1, 585.6)
γ-linolenic	6.7 (4.2, 11.3)	7.0 (4.6, 10.1)
Di-homo-γ-linolenic	30.6 (21.1, 38.6)	26.4 (20.5, 34.5)
Arachidonic	132.0 (105.9, 160.6)	104.5 (76.6, 143.4)†
α-linolenic	5.2 (3.9, 7.4)	5.0 (3.6, 6.9)
Eicosapentaenoic	16.7 (11.5, 32.3)	26.2 (14.0, 40.4)*
Docosapentaenoic	3.2 (2.3, 4.9)	2.7 (1.8, 3.9)*
Docosahexaenoic	58.8 (42.7, 78.7)	58.6 (42.6, 80.1)

* $P<.05$.
† $P<.001$.

significant for total ω-3 FA (Table 4). Unadjusted risk trend was significant for behenic acid, $OR_{Q4vs.Q1}$ 2.79 (95%CI, 1.27–6.10) and nervonic acid, 2.40 (95%CI, 1.19–4.85), and for erucic acid, 4.20 (95%CI, 1.79–9.82) and arachidonic acid, 3.81 (95%CI, 1.50–9.70). For EPA unadjusted and adjusted $OR_{Q2vs.Q1}$ were 0.39 (95%CI, 0.18–0.85) and 0.39 (95%CI, 0.15–0.97), respectively (Table 5).

DISCUSSION

Early epidemiological studies suggested possible causal association between dietary fat and PCa risk as demonstrated by dramatic changes in PCa incidence among men who moved from PCa low-incidence regions with low dietary fat intake to PCa high-incidence regions with high dietary fat intake, alluding to the overriding importance of increased exposure to environmental risk factors.[23,24] Western diet, fat in general, meat and animal fat specifically, is associated with increased PCa risk, whereas diets high in fish content are associated with reduced PCa risk,[25–27] and an African high-fiber, low-fat diet is associated with reduced risk for atherosclerosis and cancer of the large bowel.[28] Lower PCa incidence in southeast Nigeria could be related to their high-fish, low-meat diet.[6] Differences in the dietary content of oils, fats, and protein from plant versus animal sources account for a large part of nutrient diversity across African countries.[29] Although microethnic dietary diversity was minimized by conducting the study in a limited ethnogeographic region of southern Nigeria, a wide range of fasting plasma FA, 891.7 μg/mL to 7,828.8 μg/mL, with a mean of 2,527.7±752.4 μg/mL, confirmed the wide range in dietary fat intake.

Nutrition transition to high-fat diets in low-income nations is a result of human preference for palatable dishes, availability of cheap vegetable oils and fats, and urbanization,[30,31] accounting for similar FA profile across diverse economic groups in this study. Differences for some and not all FA subgroups across education rather than income strata indicate a dietary transition, particularly in the more educated group who can afford more meat and animal products and who now record higher levels of saturated, ω-6 and trans FAs. This dietary transition has been alluded to as a contributing factor to increasing cancer rates in Nigerians,[15] although no attempt has been made to compare PCa rates across socioeconomic stratification. Comparable levels of monounsaturated FAs across education and income groups can be explained by popular consumption of readily available palm fruit, palm kennel, and coconut oils, and comparable total ω-3 attributed to readily available fish. Omega-3 FAs DPA and DHA are higher in the postsecondary/college group probably because they eat the more desirable and expensive fresh water fish, rather than the cheaper commonly available frozen fishes like mackerel. Fish remains the main source of animal protein in this population,[32] a relic of the historical eating pattern of shoreline Africans.[33] Oleic and mead acids derived from animal and plant sources were highest among men with low education, suggesting deficiency of dietary essential FA.[34]

Plasma and tissue FA compositions are more objective exposure measures than dietary assessment estimations from FFQs, and concentrations in the plasma phospholipids and cholesterol

Table 4. Odds ratios and 95% confidence interval for prostate cancer risk across quartiles of sub-group plasma fatty acids in Nigerians

Sub-group fatty acid quartiles	Unadjusted OR (95% CI)	*P**	Adjusted OR† (95% CI)	*P**
Total				
Q1	1.00		1.00	
Q2	1.52 (0.70–3.30)		0.78 (0.30–2.03)	
Q3	1.66 (0.76–3.63)		1.30 (0.50–3.39)	
Q4	1.19 (0.55–2.53)	.57	0.80 (0.32–1.98)	.70
Total saturated				
Q1	1.00		1.00	
Q2	1.82 (0.80–4.17)		1.14 (0.42–3.07)	
Q3	1.16 (0.54–2.52)		1.14 (0.46–2.87)	
Q4	1.00 (0.47–2.15)	.46	1.02 (0.41–2.54)	.99
Total ω-9				
Q1	1.00		1.00	
Q2	1.44 (0.66–3.15)		0.76 (0.28–2.04)	
Q3	1.35 (0.62–2.92)		0.82 (0.32–2.10)	
Q4	1.22 (0.56–2.64)	.81	0.79 (0.31–2.03)	.95
Total ω-6				
Q1	1.00		1.00	
Q2	1.39 (0.64–3.01)		0.65 (0.24–1.76)	
Q3	2.30 (0.98–5.38)		2.33 (0.77–7.07)	
Q4	0.91 (0.44–1.88)	.14	0.55 (0.22–1.36)	.05
Total ω-3				
Q1	1.00		1.00	
Q2	0.65 (0.30–1.40)		0.50 (0.20–1.28)	
Q3	0.87 (0.40–1.93)		0.69 (0.26–1.81)	
Q4	1.07 (0.48–2.42)	.58	0.88 (0.34–2.30)	.49

* Calculated with fatty acid in each quartile as a continuous variable.
† OR adjusted for age, education, family history of prostate cancer, and waist-hip ratio.

Plasma total ω-3 FA is high across all socioeconomic groups in this population, while plasma ω-6 is significantly higher among educated men with higher income.

ester fractions better reflect medium-term (weeks to months) dietary intake. We measured fasting FAs in the combined triglycerides and phospholipids fractions rather than the more expensive sub-fraction analysis.[35] We observed that total FA per se did not explain PCa risk probably because the percentage of energy derived from fat varied widely, and we cannot confirm the 20–25% reported for rural and urban West Africa[36,37] in the absence of Nigerian food composition tables for indigenous Nigerian soups and sauces which are the major sources of dietary fats and oils. Our findings are consistent regarding ω-3 and ω-6 polyunsaturated FAs, which are reported to be associated with reduced and increased PCa risk, respectively.[38,39] There is a significant risk trend across quartiles of total ω-6 FA but the 2-fold PCa risk observed between the 3rd and 1st quartile is not statistically significant. Reports about the role of ω-6 FAs is mixed, with a significant positive association across tertiles, adjusted OR 3.6 (95%CI, 1.3–9.7),[40] but unconfirmed in human dietary intake studies,[41] while laboratory evidence remains very strong.[42] We did not observe convincing protective association for total ω-3 FAs as in studies of marine FAs,[43,44] however, the evidence for a protective effect for EPA is consistent in this data. It is possible that storage and preparation methods of fish can interfere with FA composition like other nutrient contents; fresh fish retaining a higher nutritional value than frozen fish.[45] The fact that diets rich in fish are not always associated with reduced PCa risk[46] underscores the influence of entire diets over single food items, and interactions with genetic and other environmental factors. Unlike the RR of 2.21 (95%CI, 1.14–4.29), $P<.06$ reported in a United States study,[47] our data did not show PCa risk association with trans FAs probably because of very low plasma trans FA in this population, resulting from infrequent intake of processed foods high in partially hydrogenated vegetable oils.

Regarding saturated FAs, we did not observe PCa risk association with myristic acid like other reports,[39,48] but observed significant risk trends and 2 to 6-fold PCa risk association across quartiles of behenic acid. Lack of association with palmitic acid is in agreement with the Physicians' Health Study,[46,49] but in contrast with a Norwegian study that reported a 2-fold risk with palmitic acid.[48] Our data did not show protective association with monounsaturated oleic acid as expected, given the popular report of the protective effect of diets rich in olive oil, the major source of oleic acid.[50] Rather nervonic and erucic FAs demonstrated 4-fold and 2-fold PCa risk associations, respectively, for which we have no biological explanation. Although essential linoleic (ω-6) and α-linolenic (ω-3) FAs are associated with PCa risk,[41,46,49] this was not observed in our study. However arachidonic acid, a metabolite of linoleic acid, did show a 2-fold significant risk comparing the 2nd to the 1st quartile.

One strength of our study is that we have reported pilot data from an

Table 5. Odds ratios and 95% confidence interval for prostate cancer risk across quartiles of selected plasma fatty acids among Nigerians

Fatty acid quartiles	Unadjusted OR (95% CI)	*P**	Adjusted OR† (95% CI)	*P**
Behenic				
Q1	1.00		1.00	
Q2	6.75 (2.58–17.63)		5.40 (1.79–16.36)	
Q3	1.53 (0.76–3.08)		1.32 (0.54–3.21)	
Q4	2.79 (1.27–6.10)	.000	2.47 (0.97–6.27)	.01
Erucic				
Q1	1.00		1.00	
Q2	4.20 (1.79–9.82)		2.16 (0.81–5.72)	
Q3	4.26 (1.82–9.96)		2.15 (0.82–5.64)	
Q4	1.06 (0.52–2.16)	.000	0.94 (0.40–2.20)	.16
Nervonic				
Q1	1.00		1.00	
Q2	13.6 (4.88–37.8)		5.32 (1.74–16.29)	
Q3	8.89 (3.57–22.1)		4.78 (1.76–12.97)	
Q4	2.40 (1.19–4.85)	.000	1.78 (0.79–4.00)	.003
Linoleic				
Q1	1.00		1.00	
Q2	1.15 (0.53–2.54)		0.47 (0.17–1.34)	
Q3	1.43 (0.64–3.21)		0.96 (0.34–2.72)	
Q4	0.82 (0.39–1.73)	.57	0.38 (0.15–0.99)	.12
Arachidonic				
Q1	1.00		1.00	
Q2	3.81 (1.50–9.70)		2.59 (0.85–7.86)	
Q3	1.75 (0.79–3.87)		1.93 (0.73–5.14)	
Q4	0.74 (0.36–1.50)	.003	0.75 (0.32–1.74)	.06
α- linolenic				
Q1	1.00		1.00	
Q2	1.38 (0.63–3.05)		1.04 (0.39–2.73)	
Q3	1.08 (0.50–2.31)		0.80 (0.33–1.98)	
Q4	1.19 (0.55–2.56)	.87	0.98 (0.40–2.40)	.95
Eicosapentaenoic				
Q1	1.00		1.00	
Q2	0.39 (0.18–0.85)		0.39 (0.15–0.97)	
Q3	0.57 (0.25–1.30)		0.48 (0.18–1.28)	
Q4	0.82 (0.35–1.91)	.08	1.09 (0.40–2.96)	.07
Docosapentaenoic				
Q1	1.00		1.00	
Q2	0.79 (0.35–1.79)		0.36 (0.13–1.00)	
Q3	1.55 (0.63–3.83)		0.44 (0.16–1.22)	
Q4	1.49 (0.62–3.61)	.35	0.44 (0.17–1.19)	.24

* Calculated with fatty acid concentration in each quartile as a continuous variable.
† OR adjusted for age, education, family history of prostate cancer, and waist-hip ratio.

understudied population and have provided adequate storage conditions to allow the FAs to remain stable.[51–53] Study limitations include: plasma FAs may not accurately reflect prostate levels;[41] measuring FAs only in the plasma phospholipids and triglycerides sub-fractions; and consenting PCa cases with localized or metastatic disease. A larger sample size is necessary to accommodate the wide variance in FA measures, allowing for more detailed risk analysis stratified by education status. Restricting recruitment to newly diagnosed cases will improve the precision of our findings. As we increase sample size we intend to expand our studies to simultaneously investigate genetic and antioxidant effects that have been shown in animal and in-vitro studies to have complex physiologic and cellular relationship with a number of FAs,[16] which can confound findings.

CONCLUSIONS

Plasma total ω-3 FA is high across all socioeconomic groups in this population, while plasma ω-6 is significantly higher among educated men with higher income. This data supports modest positive PCa risk association with total plasma ω-6 FA and a consistent inverse risk association with EPA, but not total ω-3 FA. Strong PCa risk association was observed for unsaturated behenic, and monounsaturated erucic and nervonic acids. Transition to diets rich in animal fat can potentially increase PCa risk even in a population on a high-fish diet, and the potential for serious implications should be viewed carefully, particularly in a region designated as low-incidence for prostate cancer. These are preliminary findings and increasing our sample size will provide adequate statistical power for risk estimations adjusted for more relevant variables within population sub-groups. Furthermore in-vitro investigations are warranted to clarify the roles and mechanisms of action of behenic, nervonic and erucic FAs in prostate carcinogenesis.

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The Association of Plasma Fatty Acids with Prostate Cancer Risk in African Americans and Africans

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Abstract: Higher risk for prostate cancer (PCa) among African Americans is partly associated with exposure to dietary fatty-acids, the carcinogenic effects of which remain controversial. Odds ratio of PCa risk was determined by unconditional logistic regression comparing highest with lowest quartiles of plasma fatty-acids in a case-control design. Mean age for 173 African Americans and 340 Nigerians was 56.9 ± 9.8 and 60.1 ± 14.0, $p<.006$, median (25th, 75th percentile) plasma fatty-acid was 2598 (2306, 3035) μg/ml and 2420 (2064, 2795) μg/ml, $p<.001$, with 48 (27.7%) and 66 (19.4%) PCa cases, respectively. African Americans recorded higher total, omega-6, and *trans*, but lower saturated and omega-3 fatty-acids, with non-significant PCa risk association for total, omega-6 and *trans* fatty acids. Positive PCa risk trend was observed in both populations with nervonic, erucic, and arachidonic acids, with docosahexaenoic acid (DHA) among African Americans, and with behenic and stearic acids in Nigerians. Non-significant negative PCa risk trend was observed with ecosapentaenoic acid (EPA) in Nigerians only. These preliminary findings need to be further explored in a larger study that will include risk analysis of fatty-acid ratios to clarify their combined impact on PCa risk.

Key words: Prostate cancer, plasma fatty acids, African Americans, Nigerians, case-control.

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African American men have consistently recorded the highest prostate cancer (PCa) incidence rate in the world. Along with increasing age and family history of PCa, African ancestry has been recognized as a significant risk factor for PCa.[1–3] The recorded incidence of PCa varies widely across the world. Based on global data of age-standardized PCa incidence in 2002, Nigeria (like other sub-Saharan African countries) was designated a low-incidence region with less than 24.5 cases per 100,000.[4] Prostate cancer incidence rates estimated from hospital data in Nigeria indicate a steady increase in the number of cases diagnosed from the 1980s to 1990s, to the extent that PCa has become the most diagnosed male cancer, with an estimated incidence rate of 61.3/100,000[5,6] despite the absence of routine screening. The need to consider the contribution of diet to this trend has been raised by researchers.[5]

Two decades before the prostate specific antigen (PSA) screening era in the 1990s, comparative studies of African Americans in Washington, D.C. and Nigerians in Ibadan demonstrated similar incidence of latent PCa, although the African Americans recorded a 10-fold higher incidence of clinical PCa.[7] Hormonal factors are considered very important in prostate carcinogenesis because the growth and differentiation of the prostate is under androgen control such that men with congenital abnormalities in androgen metabolism do not develop PCa. Differences observed between healthy indigenous Africans and African Americans in their levels of estrogen and androgen metabolites and urinary steroids were reported to depend on their respective diets, which could explain their disparate PCa rates.[8,9]

The possible link between PCa and diet was originally suggested based on observations from ecological studies that demonstrated similar trends in international differences in PCa mortality rates and national average intakes of fats in the diet,[10] such that the role of diet in PCa etiology continues to be widely studied in numerous populations. In a multicenter study that investigated the role of dietary factors in PCa risk, it was reported that PCa was associated with total fat intake in Whites, African Americans, and Asian Americans, and that 10–15% of this racial/ethnic difference in PCa incidence was accounted for by the differences in saturated fat intake.[11] Other studies have linked consumption of diets rich in red meats and fat from animal sources to increased PCa risk among African Americans, suggesting that reducing dietary intake of fat from animal sources can lead to decreased PCa incidence and mortality.[12–14] The low incidence of PCa among Nigerians in comparison with their American counterparts was attributed to their traditional diet, which unlike the Western diet, is low in animal fats and meat.[6] The recent increase in PCa incidence in Nigeria also has been postulated to have resulted from increased longevity, improved diagnosis, and exposure to a more Westernized dietary lifestyle.[15] Studying the role of dietary fat in PCa risk in genetically related populations with disparate PCa incidence and dietary fat intake can be useful in better understanding the nature of this association.

Case-control studies have reported increased risk of PCa among men with high intake of animal fat or saturated fatty acids based on dietary assessment using food-frequency questionnaires (FFQ), but only some of them included biomarker information.[16] Measurements of biological markers are believed to be more objective than estimates from FFQ, because biomarkers do not rely on the precision of food composition databases, accuracy of self-reports, or the appropriateness of FFQ items,[17] and may therefore be

more appropriate for comparing diverse populations. Fatty acids exist and are measured in sub-fractions of plasma. The fatty acid composition of plasma phospholipids reflects well the type of dietary fat eaten by individuals and has been used as an objective estimate of the type of fats proportionally consumed, even in ethnically and racially diverse cohort studies.[18–20] Fasting plasma fatty acid measurement has been suggested as most suitable for such epidemiological studies as they best reflect the usual levels of essential fatty acids. Non-fasting plasma levels can be affected by recent fat intake that may be different from the usual eating stayle.[21] In this pilot study we document the feasibility of recruiting PCa cases and controls and collecting fasting blood samples from study participants in both study sites, and shipping blood samples on dry ice from Nigeria to the U.S. to arrive within three days of shipment. We have examined whether plasma concentrations of fatty acids are associated with the risk of PCa by estimating odds ratio (OR) across quartiles of total, sub-group totals, and selected individual plasma fatty acid concentrations among culturally distinct populations of African Americans and Nigerians in a case-control design, using the lower quartile as the reference.

Methods

Population studied. Apparently healthy African American men 40 years and older and men diagnosed with PCa were recruited by media announcements and flyer distribution at community health fairs, doctors' offices, churches, barbershops, and other public places and events. In addition, PCa cases were recruited from the urology clinic and cases diagnosed not more than five years earlier identified through the state cancer register were contacted directly by mail to consider participating in the study. The cancer register did not include men diagnosed within the previous two years. In southern Nigeria, apparently healthy men 40 years and older were recruited by house-to-house invitation in two rural and two urban communities of Edo and Delta states. Prostate cancer cases diagnosed in the past five years were recruited from the urology clinic and men presenting in the general surgery and urology clinics with symptoms suggestive of prostate pathology were also recruited at the University of Benin Teaching Hospital (UBTH). Prostate cancer cases were men with abnormal digital rectal examination (DRE) and/or abnormal serum level of prostate specific antigen (PSA) above 4ng/ml who were histologically diagnosed with PCa, while controls were men with a normal prostate on DRE and PSA level of $\leq$4 ng/ml. Men with fasting blood sugar over 100 mg/dl, men on insulin, hormone treatment for PCa, anti-retrovirals, chemotherapy, a prescribed diet other than low-salt diet, those who reported weight loss within the past year, or who were diagnosed with any cancer other than skin cancer were not eligible to participate in the study. Men who were hospitalized, seriously ill, or had major surgery within the past three months were also excluded from participating in this study. All subjects signed informed consent on forms approved by the Meharry Medical College Institutional Review Board and the Research Ethics Committee of the UBTH, and they received cash and gift incentives at the completion of each of the two study visits.

Data collection. *Demographics and medical history*. During the first study visit, trained interviewers collected socio-demographic information, urology symptom history,

and dietary assessment by FFQ (to be analyzed). Height, weight, waist, hip, mid-arm circumference, biceps, triceps, and sub-scapular skin-fold thickness were measured by the principal investigator and a trained assistant while participants were wearing light clothing and were without shoes. Digital rectal examination was performed by a general surgeon or urologist after blood draw.

Blood collection. For the second study visit, participants were instructed to eat dinner before 9:00 p.m. the previous night, and then to skip breakfast until their blood was drawn the next morning before 9:00 a.m. by a certified phlebotomist/registered nurse. 30 ml fasting venous blood was drawn into three (red-, yellow-, and lavender-top) vacutainer tubes, centrifuged after standing for 30–60 minutes at room temperature, and sub-fractions separated into accurately labeled microvials. Nigerians' samples were stored at −20°C until quarterly shipment on dry ice to the principal investigator (Ukoli, F.) in the United States where they were stored together with the African Americans' samples at −40°C, and an aliquot of serum immediately shipped to a local commercial laboratory for PSA measurement. An aliquot of plasma from each participant was also shipped to a specialized research laboratory for fatty acid analyses in three annual batches. The capillary gas chromatography-electron-capture negative-ion mass spectrometry (GC/MS) method was used for the quantitative determination of plasma C8–C26 total fatty acid. After addition of the internal standard mixture to 100 μL of plasma, fatty acids were hydrolyzed from triglycerides and phospholipids, followed by hexane extraction, and derivatization with pentafluorobenzyl bromide. The resulting fatty acid pentafluorobenzyl esters were dissolved in hexane, and then analyzed in two steps: a splitless injection and a second, split injection (1:100) for quantification of the more abundant fatty acids recorded in μg/ml. This method is reported to be better than gas chromatographic analysis with flame ionization detection (GC/FID).[22]

Data analysis. The chi-squared and non-parametric tests for independent samples were used to compare cases and controls as appropriate, and unconditional logistic regression was used to estimate the OR and 95% confidence intervals (95% CI) of PCa risk across quartile categories of plasma fatty acids (μg/ml) relative to the lowest (1st) quartile for each population. Odds ratios were adjusted for age, level of education, family history of PCa, and waist-hip ratio, the variables that were significantly associated with plasma fatty acid concentration. Annual income was stratified to low (<$25,000), middle ($25,000–$49,999), and high (≥$50,000), with the equivalent cut-points for Nigerian at N35,000 and N65,000 that were amended regularly to reflect changes in the salary structure over the study period. All data analyses were performed using SPSS version 14.0 (SPSS 2001).[23] Fatty acid assay was completed for 513 participants, 173 (33.7%) African Americans and 340 (66.3%) Nigerians. We present PCa risk analysis of total fatty acid, six fatty acid sub-groups (saturated, n-9, n-7/n-5, omega-6, omega-3 and *trans*), and 21 abundant physiologically relevant plasma fatty acids for African Americans and Nigerians. Men with elevated PSA ≥4 ng/ml who did not have any prostate biopsy information at the time of data analysis, 29 (16.8%) African Americans and 48 (14.1%) Nigerians, were excluded from case-control comparisons and PCa risk analysis.

Results

Demographic characteristics. The socio-demographic and other characteristics of the African American and Nigerian cases and controls are displayed in Table 1. Mean age for the African Americans and Nigerians was, respectively, 56.9 ± 9.8 and 60.1 ± 14.0 years ($p<.006$). There were 48 (33.3%) African American PCa cases and 96 (66.7%) controls, and 66 (22.6%) Nigerian PCa cases and 226 (77.4%) controls ($p<.012$). Nigerian PCa cases were more likely to present with prostate related symptoms (27 [40.9%]) than the controls (27 [11.9%]) ($p<.001$); this was not true to the same extent of the African American participants for whom the prevalence for symptoms was one (2.1%) for PCa cases and four (4.2%) for controls. African American cases were more likely to report a family history of PCa than their controls (15 [31.2%] to 10 [10.4%]) ($p<.002$); the same was not observed in Nigerian cases and controls (three [4.5%] to four [1.8%]). The African American participants reported more years of formal education than the Nigerians; however, there was no difference by educational attainment between cases and controls within each population. There were 70 (48.6%) low-income African Americans, and 209 (71.6%) low-income Nigerians ($p<.001$). There were more low-income controls than PCa cases (53 [55.2%] and 17 [35.4%]) ($p<.04$) in the African American sample (Table 1).

Table 1.

SOCIO-DEMOGRAPHIC CHARACTERISTICS, OBESITY STATUS, AND UROLOGY HISTORY OF AFRICAN AMERICAN AND NIGERIAN PROSTATE CANCER CASES AND CONTROLS

	Distribution: N (%)			
	African Americans		Nigerians	
Characteristics	**Cases (48)**	**Controls (96)**	**Cases (66)**	**Controls (226)**
Age (years)				
<54	6(12.5)	61(63.5)**	2(3.0)	106(46.9)**
55–74	34(70.8)	31(32.3)	40(60.6)	104(46.0)
≥75	8(16.7)	4(4.2)	24(36.4)	16(7.1)
Education status[a]				
<High school	6(12.5)	11(11.5)	44(66.7)	133(58.8)
High school	16(33.3)	41(42.7)	6(7.6)	36(15.9)
Some college	3(6.2)	17(17.7)	8(12.1)	26(11.5)
College/post-grad.	20(41.7)	27(28.1)	8(12.1)	21(9.3)
Not recorded	3(6.2)	0	1(1.5)	10(4.4)

(Continued on p. 132)

Table 1. *(continued)*

	Distribution: N (%)			
	African Americans		Nigerians	
Characteristics	**Cases (48)**	**Controls (96)**	**Cases (66)**	**Controls (226)**
Job status[a]				
Not working	5(10.4)	30(31.3)**	1(1.5)	26(11.5)**
Retired	26(54.2)	11(11.5)	34(51.5)	51(23.4)
Part-time	5(10.4)	14(14.6)	3(4.5)	9(4.0)
Full-time	8(16.7)	37(38.5)	26(39.4)	132(58.4)
Not recorded	4(8.3)	4(4.2)	2(3.0)	8(3.5)
Income[a]				
Low	17(35.4)	53(55.2)*	52(78.8)	157(69.5)
Middle	16(33.3)	22(22.9)	7(10.6)	16(7.1)
High	13(27.1)	14(14.6)	4(6.1)	15(6.6)
Not recorded	2(4.2)	7(7.3)	3(4.5)	38(16.8)
Marital status[a]				
Single	7(14.6)	35(36.5)*	0(0.0)	6(2.7)
Married	20(41.7)	21(21.9)	48(72.7)	165(73.0)
Separated/divorced	11(22.9)	30(31.3)	1(1.5)	17(7.5)
Widowed	4(8.3)	6(6.3)	2(3.0)	3(1.3)
≥2 Wives/marriages	4(8.3)	4(4.2)	15(22.7)	33(14.6)
Not recorded	2(4.2)	0	0	2(0.9)
Obesity[a] (BMI)				
Normal weight (<24.9)	10(20.8)	30(31.3)	45(68.2)	153(67.7)
Overweight (25.0–29.9)	17(35.4)	29(30.2)	14(21.2)	52(23.0)
Obese I (30–34.9)	15(31.3)	22(22.9)	2(3.0)	15(6.6)
Obese II (≥35.0)	3(6.2)	15(15.6)	0(0.0)	1(0.4)
Not recorded	3(6.2)	0	5(7.6)	4(1.8)
Urology history[a]				
Family history of PCa	15(31.3)	10(10.4)*	3(4.5)	4(1.8)
BPH no symptom	7(14.6)	12(12.5)	4(6.1)	52(23.0)**
BPH with symptom	1(2.1)	4(4.2)	27(40.9)	27(11.9)

Note: probability is marked in two ways on this table. For comparisons between African Americans and Nigerians, significance of difference at the p<.001 level is marked as [a]. For comparisons between cases and controls within each group, astericks are used to mark significance of difference: *<.01; **<.001.
BMI = body mass index
PCa = prostate cancer
BPH = benign prostatic hyperplasia

Plasma fatty acids. *African American and Nigerian comparisons*. Median total plasma fatty acid was 2,597.94 μg/ml for African Americans and 2,419.95 μg/ml for Nigerians ($p<.001$). Total saturated, n-9 and omega-3 fatty acids were higher in Nigerians, while total *trans* and omega-6 fatty acids were higher in African Americans. Except for vaccenic (n-7) and mead (n-9), all other plasma fatty acids were significantly different for both populations. Essential fatty acids linoleic and α-linolenic acids, omega-6 fatty acids γ-linolenic and arachidonic, and omega-3 fatty acid docosapentaenoic acid (DPA) were about two-fold higher in African Americans than in Nigerians, while saturated fatty acid lauric acid and omega-3 fatty acid eicosapentaenoic acid (EPA) were, respectively, four-fold and two-fold higher in Nigerians (Table 2).

Case-control comparisons. Median total plasma fatty acid was lower among African American cases than among controls (2,410 μg/ml to 2,759 μg/ml, $p<.008$) and so were the medians for other sub-group fatty acids except for omega-3 fatty acid (with values of 1,026 μg/ml to 1,108 μg/ml, $p<.06$; 42.9 μg/ml to 75.7 μg/ml, $p<.001$; and 93.2 μg/ml to 77.5 μg/ml, $p<.009$, for omega-6, *trans*, and omega-3 fatty acids, respectively). Median total plasma fatty acid for Nigerian cases and controls was 2,447 μg/ml to 2,373 μg/ml, $p<.16$, and the equivalent median values for omega-6, *trans* and omega-3 fatty acids were 694.4 μg/ml to 654.0 μg/ml, $p<.06$; 15.1 μg/ml to 15.5 μg/ml, $p<.75$; and 97.1 μg/ml to 104.9 μg/ml, $p<.39$. Of the 21 physiologically abundant fatty acids in this analysis, 13 in African Americans and six in Nigerians differed significantly for cases and controls. African American cases recorded higher levels of erucic, nervonic, and docosahexaenoic acid (DHA) than their controls. Nigerian cases recorded higher behenic, erucic, nervonic, arachidonic and DPA than their controls. Omega-3 fatty acid eicosapentaenoic acid (EPA) was statistically lower in Nigerian cases than in their controls (16.7 μg/ml vs. 26.2 μg/ml, $p<.05$). Linoleic acid was lower in African American cases (707.1 μg/ml vs. 791.8, $p<.01$) but statistically similar for Nigerian cases and controls (513.4 μg/ml to 491.8 μg/ml) and α-linolenic acid was similar for cases and controls in African Americans (13.8 μg/ml vs. 15.5 μg/ml) and Nigerians, (5.2 μg/ml vs. 5.0 μg/ml) (Table 3).

OR risk estimates for sub-group fatty acids. Unadjusted and adjusted PCa risk trends across fatty acid sub-group quartiles were significant for n-9 and *trans* among African Americans, adjusted OR comparing 4th to 1st quartile for n-9, and *trans* fatty acids were respectively 0.92 (95% CI 0.21–3.95), and 4.09 (95% CI 0.28–59.59). Among Nigerians adjusted risk trend was significant for total omega-6 fatty acid, with adjusted OR comparing 3rd to 1st quartile of 2.33 (95% CI 0.77–7.07), and adjusted OR comparing 4th to 1st quartile for total *trans* FA 1.52 (95% CI 0.50–4.65). OR trends were not significant for total omega-3 fatty acid in either population (Table 4).

OR risk estimates for individual fatty acids. Unadjusted and adjusted OR trends for PCa risk across quartiles of fatty acids remained significant for four of 11 fatty acids in the African American, and for two of four fatty acids in the Nigerian study populations. Odds ratio estimates comparing 4th with 1st fatty acid quartiles are displayed in Table 5. Positive PCa risk association was observed for nervonic, erucic, and arachidonic acids in both the African American and Nigerian study populations, with respective unadjusted OR risk estimates for nervonic acid of $OR_{Q3vs.Q1}$ 2.80 (95% CI 1.01–7.75), $P_{trend}<.02$ and $OR_{Q4vs.Q1}$ 2.40 (95% CI 1.19–4.85), $P_{trend}<.001$; erucic acid $OR_{Q4vs.Q1}$ 2.95

Table 2.

COMPARISON OF MEDIAN PHYSIOLOGICALLY ABUNDANT PLASMA FATTY ACID CONCENTRATIONS (μg/ml) AMONG AFRICAN AMERICAN AND NIGERIAN STUDY PARTICIPANTS

		African Americans	Nigerians
Fatty Acids Short/Systemic Name		**Median (25th, 75th percentile)**	**Median (25th, 75th percentile)**
	Total[a]	2597.9 (2306.2, 3034.8)	2420.0 (2063.8, 2795.1)
	Saturated[b]	774.7 (695.3, 933.8)	860.4 (738.9, 989.9)
	n-9 total[b]	519.3 (446.2, 617.8)	615.5 (524.6, 763.2)
	n-7 & n-5 total	94.3 (75.4, 124.5)	98.2 (77.8, 135.5)
	n-6 total[a] (Omega-6)	1085.5 (939.9, 1243.3)	665.3 (552.7, 788.4)
	n-3 total[b] (Omega-3)	85.3 (68.3, 116.1)	99.7 (74.0, 144.8)
	Trans total[a]	61.5 (42.9, 90.6)	15.3 (11.9, 20.1)
C12:0	Lauric[b]	1.2 (0.9, 1.9)	4.2 (2.6, 8.2)
C14:0	Myristic[b]	16.2 (12.2, 24.4)	23.6 (16.3, 37.0)
C16:0	Palmitic[b]	504.8 (453.4, 607.9)	585.6 (515.7, 670.5)
C18:0	Stearic[a]	192.0 (170.2, 231.6)	179.4 (152.2, 211.5)
C22.0	Behenic[a]	20.4 (16.6, 24.5)	16.5 (13.2, 20.8)
C16:1	Palmitoleic[b]	35.2 (27.1, 59.2)	57.2 (40.5, 84.8)
C18:1	Vaccenic	39.5 (32.7, 48.4)	39.5 (31.2, 50.1)
C16:1[tr]	Palmitelaidic[a]	5.7 (3.4, 9.5)	2.0 (1.2, 2.8)
C18:1[tr]	Elaidic[a]	41.4 (27.8, 63.5)	8.6 (6.5, 11.2)
C18:1	Oleic[b]	471.0 (401.7, 566.9)	560.8 (473.2, 696.4)
C20:1	Mead	3.4 (2.5, 4.7)	3.5 (1.9, 5.6)
C22:1	Erucic[a]	0.8 (0.6, 1.1)	0.7 (0.6, 0.8)
C24:1	Nervonic[b]	25.9 (21.4, 30.4)	31.2 (26.1, 37.9)
C18:2[c]	Linoleic[a]	763.1 (655.2, 882.4)	496.2 (415.5, 584.3)
C18:3[c]	γ-linolenic[a]	12.5 (9.36, 16.8)	7.0 (4.46, 10.44)
C20:3[c]	Di-homo-γ-linolenic[a]	38.9 (33.0, 48.4)	27.1 (20.8, 35.6)
C20:4[c]	Arachidonic[a]	241.7 (202.5, 289.3)	113.6 (83.0, 146.0)
C18:3[d]	α-linolenic[a]	14.8 (11.2, 19.7)	5.0 (3.8, 7.0)
C20:5[d]	Eicosapentaenoic[b]	12.7 (7.8, 19.1)	21.6 (13.2, 37.4)
C22:5[d]	Docosapentaenoic[a]	7.0 (5.4, 9.1)	2.9 (1.9, 4.1)
C22:6[d]	Docosahexaenoic[b]	44.6 (31.1, 62.7)	58.8 (43.1, 80.1)

[a]$p<.01$ p-value African American median plasma fatty acid higher than Nigerian median
[b]$p<.01$ p-value Nigerian median plasma fatty acid higher than African American median
[c]Omega-6 fatty acid
[d]Omega-3 fatty acid
[tr]*Trans* fatty acid
Short = shorthand designation of fatty acids: Carbon length: Number of unsaturated bonds

Table 3.

COMPARISON OF PLASMA FATTY ACID CONCENTRATION (μg/ml)[a] OF PROSTATE CANCER CASES AND CONTROLS AMONG AFRICAN AMERICAN AND NIGERIAN STUDY POPULATIONS

	African Americans		Nigerians	
Fatty Acids	**Cases**	**Controls**	**Cases**	**Controls**
Total	2410 (2217, 2912)	2759 (2407, 3150)**	2447 (2087, 3024)	2373 (2014, 2751)
Saturated	740.8 (678.5, 864.2)	785.6 (707.5, 935.3)	886.5 (728.2, 975.1)	846.2 (728.2, 975.1)
n-9	488.9 (411.2, 555.7)	538.2 (471.6, 660.3)	624.6 (532.3, 875.4)	602.7 (517.4, 750.2)
n-7 and n-5	84.5 (63.7, 108.7)	103.2 (80.4, 141.3)**	95.9 (80.4, 130.0)	101.0 (76.8, 135.3)
n-6	1,026 (882.7, 1150)	1,108 (949.0, 1268)	694.4 (564.8, 880.1)	654.0(550.4, 779.5)
n-3	93.2 (75.4, 124.1)	77.5 (63.2, 101.8)**	97.1 (67.3, 145.0)	104.9 (75.3, 152.4)
Trans	42.9 (36.0, 59.7)	75.7 (48.6, 95.6)**	15.1 (10.6, 20.9)	15.5 (12.2, 20.0)
Lauric	1.2 (0.8, 1.7)	1.4 (1.0, 2.1)	4.4 (2.5, 9.0)	4.2 (2.7, 8.0)
Myristic	15.4 (10.4, 21.6)	17.8 (13.5, 24.9)	21.6 (16.2, 37.2)	24.1 (16.5, 38.3)
Palmitic	488.1 (417.9, 573.5)	521.4 (457.7, 616.9)*	603.0 (539.2, 744.1)	572.0 (503.6, 658.5)
Stearic	184.6 (167.9, 222.4)	191.6 (171.5, 233.4)	188.0 (152.0, 229.6)	175.4 (150.0, 209.1)
Behenic[a]	19.9 (17.1, 24.3)	20.4 (15.8, 24.2)	18.4 (14.8, 22.6)	15.8 (12.7, 19.8)**
Palmitoleic[b]	32.7 (22.5, 42.7)	39.9 (29.3, 64.8)**	53.0 (42.3, 73.4)	58.8 (40.2, 85.0)
Vaccenic	35.3 (30.0, 43.2)	40.8 (36.0, 49.5)**	41.2 (33.0, 52.5)	38.1 (30.3, 48.3)
[tr]Palmitelaidic[a]	4.5 (2.9, 7.5)	7.5 (4.7, 10.4)**	1.8 (1.1, 2.7)	2.1 (1.3, 2.9)
[tr]Elaidic[a]	31.2 (22.7, 41.6)	50.5 (30.1, 69.6)**	8.7 (5.9, 12.1)	8.6 (6.5, 11.0)
Oleic[b]	441.1 (366.3, 502.8)	492.4 (422.8,594.2)**	568.0 (471.9, 809.0)	550.3 (471.7, 687.7)
Mead	2.9 (1.9, 3.7)	3.8 (2.9, 5.5)**	3.5 (2.1, 5.2)	3.5 (1.9, 5.6)
Erucic[a]	0.8 (0.6, 1.2)	0.7 (0.6, 0.9)*	0.8 (0.7, 1.0)	0.7 (0.5, 0.8)**

(Continued on p. 136)

Table 3. *(continued)*

	African Americans		Nigerians	
Fatty Acids	**Cases**	**Controls**	**Cases**	**Controls**
Nervonic[b]	28.2 (22.8, 31.6)	23.9 (20.0, 27.8)**	38.0 (32.7, 48.9)	28.8 (24.3, 34.7)**
Linoleic[b]	707.1 (588.6, 819.9)	791.8 (676.1, 903.2)*	513.4 (436.3, 658.7)	491.8 (417.1, 585.6)
γ-linolenic[b]	12.0 (9.7, 14.1)	13.0 (9.2, 17.6)	6.7 (4.2, 11.3)	7.0 (4.6, 10.1)
Di-h-γ-linolenic[b]	35.8 (30.6, 42.6)	41.3 (33.8, 52.4)*	30.6 (21.1, 38.6)	26.4 (20.5, 34.5)
Arachidonic[b]	250.2 (211.7, 284.7)	233.4 (197.8, 288.8)	132.0 (105.9, 160.6)	104.5 (76.6, 143.4)**
α-linolenic[b]	13.8 (10.5, 19.0)	15.5 (11.3, 20.5)	5.2 (3.9, 7.5)	5.0 (3.6, 6.9)
Eicosapentaenoic[c]	12.7 (9.2, 19.7)	11.9 (7.0, 17.1)	16.7 (11.5, 32.3)	26.2 (14.0, 40.4)*
Docosapentaenoic[b]	6.5 (5.2, 8.9)	7.5 (5.8, 9.7)	3.2 (2.3, 4.9)	2.7 (1.8, 3.9)*
Docosahexaenoic[c]	55.0 (41.5, 72.2)	39.3 (29.4, 47.8)**	58.8 (42.7, 78.7)	58.6 (42.6, 80.1)

*$p<.05$, comparing cases and controls within each group
**$p<.01$, comparing cases and controls within each group
[a]Values expressed as median (25th, 75th percentile)
[b]African-American median plasma fatty acid higher than Nigerian median plasma fatty acid
[c]Nigerian median plasma fatty acid higher than African American median plasma fatty acid

(95% CI 1.01–8.60), $P_{trend}<.07$ and $OR_{Q3vs.Q1}$ 4.26 (95% CI 1.82–9.96), $P_{trend}<.001$; and arachadonic acid $OR_{Q4vs.Q1}$ 1.35 (95% CI 0.47–3.89), $P_{trend}<.11$, and $OR_{Q2vs.Q1}$ 3.81 (95% CI 1.50–9.70), $P_{trend}<.002$. In addition, there was positive PCa risk for myristic and DHA among African Americans with unadjusted risk estimates of $OR_{Q3vs.Q1}$ 2.48 (95% CI 0.75–8.19), $P_{trend}<.002$ and $OR_{Q3vs.Q1}$ 6.63 (95% CI 2.02–21.77), $P_{trend}<.004$, respectively. Also among the Nigerians significant positive PCa risk trend was observed for behenic acid, unadjusted $OR_{Q4vs.Q1}$ 2.79 (95% CI 1.27–6.10), $P_{trend}<.001$; and adjusted $OR_{Q4vs.Q1}$ 2.47 (95% CI 0.97–6.27), $P_{trend}<.01$; and for stearic and di-homo-γ-linolenic, with unadjusted risk estimates of $OR_{Q3vs.Q1}$ 2.25 (95% CI 1.01–5.12), $P_{trend}<.26$; and $OR_{Q3vs.Q1}$ 2.69 (95% CI 1.18–6.15), $P_{trend}<.12$; respectively. The negative risk trend for palmetoleic and oleic acids were significant in African Americans, unadjusted $OR_{Q4vs.Q1}$ 0.16 (95% CI 0.05–0.55), $P_{trend}<.05$; and $OR_{Q4vs.Q1}$ 0.38 (95% CI 0.12–1.20), $P_{trend}<.02$; respectively. Non-significant negative risk association was observed for EPA in the Nigerians, unadjusted $OR_{Q3vs.Q1}$ 0.57 (95% CI 0.25–1.30), $P_{trend}<.08$.

Table 4.

UNADJUSTED AND ADJUSTED ODDS RATIO FOR PROSTATE CANCER RISK ACROSS QUARTILES OF TOTAL AND SUB-GROUP PLASMA FATTY ACIDS OF AFRICAN AMERICANS AND NIGERIANS

	African Americans		Nigerians	
Fatty Acids	**Unadjusted OR (95% CI)**	**Adjusted OR[a] (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR[a] (95% CI)**
Total				
Q1	1.00	1.00	1.00	1.00
Q2	0.37 (0.13–1.03)	0.60 (0.15–2.33)	1.52 (0.70–3.30)	0.78 (0.30–2.03)
Q3	0.42 (0.15–1.20)	0.52 (0.15–1.85)	1.66 (0.76–3.63)	1.30 (0.50–3.39)
Q4	1.07 (0.35–3.26)	2.17 (0.52–9.05)	1.19 (0.55–2.53)	0.80 (0.32–1.98)
P_{trend}[b]	0.08	0.29	0.57	0.70
Total saturated				
Q1	1.00	1.00	1.00	1.00
Q2	0.50 (0.18–1.34)	0.53 (0.14–2.00)	1.82 (0.80–4.17)	1.14 (0.42–3.07)
Q3	1.04 (0.37–2.95)	1.72 (0.42–7.01)	1.16 (0.54–2.52)	1.14 (0.46–2.87)
Q4	1.17 (0.42–3.28)	1.82 (0.49–6.70)	1.00 (0.47–2.15)	1.02 (0.41–2.54)
P_{trend}[b]	0.28	0.25	0.46	0.99
Total n-9				
Q1	1.00	1.00	1.00	1.00
Q2	0.16 (0.05–0.50)	0.16 (0.04–0.66)	1.44 (0.66–3.15)	0.76 (0.28–2.04)
Q3	0.29 (0.09–0.95)	0.43 (0.10–1.77)	1.35 (0.62–2.92)	0.82 (0.32–2.10)
Q4	0.42 (0.13–1.38)	0.92 (0.21–3.95)	1.22 (0.56–2.64)	0.79 (0.31–2.03)
P_{trend}[b]	0.01	0.03	0.81	0.95

(Continued on p. 138)

Table 4. *(continued)*

Fatty Acids	African Americans		Nigerians	
	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)
Total n-7/n-5				
Q1	1.00	1.00	1.00	1.00
Q2	0.19 (0.06–0.55)	0.30 (0.08–1.23)	1.07 (0.46–2.52)	0.87 (0.31–2.47)
Q3	0.60 (0.20–1.82)	0.85 (0.22–3.25)	0.49 (0.23–1.07)	0.33 (0.13–0.86)
Q4	0.61 (0.21–1.81)	0.55 (0.15–2.05)	0.92 (0.41–2.07)	0.82 (0.31–2.21)
P_{trend}[b]	0.01	0.34	0.14	0.07
Total n-6				
Q1	1.00	1.00	1.00	1.00
Q2	0.53 (0.20–1.40)	0.80 (0.23–2.76)	1.39 (0.64–3.01)	0.65 (0.24–1.76)
Q3	0.64 (0.23–1.78)	0.68 (0.20–2.35)	2.30 (0.98–5.38)	2.33 (0.77–7.07)
Q4	1.35 (0.46–3.93)	1.46 (0.37–5.83)	0.91 (0.44–1.88)	0.55 (0.22–1.36)
P_{trend}[b]	0.26	0.73	0.14	0.05
Total n-3				
Q1	1.00	1.00	1.00	1.00
Q2	3.31 (1.17–9.40)	1.33 (0.36–4.91)	0.65 (0.30–1.40)	0.50 (0.20–1.28)
Q3	2.38 (0.87–6.50)	2.12 (0.52–8.74)	0.87 (0.40–1.93)	0.69 (0.26–1.81)
Q4	1.49 (0.56–3.96)	0.74 (0.21–2.60)	1.07 (0.48–2.42)	0.88 (0.34–2.30)
P_{trend}[b]	0.11	0.48	0.58	0.49
Total *trans*				
Q1	1.00	1.00	1.00	1.00
Q2	0.11 (0.03–0.44)	0.09 (0.01–0.69)	0.79 (0.35–1.79)	0.42 (0.15–1.19)
Q3	0.30 (0.07–1.29)	0.49 (0.06–4.05)	1.55 (0.63–3.83)	1.08 (0.34–3.41)
Q4	0.92 (0.17–5.02)	4.09 (0.28–59.59)	1.49 (0.62–3.61)	1.52 (0.50–4.65)
P_{trend}[b]	<0.001	0.02	0.35	0.11

[a]OR adjusted for age, level of education, family history of prostate cancer, and waist-hip ratio.
[b]Calculated with median fatty acid concentration in each quartile as a continuous variable.
Quartile (Q) 1 (lowest)
Quartile 4 (highest)
OR = odds ratio
CI = confidence interval

Discussion

Dietary fat intake has become a major focus of PCa risk-association studies since the observation of dramatic changes in the incidence of PCa among men who moved from low-incidence to high-incidence regions. Early epidemiological studies consistently suggested a possible causal association between dietary fat intake and PCa risk.[24,25] The exact role of fat in prostate carcinogenesis is yet unknown, however a number of fatty acids have been shown in animal and *in-vitro* studies to affect several physiologic and

Table 5.

UNADJUSTED AND ADJUSTED OR OF PROSTATE CANCER RISK COMPARING 4TH TO 1ST QUARTILE PLASMA FATTY ACID CONCENTRATIONS (μg/ml) OF AFRICAN AMERICANS AND NIGERIANS

	African Americans		Nigerians	
Fatty Acids	**Unadjusted OR**	**Adjusted OR[s]**	**Unadjusted OR**	**Adjusted OR[s]**
Total	1.07 (0.35–3.26)	2.17 (0.52–9.05)	1.19 (0.55–2.53)	0.80 (0.32–1.98)
Saturated	1.17 (0.42–3.28)	1.82 (0.49–6.70)	1.00 (0.47–2.15)	1.02 (0.41–2.54)
n-9 total	0.42 (0.13–1.38)*	0.92 (0.21–3.95)*	1.22 (0.56–2.64)	0.79 (0.31–2.03)
n-7 and n-5 total	0.61 (0.21–1.81)**	0.55 (0.15–2.05)	0.92 (0.41–2.07)	0.82 (0.31–2.21)
n-6 total	1.35 (0.46–3.93)	1.46 (0.37–5.83)	0.91 (0.44–1.88)	0.55 (0.22–1.36)*
n-3 total	1.49 (0.56–3.96)	0.74 (0.21–2.60)	1.07 (0.48–2.42)	0.88 (0.34–2.30)
Trans total	0.92 (0.17–5.02)**	4.09 (0.28–59.59)*	1.49 (0.62–3.61)	1.52 (0.50–4.65)
Lauric	0.86 (0.32–2.33)	2.95 (0.75–11.7)	1.21 (0.56–2.59)	1.34 (0.53–3.35)
Myristic	0.86 (0.32–2.31)**	0.70 (0.20–2.42)*	1.47 (0.64–3.34)	1.97 (0.73–5.29)
Palmitic	0.59 (0.20–1.75)	1.05 (0.27–4.06)	1.50 (0.71–3.19)	1.38 (0.55–3.45)
Stearic	0.77 (0.28–2.11)	1.11 (0.32–3.84)	1.48 (0.70–3.12)	1.42 (0.58–3.48)
Behenic	1.14 (0.40–2.24)	1.14 (0.30–4.30)	2.79 (1.27–6.10)**	2.47 (0.97–6.27)**
Palmitoleic	0.16 (0.05–0.55)*	0.02 (0.05–0.86)	1.13 (0.49–2.61)	1.07 (0.39–2.96)
Vaccenic	1.12 (0.39–3.24)**	1.12 (0.31–4.03)	1.04 (0.49–2.20)	0.48 (0.19–1.23)
[tr]Palmitelaidic	0.63 (0.22–1.74)*	0.68 (0.19–2.48)	1.00 (0.44–2.27)	1.52 (0.57–4.06)
[tr]Elaidic	0.13 (0.01–1.12)*	0.66 (0.05–8.73)	1.03 (0.44–2.41)	1.00 (0.34–2.93)
Oleic	0.38 (0.12–1.20)*	0.78 (0.19–3.24)*	1.49 (0.68–3.28)	1.49 (0.57–3.91)
Mead	0.42 (0.13–1.34)**	0.54 (0.13–2.15)	0.72 (0.33–1.59)	0.36 (0.14–0.96)
Erucic	2.95 (1.01–8.60)	3.96 (1.05–14.9)*	1.06 (0.52–2.16)**	0.94 (0.40–2.20)

(Continued on p. 140)

Table 5. *(continued)*

	African Americans		Nigerians	
Fatty Acids	**Unadjusted OR**	**Adjusted OR[a]**	**Unadjusted OR**	**Adjusted OR[a]**
Nervonic	2.56 (0.94–7.00)*	2.13 (0.59–7.69)	2.40 (1.19–4.85)**	1.78 (0.79–4.00)**
Linoleic	0.36 (0.11–1.16)*	0.77 (0.18–3.41)	0.82 (0.39–1.73)	0.38 (0.15–0.99)
γ-linolenic	0.54 (0.19–1.59)*	0.60 (0.16–2.26)	2.03 (0.91–4.54)	1.74 (0.64–4.71)
DHGL	0.46 (0.15–1.40)	0.62 (0.16–2.34)	1.30 (0.62–2.72)	0.86 (0.35–2.08)
Arachidonic	0.46 (0.17–1.23)	0.30 (0.08–1.11)*	0.74 (0.36–1.50)**	0.75 (0.32–1.74)
α-linolenic	1.00 (0.37–2.73)	1.30 (0.37–4.58)	1.19 (0.55–2.56)	0.98 (0.40–2.40)
EPA	1.26 (0.45–3.46)	0.82 (0.21–3.24)	0.82 (0.35–1.91)	1.09 (0.40–2.96)
DPA	0.88 (0.32–2.40)	1.01 (0.31–3.33)	1.49 (0.62–3.61)	0.44 (0.17–1.19)
DHA	1.57 (0.60–4.12)**	1.35 (0.40–4.61)	0.75 (0.35–1.62)	0.56 (0.22–1.40)

P_{trend} calculated with median fatty acid concentration in each quartile as a continuous variable. *$P_{trend}<.05$; **$P_{trend}<.01$
[a]OR adjusted for age, level of education, family history of prostate cancer, and waist-hip ratio.
DHGL = di-homo-γ-linolenic
EPA = eicosapentaenoic
DPA = docosapentaenoic
DHA = docosahexaenoic
OR = odds ratio

cellular processes.[16] Western diet, fat in general, and red meat specifically have been incriminated as risk factors in dietary intake studies, while diets rich in fish are reported to be associated with reduced risk.[26–28] These reported differences in the patterns of PCa risk association with dietary fatty acids can be attributed to the accuracy with which dietary assessment tools capture dietary fat intake in the population studied. For that reason plasma and tissue composition of fatty acids can be accepted as more objective measures of dietary fat exposure than estimates from dietary assessment tools like food frequency questionnaires (FFQs). We elected to measure fasting plasma fatty acids in the combined triglycerides and phospholipids fractions that better reflects medium-term (weeks to months) dietary intake, blood draw being more feasible than subcutaneous fat aspirate[29,30] in this study that includes community-based participants.

In this study total fatty acid was statistically higher in African Americans (2,597.94 μg/ml) than in Nigerians (2,419.95 μg/ml), consistent with reports of a diet higher in fat.[31] The overlapping 25th and 75th percentile limits of these measures in both populations indicate similarities in the fatty acid content of their diets, and a slow but real transition towards Westernization of the Nigerian diet, a trend that was proposed to contribute to Nigerians' increasing PCa incidence.[5,15] Total fatty acid per se did not explain PCa risk in either population, as the percentage of energy derived from fat must vary widely between the two populations given their very different plasma fatty acid profiles. We were unable to determine energy intake since there was no nutrient database for Nigerian foods. Energy derived from fat is estimated at 34% in African Americans as reported by the National Health and Nutrition Examination Survey (NHANES III),[32] and 20%–25% in both rural and urban West African countries.[33,34]

The direction of the difference in sub-group fatty acid totals between African Americans and Nigerians was not consistent, an indication of food preferences across both populations. Nigerians recorded higher saturated fatty acid, n-9 fatty acid from vegetable fats particularly red palm oil and coconut milk, and omega-3 fatty acids from their diet high in fish content.[35,36] African Americans recorded higher omega-6 and *trans* fatty acids than the Nigerians, and recorded weak-to-moderate PCa risk associations across quartiles that was statistically significant for *trans* fatty acid. We did not observe PCa risk reduction for total omega-3 fatty acid in either population, making our findings only partly consistent with other reports regarding omega-3 and omega-6 poly unsaturated fatty acids (PUFA), respectively reported to be associated with reduced and increased PCa risk.[37,38] Negative PCa risk association with ecosapentaenoic acid (EPA) that approached statistical significance was observed only among the Nigerians. Although the marine omega-3 fatty acids EPA and docosahexaenoic acid (DHA) were significantly higher among the Nigerians it is interesting to note that African American PCa cases in this study recorded significantly higher DHA levels than their controls, approaching the levels in Nigerians. This can result from an increase in the fish content of their diet or the use of omega-3 dietary supplements which contain both DHA and EPA but not α-linolenic acid, the essential omage-3 fatty acid derived only from the diet. This finding will be further investigated in the subsequent analysis of the dietary assessment information collected. The high plasma EPA and DHA among Nigerians can be attributed mainly to their diet, as fish rather than meat remains the main source of protein,[39] a relic of the historical eating pattern of shoreline Africans.[40] The PCa

protective effect of a rich fish diet is supported by studies that observed higher blood levels of long-chain omega-3 fatty acids among study controls compared with cases in a nested case-control study.[41] Native Alaskan Eskimos, a population with total omega-3 fatty acid 4.3 times that of non-natives,[42] have very low PCa incidence compared to the SEER rates for U.S. Whites.[43] In the light of numerous encouraging claims about the health protective nature of marine fatty acids such as EPA and DHA,[41,42] the lack of a negative risk association in these Nigerians with high total plasma omega-3 levels was unexpected, and so was the positive association with DHA in the African American study sample. In a small case-control study predominantly of White Americans the authors that reported a PCa risk association for the essential omega-3 fatty acid but not the marine fatty acids,[44] further underscoring the need to study the influence of balances between fatty acids within and across fatty acid sub-groups.

On the other hand, the two-fold and four-fold higher concentration of individual omega-6 and *trans* fatty acids among the African Americans compared with Nigerians deserves to be further studied to see whether these differences could contribute to some of the disparate PCa incidence in these populations. These plasma levels reflect the burden of greater consumption of fat from animal sources,[14] and hydrogenated oils of which elaidic acid is a metabolite. Refined and processed foods in the Unites States carry labels that indicate preparation with partially hydrogenated vegetable oil that contain the *trans* form of fatty acids instead of the *cis* form, which act in human tissues like saturated fatty acids, another proposed risk factor for PCa. This study implicated total *trans* fatty acid in PCa risk among African Americans with an adjusted OR of 4.09, and a very wide 95% CI because of our small study sample, and is consistent with the relative risk of 2.21 (95% CI 1.14–4.29), $p<.06$, reported from a nested case-control study conducted in 14,916 apparently healthy men based within the Physician's Health Study.[45] Our data did not demonstrate statistical evidence of positive PCa risk association with total omega-6 nor linoleic fatty acid in either population, consistent with the findings from a nested case-case control study that measured risk association across quintiles of linoleic fatty acid in whole blood,[46] but contrary to findings from a predominantly White case-control study that reported OR 3.54 (95% CI 1.0–12.53) across erythrocyte membrane linoleic fatty acid quartiles.[47] Linoleic (omega-6) and α-linolenic (omega-3) essential fatty acids have been reported to be associated with PCa risk,[44,46] and although African Americans recorded almost two-fold higher plasma total and individual omega-6 fatty acid levels than the Nigerians, no association with PCa risk was observed in either population except for arachidonic acid. We observed a three-fold PCa risk association with arachidonic acid among the Nigerians but only a weak non-significant risk association in the African Americans. One explanation for the masking of risk association in the African American population is changes that could have occurred following the diagnosis of prostate cancer. Plasma levels of arachadonic acid, a metabolite of linoleic acid, remained much higher in African Americans cases even though linolenic acid was significantly lower than in their controls. Dietary modifications reducing the relevant fats and oils can result in a reduction in the plasma level of an essential fatty acid but not in the plasma level of its metabolites. While the laboratory evidence linking omega-6 fatty acids to prostate tumor growth

is very strong, the evidence for association with dietary intake of these omega-6 fatty acids in humans remains unclear.[48]

The PCa risk association with individual fatty acids was further investigated with the intention of identifying specific dietary fats and oils that should be included or excluded from the diet to reduce PCa risk. None of these physiologically abundant fatty acids exhibited decreasing PCa risk trend across plasma quartiles in either population. However palmitoleic and oleic acids were negatively associated with PCa risk only among African American with unadjusted and adjusted ORs in the protective range. These data tend to support the popularly cited protective effect of diets rich in olive oil, a major source of oleic acid,[49] that should be explored further in both populations. Weak positive associations regarding myristic, palmitic, and stearic fatty acids are not consistent and therefore inconclusive.[38,46,50] We observed a moderate unadjusted PCa risk for stearic and behenic fatty acids of $OR_{Q3vs.Q1}$ 2.27 (1.01–5.12) and $OR_{Q4vs.Q1}$ 2.79 (1.27–6.10) only among the Nigerians. Our data also identified more than a three-fold statistically significant moderate positive PCa risk association for mono-unsaturated fatty acids erucic and nervonic acids in both populations that we intend to evaluate further in a larger study. We presently do not have any biological explanations for these PCa risk associations.

The use of population-based controls and a common protocol for both study sites are two major strengths of this study. However, study limitations include differential self-selection bias as PCa cases exposed to nutrition health information in the U.S. could have been more interested in participating in this study, an assumption that may not hold true for the Nigerians. African American cases are therefore more likely to have modified their diet in line with claims of foods and nutrients associated with prostate health, reducing the intake of animal products and taking dietary supplements, leading to higher omega-3 and lower omega-6 from pre-diagnosis levels that can mask positive risk association with omega-6 and spurious risk association with omega-3 fatty acids. The proportion of low-income African Americans was higher among the controls probably because they were more attracted by the cash incentive to participate in the study while their counterparts diagnosed with PCa were not. On the other hand, the study incentive was equally attractive to the Nigerian cases and controls. Since there was statistical difference in fatty acid levels across education but not income level strata, we controlled for education status in our risk analysis. Like previous reports, African Americans recorded significantly higher body fat and obesity rates compared to Nigerians,[51] warranting adjusting OR for waist-hip ratio. This adjustment did not significantly alter our findings; furthermore reports about adult body fat composition and PCa risk have not been consistent.[52]

Although plasma fatty acid levels may not accurately reflect levels in the prostate, misclassification of tissue fatty acid level is likely to be random, and therefore, underestimations of any real fatty acid effects are unlikely. We also do not believe that our sample storage methods affected fatty acid measurements of the Nigerians since fatty acids do remain stable under adequate storage,[53–55] as in this protocol. More important is the challenge of comparing the role of fatty acids in PCa risk across studies given the relative differences in the concentrations of the individual fatty acids depending on the

biospecimen studied (erythrocyte menbranes, platelets, adipose tissue, plasma), and the lipid subfraction of plasma that was assayed.[56–58] We measured fatty acids only in the plasma phospholipids and triglycerides subfractions. Lastly, our cases ranged from those with localized to advanced or metastatic disease and we view this as a serious but unavoidable study limitation given the difficulty in recruiting organ confined and/or newly diagnosed PCa cases in the study populations. Our small study sample and multiple statistical comparisons are also major limitations of this pilot study. These preliminary results will be used to calculate sample sizes in our future studies that will have sufficient statistical power to adequately evaluate PCa risk association of select plasma fatty acids. To improve the precision of our findings we shall limit recruitment to men who have not substantially modified their diet in the past decade or after PCa diagnosis and are not taking nutritional supplements that directly affect plasma fatty acid levels. Prostate cancer risk associations will be evaluated separately for disease stage categories, and analysis for ratios of plasma fatty acid within and between subgroups will be explored.

Conclusions. There were significant differences in the plasma fatty acid profile of African Americans and Nigerians, and these differences were retained in all individual fatty acids except vaccenic and mead acids. Individual plasma fatty acids did not appear to affect PCa risk in the populations differentially. The positive PCa risk association across quartiles of stearic, behenic, erucic, nervonic acids, and *trans* fatty acids, and the negative association with palmetoleic, oleic, and EPA should be viewed as preliminary results to be further explored in a larger study sample.

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Factors Influencing Prostate Cancer Screening in Low-Income African Americans in Tennessee

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Abstract: This study examined demographic and lifestyle factors that influenced decisions to get screened for prostate cancer in low-income African Americans in three urban Tennessee cities. It also examined obstacles to getting screened. As part of the Meharry Community Networks Program (CNP) needs assessment, a 123-item community survey was administered to assess demographic characteristics, health care access and utilization, and screening practices for various cancers in low-income African Americans. For this study, only African American men 45 years and older (n=293) were selected from the Meharry CNP community survey database. Participants from Nashville, those who were older, obese, and who had health insurance were more likely to have been screened ($p<.05$). Additionally, there were associations between obstacles to screening (such as cost and transportation) and geographic region ($p<.05$). Educational interventions aimed at improving prostate cancer knowledge and screening rates should incorporate information about obstacles to and predictors of screening.

Key words: Prostate cancer, cancer screening, African American men.

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Prostate cancer (PCa) is one of the most common cancers in men, and is the second leading cause of death for all cancer-related deaths in men in the United States.[1,2] African American men bear a disproportionate burden of prostate cancer compared with other ethnic and racial groups.[2–4] Population-based data collected through the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute indicated that African Americans had PCa delay-adjusted incidence rates between 1975–2005 that were 100% higher than their Caucasians counterparts. Furthermore, African Americans had a two-fold higher mortality than other racial and ethnic groups in the U.S.[5] Although prostate cancer-related mortality has been decreasing for all men since the 1990s, disparities disfavoring African American men persist.

The causes for PCa mortality disparities between African American and other men are multifactoral. Possible explanations include delay in diagnosing prostate cancer and subsequent poorer prognosis.[6–7] Some experts speculate that African American men have greater genetic vulnerability to prostate cancer and that prostate cancer may be biologically more aggressive in this population than in other racial groups.[8–10] In addition, African American men tend to have poorer knowledge about prostate cancer screening, report greater perceived risk of developing the disease, and worry more about the disease than Caucasian men.[11–12]

The benefits of prostate cancer screening has been more widely debated than the benefits of other types of cancer screening. This is in part because although there is evidence that PCa screening can detect early-stage prostate cancer, the evidence that early detection improves health outcomes is inconclusive.[13–16] Despite this controversy, there is a growing consensus among medical professionals, the American Cancer Society, and other cancer-related organizations that prostate cancer screening should continue until large-scale randomized clinical trials clarify whether screening reduces prostate cancer mortality. In support of this position, organizations have frequently pointed out that prostate cancer mortality has been decreasing since prostate cancer screening became widely adopted as a preventive practice.[16]

Several factors have been associated with an increase in prostate cancer screening, including having a positive family history of prostate and other cancers, being older, being employed, having a higher income, having an intention to getting screened, perceiving one's health as good or excellent, and having a usual source of health care.[17–20] In addition, several barriers to screening have been identified, including fear of a positive diagnosis, limited knowledge of prostate cancer, cost of screening, inconvenient doctors' hours, and lack of health insurance.[21–23]

The present study examines the sociodemographic factors that influence decisions to get screened for prostate cancer in low-income African Americans from the Meharry Community Networks Program (CNP) community survey. In addition, this study examines the differences in obstacles to screening by geographic region and among men who were screened versus those who were not. The impetus for this investigation is that while research has documented some factors that influence prostate cancer screening behavior, we need a better understanding of the influences and obstacles to prostate cancer screening in low-income African American men. This population has among the highest mortality rates for prostate cancer.

Methods

In 2005, the National Cancer Institute funded 25 Community Networks Programs (CNP) to focus on reducing cancer disparities in diverse, high-risk populations located throughout the United States. One of the projects funded was the Meharry Medical College Community Health Centers–Community Networks Program (Meharry CNP), which focuses on reducing and in time eliminating cancer health disparities between African Americans and others. As part of the Meharry CNP needs assessment, a 123-item community survey was developed to assess demographic characteristics (age, race, income, education, marital status, employment status), health insurance coverage, health care access and utilization, health behaviors (smoking history, alcohol use), and screening practices (including obstacles to screening) for various cancers. The survey was modeled after the Centers for Disease Control and Prevention's (CDC's) Behavioral Risk Factor Surveillance System (BRFSS) and contained many identically worded questions, including those about cancer screenings.

Population studied. The survey was administered to 1,140 African Americans in Nashville (n=342), Chattanooga (n=399), and Memphis (n=399). To maximize recruitment of African Americans, communities within ZIP codes with a majority African American presence (>50%) were targeted. Population characteristics including race, age, and gender information for all ZIP codes in these cities were obtained from the U.S. Census Bureau projected for year 2005.

Participants were recruited for the survey at community events and businesses (i.e., community centers, health fairs, barbershops). All surveys were conducted by trained project staff at each site. A series of workshops was conducted to train staff in recruiting eligible participants, obtaining written informed consent, and administering the survey. The eligibility criteria included being 18 years and older, English speaking, and resident of Nashville, Chattanooga, or Memphis for the past six months. This survey protocol was approved by the Meharry Medical College and Erlanger Health Systems Review Boards.

For this study, only African American men 45 years and older were selected from the Meharry CNP community survey database. The final sample size was 293. The rationale for selecting men over 45 was that organizations like the American Cancer Society (ACS)[24] recommend that men begin annual screenings for prostate cancer starting at age 50. They also recommend that men at increased risk (such as African Americans and men with a family history of the disease) start screening at age 45.

Data coding and analysis. The primary outcome of interest was having been screened for prostate cancer with the Prostate Specific Antigen (PSA) test in the past two years. Weight status and smoking status were two variables that were calculated. Weight status was categorized using body mass index (BMI) calculated as weight in kilograms divided by the square of height in meters. The three standard BMI categories used included normal weight ($18.5 \leq BMI \leq 24.9$), overweight ($25 \leq BMI \leq 29.9$), and obese ($BMI \geq 30$). Smoking status was categorized as former, current, or never smokers (see Table 1). Current smokers were those participants who responded *Yes* to the question *Do you smoke cigarettes now?* Participants were categorized as never smoked if they responded *No* to the questions *Have you smoked at least 100 cigarettes (5 packs of*

Table 1.

DEMOGRAPHIC AND LIFESTYLE CHARACTERISTICS OF AFRICAN AMERICAN MEN 45 YEARS AND OLDER IN THE MEHARRY CNP SURVEY

Variables	All participants N=293 (%)	Screened in past 2 years N=106 (36%)	Were not screened N=187 (64%)	p-value*
Age at interview (years)				
45 to 64	230 (79%)	74 (70%)	156 (83%)	.006
65+	63 (21%)	32 (30%)	31 (17%)	
City				
Nashville	102 (35%)	50 (47%)	52 (28%)	.003
Chattanooga	95 (32%)	30 (28%)	65 (34%)	
Memphis	96 (33%)	26 (24%)	70 (38%)	
BMI (body mass index)				
Normal weight (18.5 ≤ BMI ≤ 24.9)	115 (41%)	25 (26%)	90 (49%)	.001
Overweight (25 ≤ BMI ≤ 29.9)	80 (28%)	27 (27%)	53 (29%)	
Obese (BMI ≥ 30)	86 (31%)	46 (47%)	40 (22%)	
Smoking				
Never	132 (49%)	50 (49%)	82 (49%)	.408
Former	24 (9%)	12 (12%)	12 (7%)	
Current	113 (42%)	40 (39%)	73 (44%)	
Medical visit in the past 12 months				
Yes	207 (74%)	93 (91%)	114 (64%)	.001
No	73 (26%)	9 (8%)	64 (36%)	
Family history of any cancer				
Yes	161 (56%)	61 (58%)	100 (55%)	.632
No	128 (44%)	45 (42%)	83 (45%)	
Self-rated health				
Excellent/very good/good	179 (64%)	68 (67%)	111 (63%)	.546
Fair/poor	99 (36%)	34 (33%)	65 (37%)	
Education				
< High school	93 (33%)	31 (31%)	62 (35%)	.724
High school	119 (43%)	46 (45%)	73 (41%)	
> High school	67 (24%)	24 (24%)	43 (24%)	
Marital status				
Married/partner	94 (33%)	45 (45%)	49 (27%)	.002
Separated/divorced/ widowed	114 (41%)	40 (39%)	74 (41%)	
Single, never been married	73 (26%)	16 (16%)	57 (32%)	

(Continued on p. 118)

Table 1. ***(continued)***

Variables	All participants N=293 (%)	Screened in past 2 years N=106 (36%)	Were not screened N=187 (64%)	p-value*
Annual household income				
<$15,000	175 (63%)	52 (50%)	123 (70%)	.001
≥$15,000	103 (37%)	51 (50%)	52 (30%)	
Employment status				
Employed	123 (45%)	47 (46%)	76 (45%)	.826
Not employed	149 (55%)	55 (54%)	94 (55%)	
Health insurance				
Yes	155 (54%)	75 (71%)	80 (44%)	.001
No	133 (46%)	31 (29%)	102 (56%)	
At least one alcoholic beverage in the past 30 days				
Yes	123 (46%)	39 (38%)	84 (51%)	.028
No	145 (54%)	65 (63%)	80 (49%)	

*Chi-square test
CNP = Community Networks Program

cigarettes) in your entire life? and *Do you smoke cigarettes now?* Former smokers were those who responded *Yes* to the question *Have you smoked at least 100 cigarettes (5 packs of cigarettes) in your entire life?* and *No* to the question *Do you smoke cigarettes now?* Additionally, obstacles to screening were measured by nine items. For each item, participants had to indicate (*yes*/*no*) if the item was an obstacle.

Demographic, lifestyle, and health-related characteristics were calculated for both African American men who had a PSA test in the past two years and for those who did not. In Table 1, results are reported of chi-squared tests to examine the associations of demographic and lifestyle characteristics with screening status. In Tables 3 and 4, results are reported of chi-squared tests to examine associations between screening obstacles, and screening status and geographic region. For all chi-squared tests, a p-value of less than .05 was significant.

A binary logistic regression model was conducted (see Table 2) to evaluate the associations between demographic and lifestyle variables with having had a PSA test in the past two years. Having a PSA test within the past two years (*yes* = 1, *no* = 0) was the dependent variable. Demographic and lifestyle variables illustrated in Table 1 were only included as predictors in the logistic regression model if they had a significant (using chi-squared tests) bivariate association with screening status. The final predictor variables selected were age at survey interview, city of the participant, BMI, marital status, annual household income, health insurance status, medical visits in past 12 months, and alcohol use in the past 30 days. All data analyses were conducted

Table 2.

ODDS RATIOS (ORs) OF THE ASSOCIATION OF DEMOGRAPHIC AND LIFESTYLE FACTORS WITH PROSTATE CANCER SCREENING STATUS

	African American men (age ≥ 45)		
Variables	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**	**p-value**
Age at interview (years)			
45–64	1.00	1.00	.56
65+	2.18 (1.24 3.83)	1.25 (0.59 2.62)	
City			
Nashville	1.00	1.00	.00
Chattanooga	0.48 (0.27 0.86)	0.45 (0.21 0.999)	
Memphis	0.39 (0.21 0.70)	0.17 (0.07 0.42)	
BMI (body mass index)			
Normal weight (18.5 ≤ BMI ≤ 24.9)	1.00	1.00	.07
Overweight (25 ≤ BMI ≤ 29.9)	1.83 (0.97 3.48)	1.53 (0.68 3.45)	
Obese (BMI ≥ 30)	4.14 (2.24 7.64)	2.48 (1.16 5.32)	
Marital status			
Marital/living with a partner	1.00	1.00	.01
Separate/divorced/widowed	0.59 (0.34 1.03)	0.86 (0.39 1.89)	
Single, never been married	0.31 (0.15 0.61)	0.22 (0.08 0.60)	
Annual household income			
<$15,000	1.00	1.00	.00
≥$15,000	2.32 (1.40 3.84)	3.72 (1.58 8.73)	
Health insurance			
Yes	1.00	1.00	.21
No	0.32 (0.20 0.54)	0.63 (0.31 1.29)	
Medical visit in the past 12 month			
Yes	1.00	1.00	.00
No	0.17 (0.08 0.37)	0.21 (0.08 0.53)	
Alcohol use			
Yes	1.00	1.00	.94
No	1.75 (1.06 2.89)	0.98 (0.50 1.92)	

CI = confidence interval

using SAS/STAT software, Version 9.1 of the SAS System for Windows (SAS Institute Inc., Cary, NC, USA).

Results

Demographic and lifestyle factors for African American men 45 years and older from the Meharry CNP community survey are presented in Table 1. A total of 36% of the study participants reported having had a PSA test within the past two years. Most of the men who were screened for prostate cancer within the past two years were from Nashville, were married, were obese, had a medical visit in the past 12 months, and were 65 years and older. On the other hand, most of the men who had not been screened for prostate cancer within the past two years had annual household incomes less than $15,000 and no health insurance. Both groups of participants had similar rates of never having smoked (49%), being employed (screened = 46%, not screened = 45%), having a family history of any cancer (screened = 58%, not screened = 55%), self-rating their health as good to excellent (screened = 67%, not screened = 63%), and having less than a high school education (screened = 31%, not screened = 35%).

Relationship between demographic and lifestyle factors and prostate cancer screening behavior. As shown in Table 2, a logistic regression model was conducted to ascertain if demographic and lifestyle variables predicted screening behaviors for prostate cancer. Table 2 summarizes the odds ratios (ORs) and 95% confidence intervals (CIs).

Several of the adjusted ORs were significant for prostate cancer screening status. Compared to participants from Nashville, those from Chattanooga and Memphis were 0.45 and 0.17 times as likely to have been screened in the past two years. Obese participants were 2.48 times more likely to have been screened for prostate cancer in the past two years as participants who were normal weight, and participants who were single and/or never been married were 0.22 times as likely to have been screened as those who were married or living with a partner. Participants who did not make at least one medical visit in past 12 months were 0.21 times as likely to have screened as those participants that did. Finally, participants with an annual household income equal to or greater than $15,000 were 3.72 times more likely to have gotten screened than those making less than $15,000.

A few crude ORs became non-significant after adjusting for the other variables in model. The increased odds of having been screened for participants 65 years and older compared with participants between 45–64 years was not detected after adjustments. Additionally, the decreased odds of having been screened for participants without health insurance coverage compared with those with health insurance was not detected after adjusting for other variables. Finally, the increased odds of having been screened for participants who did not have at least one alcoholic drink in the past 30 days was not detected after adjustments.

Obstacles to screening. Obstacles to being screened for prostate cancer by geographic region are illustrated in Table 3. The obstacles were transportation issues (58%), difficulty getting time-off from work (55%), trouble remembering to schedule screenings (51%), not knowing where to get screened (44%), not having health insurance (39%), pain and discomfort of screening (38%), not having enough information about screenings

Table 3.

OBSTACLES TO CANCER SCREENING BY CITY

Obstacles	% Reported				
	All participants N=214	Nashville N=68	Chatta-nooga N=78	Memphis N=68	p-value*
Fear of finding out I have cancer	66 (31%)	28 (41%)	29 (37%)	9 (13%)	.00
Not having health insurance	82 (39%)	31 (46%)	22 (28%)	29 (43%)	.06
Cost of cancer screenings	79 (37%)	32 (47%)	21 (27%)	26 (38%)	.04
Pain and discomfort of screenings	81 (38%)	30 (45%)	28 (36%)	23 (34%)	.33
Difficulty getting time off work	115 (55%)	39 (59%)	37 (49%)	39 (57%)	.40
Trouble remembering to schedule screenings	109 (51%)	35 (51%)	37 (48%)	37 (54%)	.74
Not having enough information about screenings	77 (37%)	31 (46%)	23 (31%)	23 (34%)	.14
Not knowing where to get screened	93 (44%)	33 (49%)	33 (43%)	27 (40%)	.58
Transportation issues	122 (58%)	36 (55%)	39 (51%)	47 (69%)	.07

*Chi-square test

(37%), cost of screening (37%), and fear of getting a positive cancer diagnosis (31%). There were a few significant associations between region and obstacles to screening. For example, there was a significant association between fear of a getting a positive cancer diagnosis and region ($p<.05$). A total of 41% of participants in Nashville, 37% in Chattanooga, and 13% in Memphis reported fear of getting a positive cancer diagnosis as an obstacle. In addition, there was a significant association between the obstacle cost of screening and region ($p<.05$). A total of 47% of participants in Nashville, 27% in Chattanooga, and 38% in Memphis reported cost of screening as an obstacle.

Obstacles to being screened for prostate cancer with a PSA test by screening status are illustrated in Table 4. Both groups of men (those who screened in past two years and those who did not) reported transportation issues (screened = 61%, not screened = 56%) as the largest obstacle and fear of a positive cancer diagnosis as the smallest (screened = 40%, not screened = 26%). There were a few significant associations between screening status and obstacles to screening ($p<.05$). For example, fear of getting a positive cancer diagnosis (screened = 40%, not screened = 26%), not

Table 4.

OBSTACLES TO CANCER SCREENING BY SCREENING STATUS

Obstacles	% Reported			
	All participants N=214	Screened N=70	Not screened N=144	p-value*
Fear of finding out I have cancer	66 (31%)	28 (40%)	38 (26%)	.04
Not having health insurance	82 (39%)	38 (54%)	44 (31%)	.00
Cost of cancer screenings	79 (37%)	34 (49%)	45 (31%)	.01
Pain and discomfort of screenings	81 (38%)	32 (46%)	49 (35%)	.11
Difficulty getting time off work	115 (55%)	40 (57%)	75 (54%)	.62
Trouble remembering to schedule screenings	109 (51%)	39 (56%)	70 (49%)	.35
Not having enough information about screenings	77 (37%)	37 (54%)	40 (29%)	.00
Not knowing where to get screened	93 (44%)	37 (53%)	56 (39%)	.06
Transportation issues	122 (58%)	43 (61%)	79 (56%)	.46

*Chi-square test

having health insurance (screened = 54%, not screened = 31%), cost of screenings (screened = 49%, not screened = 31%), and not having enough information about screenings (screened = 54%, not screened = 29%) were all screening obstacles that were associated with screening status.

Discussion

African American men in this study had lower rates of screening for prostate cancer with the PSA test (36%) than men in the State of Tennessee overall (54%).[25] There are several possible explanations for this difference including that the study sample consisted primarily of low-income participants who may have limited resources to devote to health screenings. For example, 63% of participants in this study had annual household incomes below $15,000, 45% were employed, and 54% had health insurance. These rates are lower than those reported in the latest U.S. Census Bureau data for African Americans in Tennessee (18% have incomes below $15,000, 58% are employed, and 86% have health insurance).[26]

This study's results regarding the relationships between sociodemographic characteristics and screening behavior support findings from the research literature. For example, being married, having higher educational attainment, being older, having health insurance, and having a higher income were positive predictors of being screened for prostate cancer.[17–20] Additionally, in this study, obese participants were more likely

than participants with normal BMIs to have been screened, a finding that is consistent with several but not all previous studies.[27–28]

Prior research has indicated that family history of prostate cancer is associated with an increased likelihood of getting screened for prostate cancer.[8] Family history of cancer in this study was not a predictor of screening status. A possible explanation for this discrepancy is that we asked about the family history of all cancers instead of the family history of prostate cancer specifically. It may be that having a family history of a particular cancer increases the screening rates for that cancer only.

We found that making a medical visit in the past 12 months was predictive of prostate cancer screening with a PSA test in the past two years. This finding suggests that increased contact with health care systems increases the likelihood of screening for prostate cancer in African American men. Previous research has identified that health care utilization, including getting screened for cancer is associated with recommendations to do so by physicians.[29–30] Hence, in this study, men who visited their doctors in the past 12 months may be more likely to have been screened for cancers because of their doctors' recommendations during their medical visits.

An interesting finding was the differences in obstacles to screening by geographic region. The present study found that African American men reported several obstacles to being screened for prostate cancer. These included issues related to cost, transportation, time, where to get screened, and fear of finding out about cancer. The largest obstacle was transportation and the smallest was fear of a positive diagnosis. There were interesting associations between obstacles to screening and geographic region, and obstacles to screening and screening status. For example, participants in Nashville and Chattanooga were more likely than participants in Memphis to report fear of a positive cancer diagnosis as an obstacle to being screened. In addition, Nashville participants were more likely than participants at the other two sites to report cost of screening as an obstacle. This association cannot be explained by differences in the median household income because African Americans in Nashville (Davidson County, Tenn. \$30,597 $\pm$ \$1,163) have median household incomes similar to those of their Memphis counterparts (Shelby County, Tenn. \$30,440 $\pm$ \$751).[31] These results suggest that although low-income African Americans may face similar obstacles to getting screened for cancer, there are important regional differences that should be considered when developing educational programs for increasing screening rates for prostate cancer.

Another interesting finding is that participants who had been screened were more likely than participants who had not screened to report obstacles to screening. These obstacles included fear of a positive cancer diagnosis, insurance and cost issues, and a lack of information about what screening entails. These results are counterintuitive because it was expected that participants who were screened would be less likely to report obstacles to screening. One possible explanation for these results is that people who got screened may have actively worked through one or multiple obstacles, hence, they may have had a more realistic understanding of the impact of various obstacles to getting screened. Additionally, there may be obstacles that they would only find out about once they actively pursued getting screened. Participants who were not screened, in contrast, may underestimate the impact of certain obstacle because they may not have invested the time and effort trying to overcome them.

Strengths and limitations. This study has some notable strengths including that it provides information on regional differences in prostate cancer screening practices. In addition, it provides information about obstacles to screening for low-income African American men, a group that is at high-risk for prostate cancer incidence and mortality. Another strength is that this study provides information about predictors to screening in African American men. This information can be incorporated into educational programs for improving PCA knowledge, decision making, and screening rates.

Limitations of this study include that all the data are cross-sectional, hence causation cannot be inferred. In addition, all the variables were based on self-report methodology and respondents may be unwilling or may not have accurate knowledge about their health status. The validity of self-reported PSA screening is moderate, with concordance between medical chart review and self-reported PSA ranging from 71–75%.[32] It should be noted that the reliability of PSA testing data in medical reviews is unknown and these concordance figures may represent an underreporting of this relationship because they do not account for multiple sources of care. Additionally, alternate data sources such as Medicare records are not available for men younger than 65 years; hence, it is not always straightforward to confirm PSA testing though medical records in younger male populations.

Conclusion

This study identified several demographic and lifestyle variables that were significant predictors of prostate cancer screening in low-income African American men. In addition, screening status and geographic region were associated with obstables to screening for prostate cancer. Future educational interventions aimed at improving prostate cancer knowledge and screening rates in low-income African Americans should incorporate information about obstacles, and demographic and lifestyle predictors of screening.

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Association of self-reported consumption of cooked meat, fish, seafood and eggs with prostate cancer risk among Nigerians

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Background

The observation that the prevalence of latent PCa at autopsy is similar for African-American and African populations [1], and that Asian populations record latent PCa rates comparable to those of U.S. whites [2], despite large geographical differences in PCa incidence world wide, supports the suggestion that environmental cancer 'promoting' factors play a more important role than cancer 'initiating' factors in the etiology of clinically significant PCa [3,4]. Epidemiological studies have demonstrated that dietary animal fat and high energy intake are associated with increased PCa risk, while dietary marine fat is negatively associated with this risk [5]. Higher meat intake is consistently reported to be associated with increased PCa, possibly due to heterocyclic amines such as 2-amino-1-methyl-6-phenylimidazo [4,5-b]pyridine [PhIP], polycyclic aromatic hydrocarbons such as benzo [a]pyrene [BaP], and alpha-methylacyl-CoA racemase, produced in the process of grilling or frying red meat [6]. High consumption of cooked processed meats has also been reported to contribute to the high burden of PCa risk among African-Americans [7]. In China, a low-incidence region for PCa, the consumption of salted fish and preserved meats has been reported to be associated with a significant increase in PCa risk [8]. Current evidence from cohort studies supporting the association between high fish intake with reduced PCa risk is however less convincing for countries with low or high fish consumption [9,10]. Meat, fish, cheese and egg intake were not associated with PCa risk in a Netherland cohort study [11]. Like other Sub-Saharan designated low-incidence regions for PCa, Nigeria has reported an moderate upward incidence trend, with PCa becoming the most diagnosed male cancer [12,13]. This trend is postulated to result from improved diagnosis, increased longevity, and the progressive replacement of their traditional low-fat diet with a more westernized diet high in meat and processed foods. This study examined the association of self-reported consumption of cooked meat, fish, sea food, and eggs with PCa risk among Nigerians in a case-control design.

Methods

Men 40 years and older recruited by door-to-door invitation from two rural and two urban communities of Edo and Delta states of Southern Nigeria, were screened for PCa by PSA blood test and DRE examination. Also men attending the surgery and urology clinics of the University of Benin Teaching Hospital with prostate related complaints were also recruited. Trained interviewers obtained informed consent and completed the personal informa-

~ 1″ ~ 1.5″ ~ 2″ BF ~ 11″

(20gms) (40gms) (60gms) One piece of 'Big Fish (BF) ~ 60gms.
One piece of 'Small Fish'(SF) ~ 40gms.

‡ Length of serving size/portion models in inches.

Figure 1
Models of serving sizes‡ and portions of meat (M1, M2, M3) and fish (1, 2, 3, 4) utilized in interviewing participants in the Nigerian study population.

tion questionnaire, and a food frequency inventory based on the Block FFQ modified by the addition of Nigerian foods and culturally appropriate serving portions (Figure 1) for each participnats. Participants were asked to return the next day without taking breakfast, and at the second visit 30 ml fasting venous blood was collected into three tubes, a urology symptom history and digital rectal examination was conducted by a surgeon/urologist, and their physical body fat parameters were measured by a trained research assistant. Each participant received a cash incentive and gifts at the end of each study visit. PSA was analyzed by a commercial laboratory in the US. The PCa cases were histologically confirmed, and the controls were men with normal sized prostates with a PSA <4 ngs/ml.

Annual frequencies for red, white and organ meat, fish, and sea food intake were computed by adding annual frequency for each food item in that group. Food-group annual frequency <18 was labeled 'Rarely', 18–181 'Sometimes', and ≥ 182 'Frequently'. Annual quantity consumed was computed by multiplying annual frequency by unit portion size as described in Table 1. Demographic and other characteristics of PCa cases and controls were compared using Chi-square test, and odds ratio and 95% confidence interval [OR(95%CI)] of PCa risk for food items

Table 1: Computing annual intake of food items by multiplying average self-reported annual frequency of food intake by unit portion size

Annual Intake Pattern	Never	Rarely	Occasionally	Sometimes	Frequently	Every Day (Daily)	Many Times (A Lot)
Reference	0/Year	≤6/Year	1–2/Month	1–2/Week	3–4/Week	5–7/Week	≥ 2/Day
Interval Boundary	0						365 × 2
		$\frac{6}{2}$	$\frac{(12+24)}{2}$	$\frac{(52+104)}{2}$	$\frac{(156+208)}{2}$	$\frac{(260+364)}{2}$	
Mid-Interval Value	0	3	18	78	182	312	730
Frequency (3 Groups)		Rarely		Sometimes		Frequently	
Annual Intake				Mid-Interval Frequency × Unit Portion Size			
Annual Intake (4 Groups)				Transform to Quartiles			

Table 2: Demographic and other characteristics of prostate cancer cases and controls in the Nigerian study population

Characteristic	Cases n = 56	Controls n = 268	*p*-value
Residency			<0.04
Rural	25(44.6)	161(60.1)	
Urban	31(55.4)	107(39.9)	
Recruitment site			<0.001
Community	12(21.4)	251(93.7)	
Hospital Clinics	44(78.6)	17(6.3)	
Age (years)			<0.001
<54	3(5.4)	137(51.1)	
55–74	32(57.1)	112(41.8)	
≥ 75	21(37.5)	19(7.1)	
Education			<0.03
None	19(33.9)	54(20.1)	
<Secondary	23(41.1)	122(45.5)	
Secondary	1(1.8)	41(15.3)	
Post-Secondary	6(10.7)	25(9.3)	
College	7(12.5)	26(9.7)	
Annual Income (Naira)§			ns
<N45,000	47(90.4)	175(77.1)	
N45,000–N85,000	3(5.8)	20(8.8)	
≥ N85,000	2(3.8)	32(14.1)	
History of BPH			<0.001
Self-Report	22(39.3)	11(4.1)	
Obesity status			
BMI ≥ 30 (kg/m^2)	7(14.0)	16(6.2)	ns
BMI ≥ 35 (kg/m^2)	2(4.0)	32(14.1)	ns
Anthropometry (Mean)			
WHR	0.97 ± 0.09	0.92 ± 0.07	<0.001
BMI (kg/m^2)	23.9 ± 5.15	23.4 ± 3.84	ns
Height (cm)	165.1 ± 9.37	166.8 ± 7.60	ns
Skin fold thickness‡(mm)	8.9 ± 4.19	8.9 ± 4.09	ns

§ Nigerian currency
‡ Average skin fold ((biceps + triceps + sub-scapular)/3)

estimated by unconditional logistic regression controlling for age and educational status. 591(87.8%) of 673 consented men completed the FFQ, and dietary risk assessment was based on the 374 entries in the current data base.

Results

A total of 591 participants participated in this study, 334(56.5%) recruited from the community and 257(43.5%) from hospital clinics. There were 140 (23.7%) PCa cases, 78 (13.2%) with elevated PSA, and 373(63.1%) controls with mean ages 70.10 ± 10.6, 67.0 ± 10.9, and 56.09 ± 12.1 respectively, $P < 0.0001$. 127(20.1%) of the controls were recruited from the clinics

Table 3: Rate of frequent‡ intake of meat, fish and eggs among prostate cancer cases and controls in the Nigerian study population

Food item	Frequency (%) Cases	Controls	*p*-value
Chicken	4(7.1)	19(7.1)	0.67
Turkey	5(8.9)	15(5.6)	0.13
Pork	1(1.9)	18(6.7)	0.06
All white meat	7(12.7)	41(15.3)	0.67
Beef	17(30.4)	123(45.9)	0.08
Goat	1(1.8)	16(6.0)	0.18
Game	4(7.1)	36(13.4)	0.13
Skin	9(16.1)	52(19.6)	0.28
All red meat	27(48.2)	172(64.9)	0.07
Kidney/Liver	1(1.8)	22(8.9)	0.12
Gizzard	1(1.8)	5(1.9)	0.52
Tripe	0(0.0)	9(3.4)	0.30
Organ meat	4(7.1)	33(12.3)	0.09
Fresh fish	24(42.9)	122(45.5)	0.90
Dry fish	17(30.4)	92(34.3)	0.71
All fish	30(53.6)	168(62.7)	0.45
Shrimp	11(19.6)	66(24.6)	0.01
Crab	2(3.6)	16(6.0)	0.47
Snail	1(1.8)	14(5.2)	0.29
Fish & sea food	33(58.9)	195(72.8)	0.13
Egg	11(19.6)	43(16.0)	0.21

‡ Self-reported food frequency ≥ 3 times per week

and 293(79.9%) from the community. The characteristics of the 324 with their FFQ information in the database are presented in Table 2. Forty-five percent (45.9%) ate fresh fish, 43.3% beef, 16.9% eggs, and 7.2% chicken frequently, at least 3–4 times per week. The rate of frequent consumption of food groups was 227(71.6%) for fish/sea food, 198(62.3%) for red meat, 48(15.0%) for white meat, and 37(11.6%) for organ meat. Frequency pattern for meat, fish, and eggs were statistically different by education status, age, and urban/rural residency, but not by income group. The usual serving portion for fish was <40 gms for 72.4% of the participants, ≤ 60 gms of beef (51.0%), one piece of chicken (89.5%), and ≤ 2 eggs (84.6%). Pattern of intake of fish/seafood, white meat, organ meat and eggs were similar for cases and controls. Cases ate red meat (48.2% vs. 64.9%, $p < 0.07$), and shrimp (19.6% vs. 24.6%, $p < 0.01$) less frequently than controls (Table 3). PCa risk trend comparing 4th to 1st quartile annual intake was significant for red and organ meat, $p < 0.04$, with OR(95% CI) 1.74(0.59–5.17), 0.94(0.34–2.64), 1.16(0.50–2.68), and 1.18(0.50–2.81) for red meat, organ meat, fish and egg respectively (Table 4). In the study sample 2.2%, 7.1%, 8.1%, and 12.6%

Table 4: Odds ratios and 95% confidence interval (CI) for prostate cancer risk comparing lowest to highest quartiles of dietary intake of meat, fish, seafood and eggs in the Nigerian study population

	Annual Intake Quartiles Odds Ratio(95%CI)				
Food item	Q1	Q2	Q3	Q4	*p* for trend
Red meat	1.00	0.46(0.20–1.09)	0.60(0.25–1.45)	1.74(0.59–5.17)	0.04
White meat	1.00	0.71(0.31–1.62)	0.71(0.31–1.62)	1.13(0.45–2.86)	0.67
Organ meat	1.00	0.34(0.13–0.83)	0.50(0.19–1.31)	0.94(0.34–2.64)	0.04
All meat	1.00	0.69(0.30–1.57)	1.21(0.49–2.98)	2.95(0.96–9.10)	0.06
Fish	1.00	1.14(0.49–2.66)	2.41(0.91–6.42)	1.16(0.50–2.68)	0.86
All sea food	1.00	0.94(0.39–2.24)	0.75(0.32–1.76)	1.33(0.51–3.48)	0.67
Eggs	1.00	0.94(0.39–2.31)	1.34(0.52–3.45)	1.18(0.50–2.81)	0.86

reported that they did not eat red meat, chicken, fish, and eggs respectively in the previous year.

Discussion

Red meat is one of the main content of western diet proposed as a modifiable risk factor for PCa [14]. The increase in PCa incidence in Japan in the 1980s [2], and sub-Saharan Africa more recently, has been attributed to transition from the traditional low-animal fat diet to a 'westernized' diet high in animal fat, leading to modification of the natural history of PCa [12,13,15,16]. Unlike other studies that reported strong associations with red meat [14] and organ meat intake [17], our study demonstrated only a modest increased risk trend across quartiles of red and organ meat intake, but the OR for risk was not statistically significant. The fact that meat is usually boiled in this population may explain the attenuated effect of red meat since carcinogens are produced by grilling and frying [6,18]. Our findings are consistent with other reports that did not demonstrate PCa risk association with total meat, white meat [19], and egg intake [20].

Fish is the main source of protein for shoreline Africans such as Nigerians [21,22], and is more popular than meat in this population. The three commonly eaten fish are the saltwater croaker and mackerel, and the fresh water catfish, usually dried, broiled, and sometimes fried. Our data did not support the negative association between fish intake and PCa risk as reported in the study of Native Alaskan Eskimos who eat large quantities of fish [23]. Similarly a cohort study in Japan did not find PCa risk association with fish intake among men 40–69 years [24]. Japanese traditional diet, high in soybean and fish, is associated with low PCa risk [25], underscoring the importance of an entire dietary style over individual food items.

Recall error associated with the FFQ may be limited in this study given the homogeneous nature of Nigerian diet, and exposure misclassification was reduced by the use of life-size food portion models. We did not transform portion size units to actual weight, and this might attenuate statistical association if between-person differences in portion size contribute to between-person variability in amount consumed. We also did not collect information about the type of fish eaten, which together with method of preparation might be very important in cancer etiology. Despite these limitations we have no reason to disagree with the hypothesis postulated by other authors that high intake of red meat contributes to PCa risk. We however had no evidence to support the hypothesis that high intake of fish reduces PCa risk. In the absence of nutrient composition tables of Nigerian foods, we have reported preliminary results of PCa risk associations of selected food items acknowledging the limitations of FFQ in cancer risk assessment.

Conclusion

This study examined the association of self-reported consumption of cooked meat, fish, sea food, and eggs with PCa risk among Nigerians. Fish is more popular in the Nigerian population, followed by red meat, while chicken and eggs are not popular food items. The overall serving portions reported by participants are very modest. Our data did not demonstrate statistical association between frequent consumption of fish, seafood, and eggs, red, white and organ meat with PCa risk. However, consistent with previous reports, there was a modest significant increased risk trend for men in the upper quartile of quantity of red meat consumed. In contrast to other reports we did not observe any risk reduction with the quantity of fish consumed. These preliminary findings need to be confirmed in a large study sample, and future research should investigate the impact of westernized dietary transition on the development of PCa in a designated low-incidence region such as Nigeria.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FAU conceived, developed, designed, and coordinated the study, trained research staff, performed statistical analysis,

and developed the manuscript. KT participated in statistical data analysis and drafted the manuscript, EE coordinated data collection in Nigeria, ML was responsible for data entry, TO, PA, and UO examined study participants (cases and controls) and provided access to their patients, DB helped to interpret the data and to draft the manuscript. All authors read and approved the final manuscript.

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Danielle A. Jones

Project title: Regulation of the Erk signaling pathway by the PPAR gamma ligand troglitazone.

Background Information: Prostate cancer is the most frequently diagnosed cancer among men in the United States, and the second most common cause of cancer death. According to the National Cancer Institute, in 2009 there were 192,280 new cases and 27,360 deaths. African American men are at a greater risk of having prostate cancer than any other race. The reasons underlying the high incidence rate of prostate cancer among African American men are unknown. However, several risk factors for prostate cancer have been identified. Risk factors include: age (men that are over the age of 45 are at a greater risk), family history, and race (black men are at a grater risk than white or Hispanic men). Today, many researchers are conducting studies to determine the causes of prostate cancer and identify more effective methods of treating this disease.

One possible treatment for prostate cancer may be compounds that activate the peroxisome proliferator activated receptor gamma (PPAR gamma). PPAR gamma is a nuclear receptor protein that functions as a transcription factor. PPAR gamma is highly expressed in adipose tissue and plays a role in the activation of genes that stimulate lipid uptake and adipogenesis by fat cells. PPAR gamma can be activated by using the compound troglitazone. Troglitazone is an oral medication that was once used to treat diabetes mellitus. Troglitazone also reduces prostate cancer cell proliferation by inducing apoptosis.

We have previously shown that troglitazone increases phosphorylation of extracellular signal regulated kinase 1/2 (Erk 1/2) in human prostate cancer cells. Erk 1/2 belongs to the mitogen activated protein kinase (MAPK) family. MAPKs function to phosphorylate transcription factors that regulate gene expression. Erk 1/2 is activated following its phosphorylation by MEK1/2. Upon its activation Erk 1/2 contributes to the proliferation of many cell types, and is responsible for the growth of prostate cancer cells. It is not known whether troglitazone stimulated increases in Erk phosphorylation contribute to the anti-tumor effects of troglitazone.

Hypothesis/Objectives: The objective of this study was to determine whether there is a relationship between the decrease in prostate cancer cell proliferation produced by troglitazone and troglitazone-induced increases in Erk 1/2 phosphorylation. PC3 human prostate cells were used as the model cancer cell line throughout this study.

Results: Western blot analysis showed that both phosphorylated and unphosphorlated Erk 1/2 were present in PC-3 cells. Western blot also showed that troglitazone produced a dose-dependent increase in Erk phosphorylation. The greatest increase in the level of phospho-Erk was produced by a concentration of troglitazone 40 uM.

We next examined whether MEK was required for troglitazone-induced Erk phosphorylation. Western blots revealed that the MEK inhibitor U0126 blocks the phosphorylation of Erk by troglitazone in PC-3 cells. It was observed that cells that were treated with only troglitazone 40 uM showed a greater level of Erk phosphorylation than cells treated with both troglitazone 40 uM and U0126.

We next used cell growth assays to test how U0126 affects troglitazone-induced decreases in cell proliferation. Both troglitazone and U0126 alone reduced proliferation of PC-3 cells. However, combination treatment of troglitazone and the MEK inhibitor U0126 showed a greater decrease in cell proliferation compared to either drug alone.

Conclusions: The MEK inhibitor U0126 blocks the phosphorylation of Erk 1/2 by troglitazone in PC-3 prostate cancer cells. However it does not block the ability of troglitazone to reduce cell proliferation. In fact combination treatment of PC-3 cells with U0126 and troglitazone decreased the proliferation of the PC-3 cells more than either drug alone. Therefore troglitazone-induced increases in Erk phosphorylation are not required for troglitazone to reduce cell proliferation.

Prostate Cancer and Diet in Jamaican Men.

Ayokunle Osho, Tirsit Adane, Derrick J Beech, M.D., F.A.C.S., Maung Aung, MBBS, MPH, Flora A.M Ukoli, MD, MPH.

Introduction

Introduction

Epidemiologic studies suggest that environmental factors associated with Western life-style may promote the development of clinical prostate cancer. One such factor that has been implicated is dietary fat [1].
Prostate cancer is the leading cancer site among Jamaican males (30.3%) and the leading cause of cancer mortality (16.5% of total cancer deaths) [2].
According to the Jamaican Ministry of Health and Environment, the incidence of prostate cancer is 65.5 per 100,000 persons in a population of 2.8 million people [3].

Abstract

Background

There is a higher incidence of prostate cancer among populations of African descent and this could be attributed to the fact that these populations share ancestral genetic factors [4].
This was a feasibility pilot study conducted to access the demography, socio-economic status, diet and clinical tests used to diagnose prostate cancer at Cornwall Regional Hospital, Montego Bay, Jamaica. The diet data will be used to develop a culturally-specific Food Frequency Questionnaire for Jamaica.

Materials and Methods

Sample

The survey was administered to a total of 40 men. We interviewed 10 prostate cancer patients and 30 controls. The prostate cancer patients participated before or after they had seen their physician in the oncology department. The controls were obtained from Kiwanis mens' group, St Augustine church and the remaining were randomly selected within the patient population in Cornwall hospital.
Approval of the study was given by the Western Regional Health Authority and the participants gave verbal consent after a brief discussion of the study. Very few individuals opted out of the survey. 9 of the 40 surveys were self administered while the remaining 31 were conducted by the interviewer.

Data collection

Dietary assessment:
Dietary intakes were acquired using a food frequency questionnaire developed to assess the habitual diets of Jamaican adults.
Anthropometry:
Height was measured to the nearest inch using a tape rule, body weight (without shoes) was measured to the nearest 0.1 lb using a scale. The scale also measured body fat percentage. Chest, waist, hip and mid-arm circumference measurements were taken. Skin fold thickness of the biceps and triceps were taken as well.
Other information:
Information on demographic , socioeconomic status, urological history, first-degree family history of prostate cancer, tobacco and alcohol history, and history of prostate cancer screening.

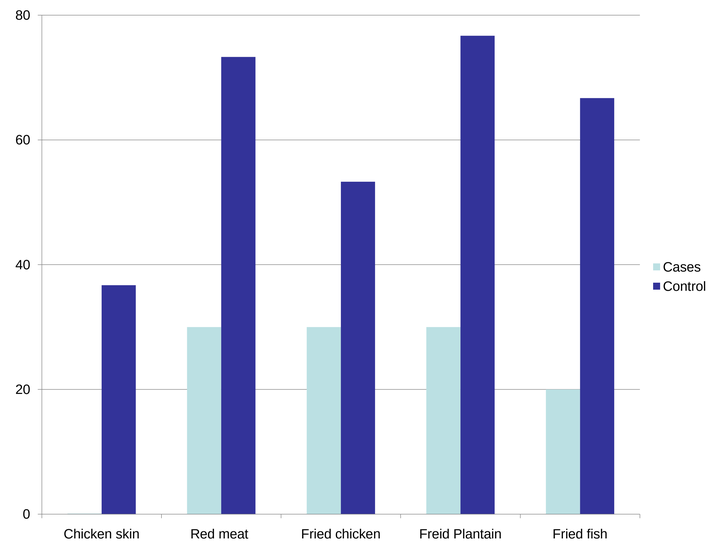
Data

Table 1. Age and Cancer Status of Subjects

Characteristics	Cases (n=10)	Controls (n=30)	Total No	%
Age Group				
≤ 35	1 (10.0)	5 (16.7)	6	15.0
35 – 64	9 (90.0)	17 (56.7)	26	65.0
≥ 65	0 (0.0)	8 (26.7)	8	20.0
Education				
Primary	2 (20.0)	11 (36.7)	13	32.5
Secondary	6 (60.0)	13 (43.3)	19	47.5
College	2 (20.0)	6 (20.0)	8	20.0
Marital Status				
Single	6 (60.0)	14 (46.7)	20	50.0
Married	4 (40.0)	16 (53.3)	20	50.0
Job Type				
Managerial	1 (20.0)	3 (16.7)	4	17.4
Tech/Service	3 (60.0)	6 (33.3)	9	39.1
Laborers	1 (20.0)	9 (50.0)	10	43.5
Not Recorded	5	12		
Urology History				
PSA Testing	7 (70.0)	16	23	
Symptoms	3 (30.0)	13	16	
BPH	5 (50.0)	4	9	

PSA: Prostate Specific Antigen; BPH: Benign Prostatic Hyperplasia

Figure 1. Fatty Food Intake.



Results

1 out of the 10 prostate cancer patients was under the age of 35, the rest were above 35 years. There was no cancer patient above 65 years either.
40% of the cases reported some type of cancer in their family. 43% of the controls reported a history of cancer in their family.
47 % of those surveyed stopped education at high school level.
There was no difference between single and married subjects.
57.5% of the subjects reported their form of employment. Majority (43.5%) of them were laborers.
Prostate specific antigen was commonly tested among cases (70%) and controls (53.3%). Only 50% of the cases had Benign Prostatic Hyperplasia at some point in their life
Eating habit was significantly different among cases and controls. According to figure 1, most of the cancer patients drastically reduced their consumption of organ meat and fried foods after diagnosis of prostate cancer. They ate more of fruits and vegetables and had less energy. Other groups of foods that are consumed consistently include rice and peas, vegetables such as corn, organ meat (beef, pork and goat). Diary consumption was low in cases and controls.
Lifestyle of smoking and drinking are common in teenage to early adulthood. Most of the participants quit smoking at some point but keep drinking, though in moderation.

Conclusions

This was a 4 week feasibility study conducted at Cornwall Regional Hospital Montego Bay, Jamaica. A lot of data were collected and analyzed. It has proved that such a survey can be conducted internationally.
No concrete conclusions can be deduced from the survey judging by the sample size. The American Food Frequency Questionnaire (FFQ) was not suitable for the survey due to the differences in diet. The different Jamaican dishes surveyed would be used to make an FFQ suitable for Jamaica. The instruments used for measurements were not standardized, making some measurements inaccurate.
Future studies using the appropriate FFQ and involving a larger sample size needs to be conducted before any major conclusions can be made about diet and prostate cancer in Jamaican men.

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Barriers to Prostate Cancer Screening among Low-Income African American Men in Nashville/Davidson County

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INTRODUCTION

Within the African-American community there is a negative perception of healthcare which may be reflected in their low screening participation. In addition to negative healthcare perceptions, studies suggest that amongst other things, lack of knowledge and transportation, relationships with primary healthcare providers and financial cost also contribute to the lack of participation amongst African-Americans. Prostate Cancer Screenings also exhibit a lack of participation amongst African-American men.

According to studies African-American men are disproportionately affected by prostate cancer. National studies have found that black men, compared with their white counterparts, have a 34 percent greater chance of being diagnosed with the disease and a 123 percent greater chance of dying from it. Despite their higher incidence and mortality rates of prostate cancer compared to their white counterparts, their participation in prostate cancer screening activities is lower. The barriers contributing to low screening rates amongst low-income African-American men in Nashville need to be identified so that an appropriate prostate cancer education intervention program can be developed to address the barriers. With the identification of a cross-section of barriers and formation of an educational program that promotes informed decision making, African American men may be able to overcome their reluctance to undergo cancer screenings involving PSA and the rectum therefore increasing the survival rate of black patients.

AIMS AND OBJECTIVES

Identify the prostate cancer screening hindrances and develop a culturally appropriate prostate cancer screening intervention program for low-income African-American men in Nashville, TN. This program will improve their level of knowledge about prostate cancer and positively change their attitude towards early detection of prostate cancer by PSA and DRE screening.

1. Convene three distinct focus groups to identify and catalog perceived barriers to prostate cancer screening among low-income African-American men.
    a. These groups will be formed to address both individual and interpersonal perspectives
    b. According to the group either individual or interpersonal perspectives will be addressed/discussed
2. Assemble a Community Advisory Board (CAB) for the development of a culturally appropriate prostate cancer education and intervention program with respect to the addressed barriers.
3. Improve the ability of the target population to make informed decisions about prostate cancer screening.

MATERIALS AND METHODS

African-American men and women 25 years and older were invited from the Nashville Community to participate in prostate cancer focus group discussions. Eligible individuals were informed through focus group flyers that described the purpose of the study, eligibility criteria, incentive, and project coordinator contact information. Flyers were posted at the health center, churches, stores, barbershops, community business and recreation centers. Prostate cancer survivors were contacted through local cancer support groups, cancer registry, and word of mouth. The project coordinator screened interested persons for eligibility and assigned them to an appropriate focus group.

Three focus groups, each consisting of ten persons, were conducted to obtain information about barriers to prostate cancer screening among self-identified African-Americans. Barriers and facilitators of prostate cancer screening will be assessed at the individual level, focus groups 1 and 2, and at the interpersonal level, focus group 3. The first group consisted of men who were at least 40 years and older and regularly screen for prostate cancer by PSA and/or DRE. Five men were diagnosed with prostate cancer and the other five were prostate cancer survivors. The second group consisted of men at least 35 years old who had never screened for prostate cancer by DRE and/or PSA. Four men were younger than 40 and six men were 40 and older. Group members for the third group were family members, wives/partners and children of African-American men who were between the ages of 25-39. Four wives/partners (30 years and older), three daughter and three sons (25-39 years of age) comprised the third group. This group assisted in indicating family members' relevant perceptions to prostate cancer screening decision making.

To minimize the cultural and gender related sensitivities an African-American man was trained as a community navigator. He conducted all focus groups at the health center conference room and a list of "probing questions" was used to facilitate discussions. He also served a modest meal and distributed $20 cash compensation towards the cost of transportation at the completion of the 2-hour session.

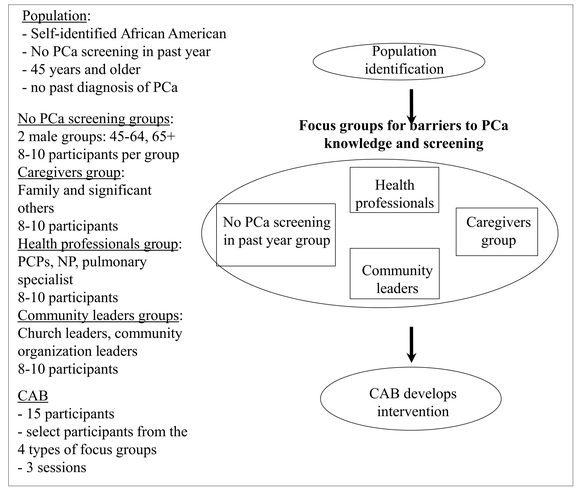
MATERIALS AND METHODS cont.

All participants were consented prior to participation, including an agreement (or refusal) to be video and audio taped during the sessions. All focus group participants were addressed by name, identification numbers were not assigned to them. The information collected was analyzed by a professional transcriber using the Atlas.ti software, with themes developed and organized by one of the study investigators (Patel, K.).

After all of the focus group meetings were conducted, 10 participants were selected to serve on a Community Advisory Board (CAB) to assist in the development of an intervention for improving knowledge, informed decision making, and screening rates for prostate cancer. The CAB consisted of seven laymen (five men, two of which were prostate cancer survivors and two women), two community leaders and one health care provider. Persons were selected based on the degree of active involvement in discussions and interest in participating; to ensure that each of the three levels of the socio-ecological model was represented 2-3 persons were selected from each focus group. Three CAB sessions were held, first the barriers indentified by the focus groups were studied, then solutions were proposed to the barriers, and lastly content materials for an educational intervention, brochure and study advertisement flyers were developed. CAB members were consented prior to their participation, served a modest meal, and received a $20 cash incentive for each of the three sessions moderated by the community navigator and one study investigator (Patel), with the PI in attendance only.

DATA ANALYSIS

RESULTS



CONCLUSION

- Information from the focus groups was used to develop content for the education intervention brochure aimed at increasing prostate cancer knowledge and encouraging prostate cancer screening.
- The CAB will generate a culturally relevant, easy to read and understand, and interactive intervention that will encourage participants to ask questions.

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•Department of Surgery Meharry Medical College
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•Mathew Walker Comprehensive Health Center
•Research Navigators

The Role of Lycopene in Prostate Cancer Risk among African American Men

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INTRODUCTION

Many of us at one time or another have been told by our parents if not by others that proper nutrition is important in staving off sickness and disease. This we are told can be achieved by eating a balance meal with plenty fruits and vegetables. But how important are fruits and vegetables in promoting good health? What nutrients are important to the human body? This paper will focus on the antioxidant, lycopene, and its impact, if any, on prostate cancer risk in African American men.

By age 65, men in the United States develop prostate cancer and by age 50 the more aggressive form of the disease is found in African American men. Prostate cancer is a problem in African-American men as they do not consume foods that contain sufficient quantities of lycopene. Some studies have indicated that the mortality rates in African-American men are much higher than other men of ethnic origins and one contributing factor that greatly influences this is the lack of a high level of lycopene found in the blood. Laboratory studies revealed that lycopene is one of the many natural carotenoids that is a very potent antioxidant that inhibits the abnormal growth of prostate cancer cells. It is found in extremely high concentrations in tomatoes and tomato products and other foods such as fresh guava, raw pink grapefruit, fresh watermelon, fresh papaya, and apricot. The aim of this research will be to examine plasma level lycopene and its association with prostate cancer risk in African American men of age 45 years and older.

AIMS AND OBJECTIVES

The goal of this study is to evaluate the role of lycopene in prostate cancer risk among African-American men in a case-control design.

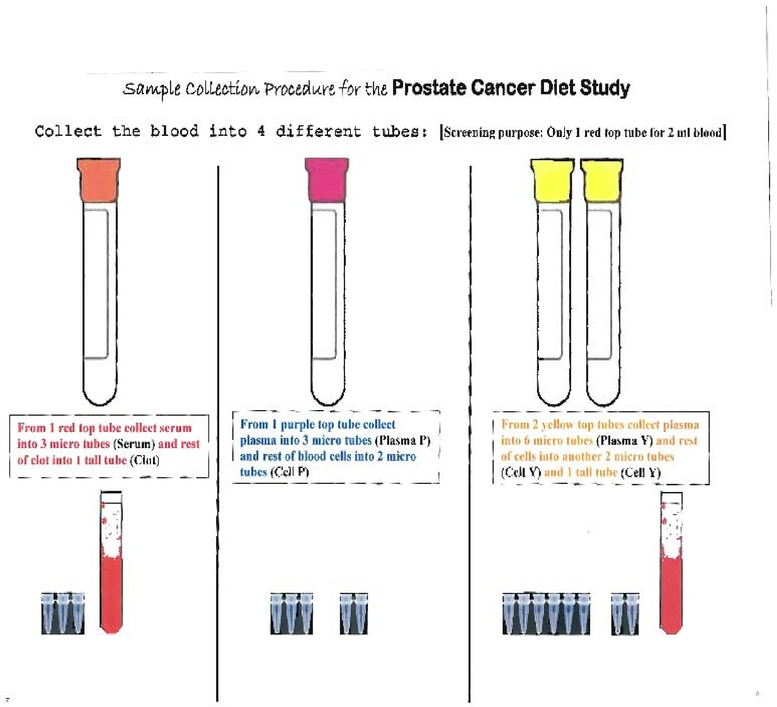
Aim 1: Accrue 50 African-American prostate cancer cases, 50 hospital-based age-comparable controls, and 50 community-based age-comparable controls living in Nashville, TN and in surrounding counties, and compare the demographics, anthropometric measurements, and dietary intake estimates of lycopene and total calories of cases and controls.

Aim 2: Compare the role of plasma lycopene in prostate cancer risk among African-Americans, controlling for anthropometric measures of body fat.

Hypothesis:

H1: Prostate cancer cases have lower plasma lycopene level than controls in both populations.
H2: Consumption of high quantities of tomato-based foods corresponds to higher plasma lycopene.
H3: Plasma lycopene remains a protective factor for prostate cancer after controlling for total calorie intake and body fat measurements.

Fig.1 Tubes used in storing venous blood specimen



MATERIALS AND METHODS

African-American men age 40 years and older and who reside in Nashville and it surrounding counties were recruited as participants for this population-based case-control study. Cases were identified as African-American men who have been diagnosed with prostate cancer within the past 5 years and the controls were those who declared to be free of prostate cancer within the past 12 months. Two age-comparable controls were selected for each case, one from the community as the case and the other from the same hospital/clinic. The study cases included men who were diagnosed with prostate cancer and the controls included men who have been screened by DRE and PSA and found to be free of prostate cancer. Men who were diagnosed with cancer for more than five years; patients on chemotherapy or hormonal treatment for cancer therapy, other hormones such as insulin, steroids, and anti-retroviral medication; severely ill or institutionalized; patients on prescribed diet modification as part of treatment management for any medical condition. (Except low-salt diet.); and men diagnosed with any other cancer apart from non-melanoma skin cancer were excluded from the study. For the controls, we excluded those who have been diagnosed with prostate cancer at any time; severely ill or institutionalized; patients on prescribed diet modification as part of treatment management for any medical condition; diagnosed with any other cancer apart from non-melanoma skin cancer; and those who currently resided outside TN. We excluded institutionalized persons as their diet may have been different from their usual diet before they became institutionalized. The hypothesis of this study assumed that dietary patterns have not been changed drastically in recent year. Also excluded were men on selected treatments as the hormonal milieu may have been modified drugs such as hormones, anti-retrovirals, and chemotherapy.

Participants were informed about the study including the procedures, benefits, risks, and confidentiality issues. They were informed that participation was voluntary and about their right to withdraw from the study or refuse to participate in the study at any time. In addition, they were informed that the data collected would be used exclusively for this research. Participants were also informed about prostate cancer diagnosis, pathology, PSA measures and that treatment would only be abstracted from their medical records if they give the permission for that to be done. All participants were asked to read and sign a HIPAA form that shows how their information would be protected and the list of persons with whom we may share this information with if the need arises.

Data collected were done in two parts. For the first part of data collection, processed participants completed a self-administered questionnaire which involved collecting personal and medical information, including prostate biopsy information. Participants also completed a dietary assessment in the form of food frequency questionnaire (FFQ) that includes life-size food portion models to compare annual frequency and serving size consumption of selected food items like red meat, dairy product, tomato-based foods, fruits and vegetables across cases and controls. Their physical measurements such as height, weight, body-fat percent, waist, hip, mid-arm circumference, biceps, triceps and subscapular skin folds were also measured and recorded. The second part of data collection involved specimen collection of fasting venous blood, 30ml. This was only once with a multi-draw needle, into three separate tubes to provide serum and plasma to measure lycopene.

DATA ANALYSIS

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RESULTS

CONCLUSION

REFERENCES

ACKNOWLEDGEMENT

African-American prostate cancer screening program and study participants, Washington DC and Nashville metropolitan areas, Benin-City, Warri, and Udo of Southern Nigeria, surgeons/urologists, patients and staff of the surgery department University of Benin Teaching Hospital and affiliates (Udo and Warri health centers, Specialist hospitals Benin and Warri, and Eku Baptist Hospital), Howard University Cancer Center, Washington DC, the Department of Surgery Meharry Medical College, research assistants Clare Tay, Samali Mayengo, Luke Ani, Esther Ukoli, Jennifer Murphy & Libnir Telusca. Project was funded mainly by the Department of Defense IDEA AWARD # DAMD17-02-1-0068 and HBCU Partnership. W81XWH-05-1-0229. Partial-funding from the Government of the District of Columbia and New faculty award HUCC.

MEHARRY MEDICAL COLLEGE
INSTITUTIONAL REVIEW BOARD
CONTINUING REVIEW FORM (CRF)

Principal Investigator Flora A. M. Ukoli, M.D., M.P.H. Department Surgery

Study Coordinator _____

Title of project:
Lycopene in Prostate Cancer Risk among African-Americans and Nigerians:
A Case-Control Study

Funding Source Department of Defense, DOD

IRB SUBMISSION REQUIREMENTS
Expedited: **2 copies of CRF (1 original + 1 copy), 2 copies of consent forms (clean copy), 2 copies of consent forms (tracking copy), 2 copies of last approved stamped consent forms**

Full Board: **18 copies of CRF (1 original + 17 copies), 18 copies of consent forms (clean copy), 18 copies of consent forms (tracking copy), 18 copies of last approved stamped consent forms**

SUBMISSION CHECKLIST (PLEASE COLLATE ALL SUBMISSIONS)

☑ ***CONTINUING REVIEW FORMS (CRF)***

☐ ***CLEAN COPIES OF NEW CONSENT FORMS with current revised date (unstamped)***

☑ ***LAST APPROVED STAMPED CONSENT FORMS***

☐ ***TRACKING COPIES OF REVISED CONSENT FORMS***

☐ ***OTHER (please list)***_____

☐ ***RECERTIFICATION of IRB training for participants who have contact with human subjects***

CONFLICT OF INTEREST (COI) STATEMENT

YES ◉ NO ○ Has a COI developed since the submission of the Human Subject Review Form (HSRF) **or** previous IRB continuing review for the Principal Investigator/spouse or research personnel? (i.e., stock or stock options, interest in technology, consultant to sponsor, proprietary interest)?

PROJECT DESCRIPTION

1. **PROJECT STATUS (check what applies):**

☑ ***CONTINUING with NO CHANGES*** in procedure, risks, number of subjects or class of human subjects since the last review.

☐ ***REVISED*** since the last review.

☐ ***NO SUBJECTS HAVE BEEN ENROLLED TO DATE.***

☑ ***RECRUITMENT/ENROLLMENT CONTINUES.***

☐ ***SUBJECTS NO LONGER BEING ENROLLED, but continue to receive research intervention (e.g., blood draws, receiving medications).***

☐ ***SUBJECTS NO LONGER BEING ENROLLED; only for long-term follow-up.***

☐ ***DATA ANALYSIS ONLY***

☐ ***COMPLETED***. NO FURTHER RECRUITMENT OR CONTACT WITH HUMAN SUBJECTS IS PLANNED, *NOR WILL ANY FURTHER ANALYSIS OF SAMPLES OR DATA GATHERED FROM PATIENTS BE PERFORMED*.

☐ ***I AM NO LONGER CONDUCTING THIS PROJECT.*** (If you check this option your IRB approval will end and the IRB will no longer review your project. If you wish to resume the study later you must submit it to the IRB as a new project.)

☐ ***NEVER INITIATED: Reason***
Not funded ☐ *No enrollment* ☐ *Other* ☐ _____

_____

☐ ***FUNDING****:* If industry-initiated, has funding been provided for continuing review: Yes/No

YES ○ NO ○

2. **HUMAN SUBJECTS** from the following population(s) are involved in this study:

☐	Minors	☐	Meharry Medical College employees
☐	Pregnant women	☐	Meharry Medical College students
☐	Fetuses or abortuses	☐	Mentally disabled or retarded
☐	Inpatients	☐	Prisoners
☑	Outpatients	☐	Human-derived biological materials
☐	Emancipated minor	☐	Other _____

3. Please indicate **STUDY SITES**:

- [x] Meharry Medical College
- [ ] Vanderbilt Medical Center
- [ ] Metro General
- [ ] Non-U.S.A. Site
- [ ] Murfreesboro Veterans Administration
- [ ] Other Vanderbilt Sites
- [ ] Other _____ (Please Specify)

If you have added study sites since the last review, attach certifications that each new site approves the use of its facilities for your research. Certification can be a letter from the site's institutional review board or an appropriate institutional official.

4. Does this project use the Meharry Clinical Research Center's facilities or services? Yes ◉ No ○

PROGRESS REPORT

5. NUMBER OF SUBJECTS ORIGINALLY APPROVED BY THE IRB TO BE ENROLLED IN THE STUDY. 300

6. HAS THE IRB APPROVED INCREASES OR DECREASES IN THE NUMBER OF ENROLLEES IN THE STUDY? YES ○ NO ◉

   A. IF YES, NUMBERS CHANGED FROM _____ TO _____
   DATE OF IRB APPROVAL _____

7. NUMBER OF SUBJECTS WHO HAVE SIGNED CONSENT FORMS (i.e., including withdrawals, screen failures) SINCE THE LAST REVIEW. 70

   A. How many of the subjects withdrew from the study? Explain in #12. None

   B. How many of the subjects in the study were lost to follow-up? Explain in #12. None

8. HOW MANY SUBJECTS HAVE BEEN ENROLLED IN THE STUDY TO DATE? (From the beginning of the study). 175

   A. **How many of the subjects have completed the study, including follow-up?** 175

9. NUMBER OF SUBJECTS ENROLLED SINCE THE LAST CONTINUING REVIEW. If 0, explain below.

(Explain) Low number of potential participants, Inadequate advertisement 0

10. NUMBER OF SUBJECTS YET TO BE STUDIED. This must correspond with the total number the IRB approved in the original application, or with the IRB-approved changes in that number (#6A). ***If no patients have been enrolled by the third time this project is reviewed, IRB approval will automatically be withdrawn.*** 125

11. Have any SERIOUS ADVERSE EVENTS occurred since the last review? **This refers to all study sites.**

    Yes ○ No ◉ If YES, how many? _____

12. If the SERIOUS ADVERSE EVENTS occurred at Meharry Medical College/NGH, were these reported to the study sponsor, FDA, and the IRB?

Yes ○ No ○ Not applicable ◉

13. Were any of these serious adverse events unanticipated in the protocol or not mentioned in the consent form?

Yes ○ No ○ Not applicable ◉

A. **Was the consent form modified to include the serious adverse event(s)?**

Yes ○ No ○ Not applicable ◉

14. If a Multi-center site, have there been any Data Safety Monitoring Board reports sent by the sponsor?

Yes ○ No ○ Not applicable ○

A. If yes, how many? _____

B. Attach any copies that have not been submitted to the IRB

15. SUMMARY OF RESULTS TO DATE. If none, explain why. If applicable, provide copy of publication, progress report, etc.

The project has recruited 175 participants, 57 from Nashville site and 122 from the Nigeria site. Recruitment of new participants has since stopped at the Nigerian site. In 2009 we did not recruit any prostate cancer case in Nashville. Stored study samples include serum, plasma, blood clot and urine. 177 previously stored samples (81 samples from Nigeria), have been analyzed for lycopene by the study collaborator Myron Gross, Ph.D., at the University of Minnesota. 55 of these samples are from prostate cancer cases while the reminder are from controls. The Nashville site is yet to meet its accrual goal especially prostate cancer cases. We revisited our recruitment strategy at the Nashville General Hospital (NGH) and the Matthew Walker Comprehensive Health Center (MWCHC) in Nashville (where we just completed a very successful prostate cancer education and screening program), and intend to improve the recruitment of cases in 2010. This will be achieved by distributing flyers in the urology clinic of the NGH and at MWCHC. We have identified 80 men at the MWCHC with elevated PSA awaiting screening resolution. This will serve as a promising source of potential study eligible men that will receive a mailed invitation/flyer to participate in the study.

PLEASE ATTACH A CURRENT COPY OF THE CONSENT FORM.
IF CLOSED TO ENROLLMENT, CONSENT FORM IS NOT NECCESARY.

I certify that the information in this report is accurate, and that the protocol and method of obtaining informed consent which were approved by the IRB, have been followed during the period covered by the PROGRESS REPORT.

Date: _____ Principal Investigator _____

Yes ○ No ○ Not applicable ◉

13. Were any of these serious adverse events unanticipated in the protocol or not mentioned in the consent form?

Yes ○ No ○ Not applicable ◉

A. **Was the consent form modified to include the serious adverse event(s)?**

Yes ○ No ○ Not applicable ◉

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I certify that the information in this report is accurate, and that the protocol and method of obtaining informed consent which were approved by the IRB, have been followed during the period covered by the PROGRESS REPORT.

Date: 03/03/2010 Principal Investigator _____