Award Number:

W81XWH-09-1-0638

TITLE:

Reducing Prostate Cancer Disparities through Behavioral and Biologic Epidemiologic Approaches

PRINCIPAL INVESTIGATOR:

Bettina Drake, PhD, MPH

CONTRACTING ORGANIZATION:

The Washington University
St. Louis, MO  63130-4862

REPORT DATE:

September 2010

TYPE OF REPORT:

Annual summary

PREPARED FOR:  U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland  21702-5012

DISTRIBUTION STATEMENT:

   x  Approved for public release; distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.
**Purpose:** This study seeks to define the optimal dose of vitamin D supplementation in Blacks needed for future intervention efforts in the prevention of prostate cancer.

**Scope:** Study subjects were randomized to placebo, 1000IU, 2000IU, or 4000IU of vitamin D3 per day to determine the minimum dose of vitamin D needed to achieve an optimal level. After 3 months of supplementation, plasma levels of 25(OH)D and PSA are determined and compared to baseline levels. We also assessed 25(OH)D and PSA 6 months. The goal was to enroll 320 participants, including 100 men, into the study. A 3-phase eligibility and consent process was used. Only people who were AA, English-speaking, and 30-80 years old were approached to participate in the study; 2. Basic non-clinical eligibility criteria were assessed; 3. Primary care contacts were contacted to assess clinical eligibility. To encourage retention, a case-manager approach was implemented which included biweekly calls and monthly pill bottle exchange visits.

**Up-to-date findings:** We consented 572 individuals and exceeded our recruitment goals with 329 participants enrolled in the study, including 107 men. Retention for the 3- and 6-month assessment was 90.54% and 89.13%, respectively. The supplementation and follow-up periods for this study have recently been completed.
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>4</td>
</tr>
<tr>
<td>Body</td>
<td>4</td>
</tr>
<tr>
<td>Key Research Accomplishments</td>
<td>6</td>
</tr>
<tr>
<td>Reportable Outcomes</td>
<td>6</td>
</tr>
<tr>
<td>Conclusion</td>
<td>6</td>
</tr>
<tr>
<td>References</td>
<td>7</td>
</tr>
<tr>
<td>Appendices</td>
<td>8</td>
</tr>
</tbody>
</table>
INTRODUCTION
For my cancer epidemiology research to flourish, the next phase of my training should include mentorship and training on the use of behavioral and biologic epidemiological methods concurrently. I seek to utilize this award to accomplish four main objectives: 1) To increase knowledge in and integrate the application of biologic and behavioral epidemiological methods in prostate cancer disparity research; 2) To increase my publication record; 3) To seek and obtain additional funding, specifically an R01, by the end of year four; 4) To strengthen skills in managing research teams and to develop relationship with colleagues who might serve as co-investigators on future projects. The main goal of the project I am proposing for this career development award is to determine the impact vitamin D has on prostate-specific antigen (PSA) levels. We will be able to assess behaviors such as adherence to vitamin supplementation, diet and as well as sun exposure. The future potential of this project is great. We will be able to demonstrate in the highest risk group for prostate cancer, a tangible prevention strategy that is supported by sound epidemiology and has strong potential for dissemination.

BODY
Training Plan
Dr. Giovannucci, my mentor, has included me into his research team. In addition to guiding my research efforts, he has also been instrumental in making important connections for me within our field, allowing me to develop relationships with researchers that I otherwise would not. Currently, I am an Assistant Professor at Washington University in St. Louis; however, I maintain an active collaboration with Dr. Giovannucci and other investigators at Dana-Farber Cancer Institute and Harvard School of Public Health.

Dr. Giovannucci and I meet by phone on a regular basis to discuss methodological and analytical approaches, interpret outcomes, and outline manuscript ideas. We continue to work closely on the vitamin D supplementation project presented in this proposal. When we meet by phone we discuss the following topics: 1) Progress on manuscript and grant writing projects; 2) How my research is addressing prostate cancer disparities through biologic and behavioral approaches; 3) What is missing from my research program to address #2; 4) New research ideas. These discussions have resulted in an institutional award through the Nutrition Obesity Research Center at Washington University as well as the submission of an R03 on the prognostic effect of vitamin D on prostate cancer.

The objectives of this training award include: 1) To increase knowledge in and integrate the application of biologic and behavioral epidemiological methods in prostate cancer disparity research; 2) To increase my publication record; 3) To seek and obtain additional funding, specifically an R01 by the end of year four; 4) To strengthen skills in managing research teams and to develop relationship with colleagues who might serve as co-investigators on future projects.

Objective 1: This objective is being met through the conduct and participation in the research plan outlined below. Shortly, we will begin the analysis of this study which will allow me to delve further in to the application of behavioral and biological factors on prostate cancer disparities.

Objective 2: At the start of this award, I had a number of papers in progress. I have published 4 publications in the past year, one in the Journal of the American Medical Association. My paper-writing plan has shown to be effective. I have a number of papers currently in progress as well as several papers that will soon be in progress after the assays are conducted from the vitamin D supplementation trial. Data collection has recently ended for this study and data analysis will begin within the next 2-3 months.

Objective 3: Over the previous year, I have had numerous experiences in grant-writing and have also been successful in both federal and institutions grants. I plan to build on my currently funded research to apply for a Health Disparity Award through the PCRP at DOD in the summer of 2011. In addition to grant-writing experience, I had the opportunity to participate on an NIH
review panel for R21 grants. This experience has positively impacted my approach to writing grants.

Objective 4: With my recently funded projects, I have the opportunity to hire and manage research assistants, study protocols and budgets. Through my collaborations with Dr. Giovannucci, as well as my current faculty appointment, I have established collaborations with other investigators and am currently collaborating on research projects, grant proposals and manuscripts.

Research

The research project proposed will examine differences in PSA levels associated with vitamin D intake (oral supplementation in three doses) and uptake (plasma measured 25(OH)D) among Black participants. PSA levels will be assessed, in men only (N=100), at baseline, 3-, and 6-month follow-up.

Our aims and hypotheses are as follows: Aim 1. To examine the influence of oral vitamin D supplementation on PSA levels. We will examine whether vitamin D supplementation is associated with plasma levels of PSA, and whether a threshold effect exists within this association.

Hypothesis 1.1: Higher levels of vitamin D supplementation will be associated with lower PSA levels.

Hypothesis 1.2: Vitamin D uptake (i.e. 25(OH)D levels) will be inversely associated with PSA levels.

The supplementation and follow-up periods for this study has recently completed. We are planning to analyze the blood-work within the next month. How current results are focused on recruitment and retention successes.

This study addresses the critical areas of cancer prevention and racial disparities by defining the optimal dose of vitamin D supplementation in Black men needed for future large intervention efforts in the prevention of prostate cancer. Study subjects were randomized to placebo, 1000IU, 2000IU, or 4000IU of vitamin D3 per day to determine the minimum dose of vitamin D needed to achieve an optimal level. Supplementation occurred during the winter months, to reduce sun exposure. After 3 months of supplementation, plasma levels of 25(OH)D and PSA levels are determined and compared to baseline levels. We also assessed vitamin D and PSA levels 3 months post supplementation.

The recruitment goal was to enroll 320 participants, including 100 men, into the study. A 3-phase eligibility and consent process was used to reach this goal. 1. Only people who were AA, English-speaking, and 30-80 years old were approached to participate in the study. 2. Among these individuals, basic non-clinical eligibility criteria were assessed. 3. Primary care physicians of the remaining individuals were contacted to assess clinical eligibility. Targeted recruitment efforts focused on obtaining individuals who met the first phase eligibility criteria. Potential participants were identified at public housing sites, faith-based organizations, community organizations and through participant referrals. To encourage retention, a case-manager approach was implemented and research assistants made biweekly phone calls and monthly pill bottle exchange visits with participants.

Through our recruitment efforts, we consented 572 individuals and exceeded our recruitment goals with 329 participants enrolled in the study, including 107 men. During year 1, with 2.5 months of recruitment, we enrolled 46 participants. During years 2 and 3 with 6 months of recruitment each year, we enrolled 166, and 117 participants, respectively. Retention for the 3- and 6-month assessment was 90.54% and 89.13%, respectively.

Our strategies and lessons learned are relevant to other researchers conducting research in a population, such as this one, that has historically been challenging to recruit and retain into clinical studies.
Data analysis will begin in the next 2-3 months. We will examine the influence of 25(OH)D uptake on the difference between baseline, 3-month, and 6-month PSA levels as well as the difference between baseline and 6-month PSA level to assess if lack of significant change may be attributable to vitamin D supplementation. All analyses will be conducted first as intent-to-treat and include all subjects, followed by analyses of only compliers. In the primary analysis, we will utilize the randomized trial structure to assess the association between vitamin D intake and PSA change. As a secondary analysis, we will assess the association between 25(OH)D uptake, categorized in tertiles (below 32 ng/mL), acceptable (32 - 40 ng/mL) and optimal (40 ng/mL and over)), and PSA change.

KEY RESEARCH ACCOMPLISHMENTS

- Successful recruitment and retention of participants into the study. We met and slightly exceeded our recruitment efforts of 329 (320 proposed) participants of which 107 (100 proposed) were men. Our 3-month retention rates exceeded 90%.
- Funding from the Nutrition Obesity Research Center at Washington University School of Medicine to conduct a nested case-control study that will assess the effects of pre-treatment vitamin D and leptin levels on prostate cancer recurrence titled, “Obesity and vitamin D related effects on prostate cancer recurrence”

REPORTABLE OUTCOMES

- Assistant Professor position at Washington University School of Medicine
- An R03 submission to the Cancer Epidemiology Section of NCI
- Funding from the Nutrition Obesity Research Center at Washington University School of Medicine to conduct a nested case-control study that will assess the effects of pre-treatment vitamin D and leptin levels on prostate cancer recurrence titled, “Vitamin D related effects on prostate cancer recurrence”

CONCLUSION

The proposed study will be among the first to examine the impact of vitamin D supplementation/uptake on PSA among Blacks in a non-patient sample. As a result of our work, we will learn more about the complicated biological relations between vitamin D and PSA. Additionally, this work will make an important contribution to our understanding of the role of vitamin D as a possible pathway for racial/ethnic prostate cancer disparities. We may derive preliminary public health messages regarding the association between vitamin D and these important cancer biomarkers. Further, it provides an excellent vehicle for the development of my skills in behavioral and social science, while continuing development of my expertise in epidemiology. The types of interventions that may evolve from my research program are prostate cancer prevention interventions targeting diet (vitamin D) consumption among the most at-risk groups. With the knowledge and experience gained from this award, I will make significant contributions to the development of effective studies that focus on the interactions
between biologic and behavioral factors that contribute to prostate cancer disparities and how we can address the problem through a transdisciplinary approach to reduce the cancer burden.

There are many factors associated with vitamin D and its effects on prostate cancer. My future research will begin incorporating genetic polymorphisms within the vitamin D pathway as well as additional behavioral factors such as dietary intake and sun exposure behaviors that will provide a more complete representation of the mechanisms behind vitamin D effects.

REFERENCES
N/A

APPENDICES
Curriculum vitae
Bettina Fisher Drake, MPH, PhD

**SUMMARY:** My work focuses on the interactions between the social/behavioral and biological determinants of cancer disparities, an understanding of which may lead to the development of more effective disease prevention strategies. The objectives of my research program are: 1) to identify the modifiable and non-modifiable risk factors for cancer as well as the at-risk groups for these factors; 2) to utilize epidemiologic methods to understand the interactions between behavioral and biologic determinants of adverse cancer outcomes; 3) to contribute to the translation of epidemiological findings into behavioral interventions at the individual and population level.

**CITIZENSHIP:** U.S.A

**ADDRESS:** (Office) Washington University School of Medicine
Prevention and Control
660 S. Euclid, Campus Box 8100
St. Louis, MO 63110

**PRESENT POSITION:** Assistant Professor, Washington University School of Medicine

**EDUCATION:**

**Undergraduate**
2000 Honors Premedical Academy
Baylor College of Medicine and Rice University

2001 B.S., Biochemistry major, Sociology minor
Baylor University
Baylor Interdisciplinary Core

**Graduate**
2003 M.P.H., Public Health, Epidemiology concentration
University of North Texas Health Science Center
Thesis: *Tracking of Cholesterol Among Individuals With and Without Diagnosed Cardiovascular Disease*
Advisor: Antonio René, PhD

2006 Ph.D., Epidemiology
University of South Carolina, Arnold School of Public Health
Dissertation: *Prostate Cancer Disparities in South Carolina: Treatment and Survival*
Advisor: James Hébert, ScD
Postgraduate
2006-09  Alonzo Smythe Yerby Postdoctoral Fellowship, Social Epidemiology
Harvard School of Public Health
Mentors: Gary G. Bennett, PhD and Karen M. Emmons, PhD

ACADEMIC POSITIONS/EMPLOYMENT
2000  Researcher, Organic Chemistry Department, Baylor University
2001  Researcher, Center for Drug Discovery, Baylor University
2001  Researcher, Center for Community Research and Development, Baylor University
2001  Research Assistant, Texas Public Health Training Center
2002  Project Evaluator, Tarrant County Health Department
2002  Intramural Research Training Awardee, National Institute on Aging
Mentor: Larry Brant, Ph.D.
2002-03  Research Assistant, University of North Texas Health Science Center
Mentor: Daisha Cipher, Ph.D.
2003-04  Graduate Research Assistant, Office for the Study of Aging, University of South Carolina
Mentor: Jim Laditka, Ph.D.
2002-05  Graduate Research Assistant, Community-Based Participatory Research Project, University of South Carolina
Mentor: Robert McKeown, Ph.D.
2004-06  ASPH/CDC/PRC Predoctoral Research Fellow, University of South Carolina
2006-09  Alonzo Yerby Postdoctoral Research Fellow, Harvard School of Public Health
2009-present  Assistant Professor, Washington University School of Medicine

CERTIFICATIONS
2004  Dementia Specialist

HONORS & AWARDS
2000  Order of Omega Honor Society
2002  Intramural Research Training Awardee, National Institutes of Health
2003  Leon Brachman Community Service Award, University of North Texas Health Science Center
2003  Outstanding Public Health Student, University of North Texas Health Science Center
2003 Delta Omega Public Health Honor Society, Alpha Sigma Chapter
2004-06 ASPH/CDC/PRC Pre-doctoral Research Fellow
2006 Outstanding Epidemiology Student, University of South Carolina
2007-12 NIH Health Disparities Loan Repayment Program Awardee

COMMITTEES/LEADERSHIP POSITIONS
2003-06 Steering Committee, Heart, Soul, Mind & Strength Community-Based Project, University of South Carolina and United Methodist Convention
2002 Leadership Team, Campus-Community Partnerships for Health, University of North Texas Health Science Center
2004-06 Evaluation Committee, Arnold School of Public Health, University of South Carolina
2004-06 South Carolina - African-American Prostate Cancer Network
2004-06 Research Taskforce, South Carolina Cancer Alliance
2004-05 Vice President, Dan’s Student Advisory Council, University of South Carolina
2005-06 Core Team and Education Subcommittee, South Carolina Cancer Disparities Community Network, University of South Carolina
2006- Prostate Health Education Network
2006-2009 Associate Member, Dana-Farber/Harvard Cancer Center, Cancer Disparities Program-in-Development
2007 New Investigators’ Workshop, American Society of Preventive Oncology
2007 NCI Professional Development Workshop, CMBB/CRCHD
2008 Workshop on Behavioral Methodologies in Cancer Research for Underrepresented Investigators, NCI and Kellogg Health Scholars Program
2009-present Alvin J. Siteman Cancer Center, Member
2009-present Program for the Elimination of Cancer Disparities (PECaD), Leadership Team Member, Prostate Cancer Community Partnership-Co-Chair, Disparities Elimination Advisory Committee, Member
2010-present Nutrition Obesity Research Center, Washington University School of Medicine, Full Member

PROFESSIONAL SOCIETIES AND ORGANIZATIONS:
2001- American Public Health Association
2001- Baylor University Alumni Association
2004- Gerontological Society of America
2006- American Society of Preventive Oncology
2007- American College of Epidemiology

EDITORIAL/REVIEW RESPONSIBILITIES
2008- Reviewer: Annals of Epidemiology; Cancer Causes & Control; Social Science & Medicine; Journal of Healthcare for the Poor and Underserved; Progress in Community Health Partnerships: Research, Education, and Action
2010 NCMHD Special Emphasis Review Panel ZMD1 PA (07), Faith-Based R21

TEACHING
2000 Teaching Assistant, Organic Chemistry Laboratory
Baylor University Chemistry Department
2003 Instructor, Upward Bound Bridge Biology
Upward Bound Math and Science Program
Wiley College
2003 Instructor, Texas Assessment of Knowledge and Skills (TAKS) Science Preparation
Upward Bound Math and Science Program
Wiley College
2005 Teaching Assistant, Epidemiologic Methods
Department of Epidemiology & Biostatistics
Arnold School of Public Health, University of South Carolina
2007 Master’s Thesis Committee
Arnold School of Public Health, University of South Carolina
Kamala Swayampakala, MPH
“Independent and Joint Effects of Race and Geographic Location in Primary Treatment of Prostate Cancer and PSA Outcome in South Carolina”
2008 Instructor, Race, Ethnicity, and Health: Perspectives from the Behavioral and Social Sciences
Department of Society, Human Development and Health
Harvard School of Public Health
2008 Mentor, Continuing Umbrella of Research Experiences (CURE) & Boston Latin School of Science Mentorship Program
Nicole Thornhill
“Adherence to Vitamin D Supplementation among Blacks”
2010 Invited Guest Lecture, *Cancer Epidemiology*
St. Louis University School of Public Health
Course Instructor (Tekeda Ferguson, PhD)

**PRESENTATIONS**

**Oral**


**Poster**


**RESEARCH SUPPORT:**

**Current**

PC081669  Drake (PI)  09/01/09 – 08/31/11

Department of Defense

**Title:** Reducing Prostate Cancer Disparities Through Behavioral and Biologic Epidemiologic Approaches

The main goal of this training award is to extend my training in epidemiology with strong training in social and behavioral science so that I can bridge biologic and social/behavioral methods to address disparities in prostate cancer incidence and mortality. I have a strong background in epidemiology- my goal for this career development award is to develop additional expertise in behavior and social science so that I can become a behavioral epidemiologist focused on prostate cancer disparities.

Role: PI

U54 CA153460  Colditz (PI)  9/1/10 – 6/30/15

National Institutes of Health (NCI)

**Title:** The Program for the Elimination of Cancer Disparities (PECaD)

The goals of this project is to create a national model for eliminating disparities in cancer through community-based partnerships and community based participatory research (CBPR); to increase access by breaking down barriers to quality cancer care; and to be a catalyst for change in our region by fostering healthy communities. The program includes a leadership core, community outreach component, full and pilot research projects, and a training program.

Role: Leadership Core and Evaluation Lead
U54 CA153460 Colditz (PI) 9/1/10 – 6/30/12
National Institutes of Health (NCI)
Title: Increasing Minority Recruitment in Prostate Cancer Biorepository Studies (PECaD)
In partnership with our prostate cancer community partnership, the goal of this project is to evaluate barriers to participation in prostate cancer tissue collection for research purposes (biorepository), position navigation/recruitment staff in clinics, and provide information to the community in collaboration with our partners.
Role: Project Lead

Nutrition Obesity Research Center Drake (PI) 10/1/2010 – 9/30/2011
Washington University School of Medicine
Title: Obesity and vitamin D related effects on prostate cancer recurrence
This study is a nested case-control study that will assess the effects of pre-treatment vitamin D and leptin levels on prostate cancer recurrence.
Role: PI

Completed
Dana-Farber/Harvard Cancer Center Bennett (PI) 01/01/2006 – 12/31/2010
Title: Cancer Risk Factors and Vitamin D Supplementation in Blacks
This study is a vitamin D supplementation trial of 4 levels (placebo, 1000IU, 2000IU, 4000IU) to determine the dosage of vitamin D that can get an individuals blood levels to an optimal levels.
We are also assessing the effect of vitamin D on biomarkers for prostate and colorectal cancer
Role: Co-PI

BIBLIOGRAPHY:
Peer Reviewed Manuscripts and Book Chapters


Non-Peer Reviewed Manuscripts and Book Chapters