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TITLE: Inflammatory Processes, Emotion Regulation, and Depression in Prostate Cancer Survivors

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CONTRACTING ORGANIZATION: University of California, Irvine, CA

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14. ABSTRACT

The period following radical prostatectomy or radiation therapy for localized prostate cancer is marked by relatively rapid changes in prostate-specific physical functioning. This can be a critical period marked by increased depression and poor adjustment for men, though substantial heterogeneity across men exists. Depression, when occurring in the context of cancer, can compromise important functional and health outcomes. However, little research has sought to examine the unfolding risk and occurrence of depression following prostate cancer treatment. A primary goal of this research is to specify and test a theoretically-driven model of how psychological and contextual vulnerabilities shape trajectories of depression in the year following prostate cancer treatment. This approach will allow for identification of which features characterize patients in whom depression is persistent and to whom intervention can be targeted, and which processes are promising targets for intervention. To date, accomplishments have included project initiation and procurement of project staff, and a focus on patient recruitment and enrollment. To date, 32 participants are enrolled Understanding of the nature and structure of depression as it is experienced by this patient group will have implications for both assessment and treatment of depression in prostate cancer patients and ultimately the efficacy of interventions aimed at reducing the intensity of that depression.

15. SUBJECT TERMS

Prostate Cancer; Depression; Proinflammatory Cytokines; Emotion Regulation; Health-Related Quality of Life; Biobehavioral

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TABLE OF CONTENTS

1. Introduction.

The period following radical prostatectomy or radiation therapy for localized prostate cancer can be a critical period marked by increased depression and poor adjustment for men, though substantial heterogeneity across men exists. Depression, when occurring in the context of cancer, can compromise important functional and health outcomes. A primary goal of this research is to specify and test a theoretically-driven model of how psychological and contextual vulnerabilities shape trajectories of depression in the year following prostate cancer treatment. This approach will allow for identification of which features characterize patients in whom depression is persistent and to whom intervention can be targeted, and which processes are promising targets for intervention. This research seeks to: 1) investigate how psychological and contextual vulnerabilities (including disease-related and general stressors and PTSD symptoms), emotion-regulating processes, and proinflammatory cytokines shape trajectories of depression in men with prostate cancer in the year following treatment (main effects hypothesis); 2) examine emotion regulating processes as a proximal mediator of psychological and contextual vulnerabilities' effects on depression; and 3) examine proinflammatory markers as a proximal mediator of psychological and contextual vulnerabilities' effects on depression. The study employs a longitudinal research design set to begin prior to initiation of cancer treatment (Time 1) in 150 men, with subsequent assessments at 1- and 2-months post-treatment, and every 2 subsequent months through month 12. We will primarily recruit patients from the UC Irvine Medical Center and the Long Beach Veteran's Affairs Medical Center as well as from cancer treatment facilities and community clinics throughout the Orange County catchment area.

2. Keywords

- Prostate Cancer
- Depression
- Proinflammatory Cytokines
- Emotion Regulation
- Health-Related Quality of Life
- Biobehavioral

3. Accomplishments

a. What were the major goals of the project?

	Targeted Completion Period (currently in project month 11)	Percent Completion to Date
Major Task 1: IRB Approval for Protocol	Months	
Subtask 1: U.S. Army Medical Research and Materiel Command (USAMRMC) ORP Human Research Protection Office (HRPO) approval will be obtained PRIOR to initiation of the project.	1-3	100%
Subtask 2: Secure IRB approval from the VA (UCI IRB will serve as the primary IRB of record)	1-3	100%
Subtask 3: On-going IRB maintenance and reporting (VA IRB)	4 - 36	n/a
Subtask 4: On-going IRB maintenance and reporting (UCI IRB)	1 - 36	n/a
Milestone(s): UCI IRB approval of UCI IRB HS# 2018-4643 (including ethical review by the Chao Family Comprehensive Cancer Center)	1	100%
Major Task 2: Staff Hiring and Training		
Subtask 1: Hire and train research coordinator at the VA Long Beach	1	100%
Subtask 2: Hire and train research coordinator, data compliance coordinator, and project manager at UCI	1	100%
Major Task 3: Patient Recruitment		
Subtask 1: Employ planned clinic-based methods of patient recruiting, screening, and enrollment. This will occur at both the VA and UCI clinics. Hoyt will oversee all recruitment, screening, and enrollment activities with as needed input and involvement of Drs. Gupta, Ahlering, and Wenzel.	4 - 24	on-going
Subtask 2: Monitor recruitment and assure adherence to projected recruitment timeline	4 – 24	
Milestone(s): Hoyt (with Ahlering) have pilot tested UCI-based clinic recruitment, which has shown to be feasible.	1	100%

Major Task 4: Research Assessments/Data Collection		
Subtask 1: Finalize measurement plan and online data collection platform	1	100%
Subtask 2: Obtain questionnaire and interview data according to the assessment schedule for all enrolled patients. This will involve careful patient tracking and scheduling, EMR data extraction, and conduct of patient data collection sessions.	3 - 36	on-going
Subtask 3: Obtain samples of plasma for biomarker analysis. This will involve scheduling patients for phlebotomy, transport of samples to the lab, and oversight of sample preparation and storage.	3 – 36	on-going
Major Task 5: Data Analysis and Dissemination		
Subtask 1: Data storage, protection, monitoring, and cleaning will be ongoing throughout data collection.	3 – 36	on-going
Subtask 2: Laboratory assays will be conducted to measure pre-identified proinflammatory cytokine markers.	34 – 35	0%
Subtask 3: Planned data analysis will be conducted to test primary hypotheses.	35 - 36	0%
Subtask 4: The study team will initiate the dissemination plan as appropriate to study findings. This will include preparation of primary and secondary papers for publication, scientific conference presentation, and communication within the cancer care community.	35 - 36	0%

b. What was accomplished under these goals?

The project began work in early 2020. Year one activities/accomplishments have included finalizing IRB approvals across sites (Major Task 1), hiring and training project staff (Major Task 2), establishing recruitment and data collection procedures (Major Tasks 3 and 4), and initial recruitment and enrollment (Major Task 3).

Initiation of application for IRB approval was immediate and initially included the University of California IRB and the IRB at the VA Long Beach Medical System. Project staff at both UC Irvine and the VA Long Beach were secured and trained in order to help establish, implement, and supervise the daily functioning of the study. The project staff, along with PI, worked to create strong referral processes with medical oncologists and urologists, physician's assistants, research personnel, and administrative staff within the recruitment environments.

Initial work involved establishing and piloting the recruitment and patient protocol. This included consulting with the project statistician to discuss and confirm our study design in the earliest phases. The team also engaged in ongoing consultation with a specialist in biological-markers in order to finalize procedures for the collection, storage, transport, and analysis of biological samples. The PI also conducts monthly meetings with key study team members.

The preponderance of activity to date has been on patient recruitment, screening, and data collection (simultaneous activities). Patient recruitment began immediately following IRB and compliance approvals. Recruitment procedures have been designed to identify every eligible patient in several Urological clinics at UCIMC and all patients at the VA. Since beginning, research staff have identified and screened 106 potential participants. Of these, 55 patients were ineligible, 12 declined participation, and 17 are either pending (waiting to make treatment decisions) or have left care. To date, 32 individuals have consented to participate in the study and are in various phases of completion.

Enrolled participants range in age from 51-73 years (mean=62.5, SD= 5.5). We have been very successful in enrolling men from ethnic minority groups. The largest portion of participants self-identify ethnicity as African-American/Black (47%) and the remainder self-identify as non-Hispanic White (30%), Hispanic/Latino (13%), or other/mixed race (10%). The majority of participants report either current full-time(38%) or part-time (16%) employment. Participants also report being unemployed (16%%) or retired (22%). Nearly 13% report a form of permanent disability. We have also been able to enroll men at lower levels of socio-economic status: 61% of participants report annual family income of less than $30,000 (26% report making less than $15,000 per year). The education level of enrollees varies widely with 23% completing less than a high school education (no degree/GED), 30% completing high school (or GED), 13% with some type of vocational training post high school, 13% with a 2-year college degree, 7% with a 4-year degree, and 16% with advanced degrees.

participant protocols or study procedures. Based on experience, study participation continues to appear to be tolerable and acceptable to enrolled subjects. This includes repeated careful assessment of depressive symptoms by questionnaire and clinical diagnostic interview.

We are beginning to learn some about the levels of depression in the sample. Twenty percent of our sample reported a prior history of major depression and 13% of participants met DSM-IV diagnostic criteria for major depression during the course of their participation. Of these, 50% did not have a significant depression history. In terms of depressive symptoms as measured by the CES-D, the sample, on average, reports low to moderate symptoms across time with elevated symptoms at baseline (pre-treatment). Approximately 13% of participants scored above clinical cut-off for elevated depressive symptoms on the CES-D at baseline. Of additional note, 40% of participants met DSM-IV diagnostic criteria for adjustment disorder related to their prostate cancer diagnosis during the course of participation. Of course, these observations are preliminary and incomplete.

c. What opportunities for training and professional development has the project provided?

Nothing to report.

d. How were the results disseminated to communities of interest?

Nothing to report.

e. What do you plan to do during the next reporting period to accomplish the goals?

The plan for the next reporting period is to continue (and increase) all on-going activities related to participant screening and enrollment, data collection, and data management. With the relaxation of current COVID-19 safety precautions and widespread availability of the COVID-19 vaccine, we anticipate an increasing rate of enrollment activities across the next reporting period.

4. Impact

a. What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

b. What was the impact on other disciplines?

Nothing to report.

c. What was the impact on technology transfer?

Nothing to report.

d. What was the impact on society beyond science and technology?

Nothing to report.

5. Changes/Problems

a. Changes in approach and reasons for change

Nothing to report.

b. Actual or anticipated problems or delays and actions or plans to resolve them

The most significant problem that has contributed to slowed progress has, of course, been related to emergency changes in work, practice, patient care, and policy in response to the COVID-19 pandemic. Throughout the pandemic period (and currently) we have been able to maintain most study activities.

safety response recommendations. This included remote working, limitations in patient contact, and employment of strict safety precautions. The result has been significantly slower than anticipated rate of patient accrual. Our institutional response has been coordinated and extensive. UC Irvine immediately established an Office of Contract Tracing and Vaccination Services that made a response team available at all times. They coordinated a large-scale campus and community vaccination program. At present, all study team members have received COVID-19 vaccination. All medical and university employees, as well as patients, have access to the vaccine. The regional response has also been strong and at the time of this report, Orange County is at the lowest risk tier since the beginning of the pandemic. Governor Gavin Newsom has announced that he anticipates state-wide return to most activities by mid-June 2021. Thus, we anticipate a corresponding return to all study activities at both UC Irvine and the VA Long Beach.

c. Changes that had a significant impact on expenditures

Nothing to report.

d. Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report.

e. Significant changes in use or care of human subjects

Nothing to report.

f. Significant changes in use or care of vertebrate animals.

Nothing to report.

g. Significant changes in use of biohazards and/or select agents

Nothing to report.

6. Products

Nothing to report.

7. Participants & Other Collaborating Organizations

a. What individuals have worked on the project?

Name:	Michael A. Hoyt, PhD
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	https://orcid.org/0000-0003-2274-1902
Nearest person month worked:	3
Contribution to Project:	Dr. Hoyt has directed all study activities and has led and coordinated the study team.
Funding Support:	n/a

Name:	Karen Llave, MS
Project Role:	Project Manager
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	6
Contribution to Project:	Manages day to day operations.
Funding Support:	n/a

Name:	Kareem Torres
Project Role:	Patient Recruiter
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	6
Contribution to Project:	Responsible for patient recruitment, screening, enrollment, and scheduling activities.
Funding Support:	n/a

Name:	Chelsea McKinney
Project Role:	Data Compliance Manager
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	.1
Contribution to Project:	Assists with data compliance and IRB materials.
Funding Support:	n/a

Name:	Lari Wenzel, PhD
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	eRA COMMONS USER NAME: LARI_WENZEL
Nearest person month worked:	.4

Contribution to Project:	Contributes to project meetings, study operations, and problem-solving.
Funding Support:	n/a

Name:	Kathrynn Osann, PhD
Project Role:	Biostatistician
Researcher Identifier (e.g. ORCID ID):	eRA COMMONS USER NAME: KOSANN
Nearest person month worked:	.3
Contribution to Project:	Statistical oversight and guidance.
Funding Support:	n/a

Name:	Thomas Ahlering, MD
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	eRA COMMONS USER NAME: AHLERING
Nearest person month worked:	.1
Contribution to Project:	Provides medical expertise and consultation; assists with clinic-based recruitment activities.
Funding Support:	n/a

b. Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report.

c. What other organizations were involved as partners?

1. **Organization Name:** VA Long Beach Healthcare System
2. **Location of Organization:** Long Beach, CA
3. **Partner's contribution to the projec**t*:*

- **Collaboration**: The VA Long Beach serves as a study recruitment site and key study partner. Dr. Pankaj Gupta, Chief of Oncology, is the site PI and a study Co-Invesigator. Current the VA Long Beach team includes the following:

Name:	Tamayo Johnson, RN, CCRC
Project Role:	VA Site Project Coordinator
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	9
Contribution to Project:	Provides organization of day to day activities at the VA Long Beach.
Funding Support:	n/a

Name:	Pankaj Gupta, MD
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	eRA COMMONS USER NAME: gupta013
Nearest person month worked:	1
Contribution to Project:	Serves as local PI at the VA Long Beach. Oversees VA-based activities.
Funding Support:	n/a

8. Special Reporting Requirements

Nothing to report.

9. Appendices

Nothing to report.