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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> As more men live with their prostate cancer, they face increased risk of cardiovascular disease (CVD); this risk is intensified by treatment type, in particular androgen deprivation therapy (ADT). There is a paucity of data exploring the risk of CVD among minority men with prostate cancer overall or by treatment type. The purpose of this study is to examine race-specific CVD risk in men with prostate cancer, overall and by treatment type. 2000 prostate cancer cases (1000 each African American and Caucasian) have been identified and over 1200 have been abstracted. Overall, ~75% of men had a post-diagnosis lipid profile drawn. However, lipid monitoring was lacking among those ever on ADT, predominantly in the Caucasian group, demonstrating a potential gap in CVD risk factor monitoring in a high-risk group. In our population, ADT increased cholesterol levels in both African-American and Caucasian men with prostate cancer suggesting a need for guidelines for regular screening of men treated with ADT. We are now exploring the role of pre- and post-diagnosis of hypercholesterolemia, use of cholesterol-lowering medications, and the role of additional cardiovascular risk factors (e.g. hypertension, diabetes) on risk of events in this population of African-American and Caucasian prostate cancer cases.					
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## **Introduction**

Racial differences in the overall health of men living with prostate cancer are an important but understudied area of research. As more men live with their prostate cancer, they face increased risk of cardiovascular disease (CVD) events; this risk is intensified by treatment type. There is a paucity of data exploring the risk of CVD among minority men with prostate cancer overall or by treatment type. As African Americans, in general, are less likely to have CVD risk factors under control and are more likely to experience CVD events, we are (1) examining if African-American men with prostate cancer are more likely to have worsening CVD risk factor profiles and more CVD events than Caucasian men with prostate cancer during a follow-up period of 5 years past diagnosis and (2) examining if androgen deprivation therapy for prostate cancer is associated with worsening CVD risk factor profiles and more CVD events during a follow-up period of 5 years past diagnosis, and to determine whether race modifies these associations. This is a retrospective cohort study of men newly diagnosed with prostate cancer at Henry Ford Health System between years 1998 and 2006. As men undergoing prostate cancer treatment interface with the medical care system, there are considerable opportunities to assess their CVD factor profiles. If African-American men with prostate cancer are more likely to have worsening CVD risk factor profiles and to experience CVD events than their Caucasian counterparts, this could reveal an important and modifiable opportunity to reduce a disparity in the overall health of men with prostate cancer. Although treatment type may be associated with CVD risk factor changes and events, to-date only one study has examined this association in African-Americans. Results from this investigation will be used to identify the need to couple

therapy with risk factor monitoring and will stimulate future research into potential underlying causes for these disparities.

## **Body**

As outlined in the approved statement of work, the following tasks have been completed:

- obtained Human Subjects Regulatory Board Approval;
- obtained and maintained Henry Ford Health System (HFHS) Institutional Review Board Approval for Human Subject Research;
- created Access database for direct medical record abstraction data entry;
- created, piloted and revised medical record abstraction tool;
- created electronic cohort of 2,000 prostate cancer cases (1,000 each African-American and Caucasian);
- developed and implemented quality control procedures;
- on-going database management;
- patient addresses have been geocoded to determine neighborhood-level SES indicators.

A total of >1,200 medical chart abstractions are underway or completed, and a remaining ~700 (~one-third) need to be completed, which places us on track for completion of abstraction within the allotted study period. Data cleaning is on-going, with creation of SAS program files that can be used again once abstraction is completed. Literature reviews are on-going for manuscript preparation and an outline for manuscript I is in the process of being finalized.

As described in the statement of work training activities include completing the following courses: Epid 787 “An Introduction to Multilevel Analysis in Public Health” at the University of

Michigan in July, 2010. This course covered analysis techniques that will be needed for analyzing the geocoded SES variables that are being collected for the current study. The PI also completed the following course: Epid 777 “Geographic Information Systems for Epidemiology” at the University of Michigan in July, 2011, which covered an analytic tool that is key to the SES component of this research. Additionally, the PI has regularly attended the HMORN Cancer Research Network annual meeting. The PI submitted and presented an abstract at the second Innovative Minds in Prostate Cancer Today (IMPACT) conference (March, 2011) and this poster is included in the appendix.

Preliminary analyses have begun using the electronically obtained data on the cohort of 2,000 men. In cross-sectional studies, Androgen Deprivation Therapy (ADT) is associated with cholesterol levels<sup>1</sup> and ADT may also be associated with worsening risk factor profiles.<sup>2</sup> We examined the relationship of ADT use (ever/never) with total cholesterol level pre- and post-diagnosis (see poster in appendix).

The analytic sample consisted of 2000 prostate cancer cases (1000 each African American and Caucasian) identified from the Henry Ford Health System (HFHS) tumor registry. African-American and Caucasian prostate cancer cases were age (+/- 5 years) and date of diagnosis (+/- 1 year) matched. Information on cholesterol levels 1 year prior to diagnosis to 5 years post-diagnosis and ADT use (ever/never) were obtained from electronic corporate data stores at HFHS. Linear mixed models were fit to examine whether there was a racial difference in change in cholesterol level, adjusting for first measured cholesterol, by ADT.

A total of 7,528 cholesterol measures were available. Pre-diagnosis, 1077 men (54%) had  $\geq 1$  cholesterol level measured and post-diagnosis, 1489 men (74%) had  $\geq 1$  cholesterol level

measured. After diagnosis, there was a racial difference in number of men with cholesterol measures by ADT use ( $P < 0.001$ ); among those ever using ADT, more African-American men had  $\geq 1$  cholesterol measure, while among those never using ADT, more Caucasian men had  $\geq 1$  cholesterol measure. After adjusting for first measured cholesterol, there was evidence for a race by ADT interaction with change in cholesterol level ( $P = 0.06$ ). Compared to Caucasians never on ADT, both Caucasian and African-American men ever on ADT had an increase in cholesterol whereas African-American men never on ADT had a decrease in cholesterol (Table 1).

**Table 1:** Change in cholesterol level by Androgen Deprivation Therapy (ADT) and race

	<b>C / No ADT</b>	<b>AA / No ADT</b>	<b>C / ADT</b>	<b>AA / ADT</b>	<b>P-Value</b>
		<b>Est (SE)</b>	<b>Est (SE)</b>	<b>Est (SE)</b>	
Cholesterol	Ref	-1.33 (1.13)	1.64 (1.50)	2.52 (1.52)	0.0661

C, Caucasian; AA, African-American; Est, Estimate; SE, standard error

To our knowledge, this is the first investigation examining change in cholesterol levels by ADT use and race, adjusted for baseline cholesterol levels. Given that the 1-year pre-diagnosis time frame only yielded 54% with a baseline cholesterol level, we obtained IRB approval to obtain the most recent pre-diagnosis cholesterol level not restricting to the 1 year time period, which improves our ability to adjust for baseline cholesterol levels in this cohort. These preliminary analyses are continuing, and we plan to refit our models adjusting for the additional baseline cholesterol levels, as well as CVD medication use and an indicator variable for number

of visits with a healthcare provider to our models. In preparation for this, we are in the process of coding our cholesterol medications for use in analysis.

### **Key Research Accomplishments**

- Cholesterol profile of men with prostate cancer varies by race and treatment type. This abstract was submitted and accepted for poster presentation to the IMPACT meeting.

### **Reportable Outcomes**

Cassidy-Bushrow, AE. Mahan, M. Rybicki BA. Cholesterol profile of men with prostate cancer varies by race and treatment type. 2011. Second Innovative Minds in Prostate Cancer Today (IMPACT) conference, Orlando, FL, March 2010.

### **Conclusions**

In our study population of men with prostate cancer, most had cholesterol screening at least once within the 5-years post-diagnosis. As demonstrated by others, ADT was associated with an increase in cholesterol level. However, cholesterol monitoring overall was lacking among those ever on ADT, predominantly in the Caucasian group, demonstrating a potential gap in CVD risk factor monitoring in a high-risk group. Given that ADT increased cholesterol levels in both African American and Caucasian men with prostate cancer, guidelines for regular screening of men treated with ADT are warranted. Additional work planned as part of this study includes examination of pre- and post diagnosis of hypercholesterolemia, use of cholesterol-lowering medications, and the role of additional cardiovascular risk factors (e.g. hypertension,

diabetes) on risk of events in this population of African-American and Caucasian prostate cancer cases. Abstraction is continuing and is on-track for completion within the study time frame, with analysis and manuscript preparation on-going in anticipation of completed datasets.

## References

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2. Smith MR, Lee H, McGovern F, Fallon MA, Goode M, Zietman AL, Finkelstein JS. Metabolic changes during gonadotropin-releasing hormone agonist therapy for prostate cancer: differences from the classic metabolic syndrome. *Cancer.* 2008;112:2188-2194.

