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Physical Activity, Sedentary Behavior and Health Related Quality of Life in Prostate Cancer Survivors in the Health Professionals Follow-up Study

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Abstract

Purpose—Many prostate cancer survivors experience compromised health-related quality of life (HRQOL) as a result of prostate cancer. We examined relationships between types and intensities of activity and sedentary behavior and prostate cancer-related HRQOL, overall, and by demographic, disease, and treatment characteristics.

Methods—Associations between post-diagnosis activity and sedentary behavior and HRQOL domains (urinary incontinence, urinary irritation/obstruction, bowel, sexual and vitality/hormonal) were prospectively examined in men diagnosed with non-metastatic prostate cancer in the Health Professionals Follow-up Study (n=1917) using generalized linear models.

Results—After adjusting for potential confounders, higher duration of total, non-vigorous, and walking activity was associated with higher vitality/hormonal functioning scores (*p*-trends,< 0.0001). Effects were small (*d*= 0.16–0.20), but approached clinical significance for men in the highest versus lowest activity categories. Survivors who walked ≥90 minutes/week at a normal pace, or faster, reported higher hormone/vitality scores (*p*=0.001) than men walking <90 minutes at an easy pace. Weight lifting was associated with increased urinary incontinence (*p*-trend,0.02). Total activity was associated with higher hormone/vitality functioning in men who were ≥5 years

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post-treatment, had more advanced disease (Gleason score ≥7), and had ≥1 comorbid condition. No relationships were observed between vigorous activity or sedentary behavior and HRQOL.

Conclusions—Increased duration of non-vigorous activity and walking post-diagnosis was positively associated with better hormone/vitality functioning. Specifically, engaging in ≥5 hours of non-vigorous activity or ≥3 hours of walking per week may be beneficial.

Implications for Cancer Survivors—Encouraging men to engage in non-vigorous activity and walking may be helpful for managing prostate cancer-related HRQOL.

Keywords

bowel functioning; hormone functioning; physical activity; prostate cancer survivors; sedentary behavior; sexual functioning; urinary functioning

Introduction

Many prostate cancer survivors experience numerous side effects as a result of prostate cancer or its treatment. Treatment with surgery, radiotherapy, and/or hormone therapy [1] have been associated with many negative physical (e.g., urinary incontinence, impotence, bowel dysfunction, osteoporosis, muscle atrophy, strength loss, erectile dysfunction)[2–5]; and psychosocial (e.g., increased depression and fatigue; reduced self-esteem, sexual confidence, vitality) side effects and reduced overall and prostate cancer -specific health-related quality of life (HRQOL) [4, 2, 6] although the type and severity of symptoms and impact on general and disease-specific HRQOL may vary by treatment [7, 8]. While some treatment-related side effects are acute, many are chronic or have a delayed onset [6] and poorer cancer-related HRQOL has been associated with reduced overall survival [9]. Thus, identifying modifiable factors that influence prostate cancer-specific HRQOL is important. Sedentary behavior and physical activity are two modifiable lifestyle factors with potential to ameliorate treatment-related side effects [10–12] and increase disease-free survivorship in prostate cancer survivors [13, 14].

Cross-sectional studies [15–17] and randomized controlled trials of prostate cancer survivors [10, 18, 11] indicate physical activity may enhance general and cancer-specific HRQOL. However, these findings are not consistent, with some studies reporting benefits and others finding no effect, and most studies have been small and conducted during active treatment [10, 18]. Moreover, few studies have considered lower intensity physical activities which have more recently been associated with reduced functional decline in older cancer survivors [19] and improved HRQOL in colorectal cancer survivors [20]. In contrast, increased sedentary behavior has been consistently associated with adverse health outcomes including poor cardiovascular health, type 2 diabetes and premature mortality in the general population [21]. Emerging evidence indicates increased sedentary behavior may also adversely influence health and disease outcomes and compromise general and cancer-specific HRQOL in cancer survivors [22, 12, 23–26]. Although, findings in this area are somewhat equivocal with some studies observing negative effects and other finding no effect [27–30]. Also, most studies are cross-sectional and none have examined sedentary behavior and prostate cancer-specific HRQOL.

Several recent papers have identified understanding a) the relationship between specific types and/or intensitities of physical activity and specific outcomes [31–33, 11] and b) potential associations between sedentary behavior and patient reported outcomes [33, 12] as important research priorities in cancer survivorship. We sought to fill these gaps in the literature by examining the relationships between, not only total physical activity, but different types (e.g. weight lifting, walking) and intensities (vigorous and non-vigorous) of physical activity and prostate cancer-specific HRQOL among prostate cancer survivors. In addition, we examined the relationship between sedentary behavior and prostate cancer - specific HRQOL for the first time. Finally, we examined potential subgroup effects by demographic and disease characteristics in an attempt to further refine these relationships. We hypothesized that higher physical activity duration and less sedentary time would be significantly associated with improved HRQOL.

Material, Patients and Methods

Participants

The Health Professionals Follow-up Study is a prospective study of 51,529 U.S. male health professionals who enrolled in 1986 by completing a mailed questionnaire. Participants provided information regarding medical diagnoses, medications, and lifestyle factors and complete biennial follow-up questionnaires to update this information (response rate 96%). After participants report a prostate cancer diagnosis, medical records and pathology reports are obtained to confirm the diagnosis and record clinical T-stage, Gleason score, treatments, prostate-specific antigen (PSA) values at diagnosis and after treatment (to identify events of biochemical recurrence), and metastasis. Biennial follow-up questionnaires were completed by prostate cancer survivors to update data on treatment, PSA levels and clinical progression. In 2010, this questionnaire included the Expanded Prostate Cancer Index Composite Short Form (EPIC-26;[34]) to assess HRQOL outcomes. The present analyses includes men who were diagnosed with non-advanced disease prior to 2008, were post-treatment, and had provided data on pre-diagnosis as well as post-treatment physical activity and sedentary behavior in 2008, and at least one HRQOL subscale in 2010. Of those men who were sent the 2010 HRQOL questionnaire (n= 2241), we had complete data on 85.6% (n=1917). This study was approved by the institutional review board of the Harvard School of Public Health. A schematic of the study design and measures is provided in Figure 1.

Measures

Physical Activity—Physical activity was assessed biennially using a validated assessment [35] beginning in 1986. Men reported average weekly time spent during the past year participating in: walking to work or for exercise; jogging <10 min/mile); running (≥10 min/mile); bicycling; lap swimming; tennis; squash or racquetball, and calisthenics or rowing. Data on participation in heavy outdoor work and weight training were added in 1988 and 1990, respectively. Men could select from the following time categories: 1–4 minutes (mins), 5–19 mins, 20–39 minutes, 40–80 minutes, 1.5 hours, 2–3 hours, 4–6 hours, 7–10 hours, 11–20 hours, 21–30 hours, 31–40 hours, 40+ hours. For those intervals that were a range, the midpoint was used as a measure of weekly time spent in that activity. Each activity was assigned a metabolic equivalent task (MET) value using the compendium of

physical activities [36] and classified as non-vigorous (MET value <6) or vigorous (MET value ≥6). Time spent in all activities was summed to obtain total weekly physical activity duration. Weekly duration of vigorous, non-vigorous, walking, and weight lifting were also calculated (see Figure 1 for details). Activity categories were based on those used in previous analyses [37, 14]. Men also self-reported their walking pace at multiple assessment time points by selecting one of the following categories to classify their "usual walking pace outdoors": easy/casual (<2 mph); normal/average (2–2.9 mph), brisk (3–3.9) and very brisk/striding (≥4 mph). Physical activity assessed in 2008, the time point immediately prior to HRQOL assessment, was used as the primary exposure to reduce the potential of HRQOL affecting physical activity levels. Additionally, we adjusted for pre-diagnosis physical activity in multivariate models.

Sedentary Behavior—Sedentary behavior was assessed biennially beginning in 1990. Men self-reported weekly time spent in the following sedentary activities during the past year: sitting at work, sitting while driving, sitting or lying watching TV or VCR, sitting at home reading, sitting at home working on a computer, and other sitting at home. The time spent in each activity per week was summed and divided by seven and then examined in quartiles of total daily sedentary hours. We used sedentary time in 2008, the time point immediately prior to HRQOL assessment, as the primary exposure, and adjusted for pre-diagnosis sedentary time.

HRQOL—In 2010, the 26-item EPIC-26 questionnaire [34] was used to assess participants' frequency and severity of symptoms influencing HRQOL over the last 4 weeks within 5 domains: urinary incontinence (e.g., urine leaking, urinary control), urinary irritation/obstruction (e.g., pain/burning/bleeding during urination, need to urinate frequently) and bowel (e.g., urgency to have bowel movement, bloody stools), sexual (e.g., erection frequency/quality, ability to function sexually) , and vitality/hormonal function (e.g., hot flashes, depression, changes in body weight). Multi-item scale scores were transformed linearly to a 0 to 100 scale with higher scores representing better HRQOL (e.g. better sexual, vitality/hormonal, or bowel function, and *less* urinary incontinence or urinary irritation/obstruction).

Data Analysis

Generalized linear models were used to examine relationships between 2008 total, vigorous, non-vigorous, walking, and weightlifting activity (categories), sedentary time (quartiles), 2010 walking pace (categories), and each EPIC-26 subscale. Initial models (Model 1) controlled for age at diagnosis (continuous) and time since treatment (continuous). Next, each model was adjusted for stage (T1, T2, T3), Gleason score (<7, 7, >7), primary treatment type (radical prostatectomy, radiation, hormone therapy, active surveillance, other), PSA at diagnosis (<4, 4 to <10, 10 to ≤20, >20), body mass index (BMI; continuous), and presence of comorbidities (yes/no) from participant report of myocardial infarction, stroke, emphysema/chronic obstructive pulmonary disease, Parkinson's disease, coronary artery bypass or coronary angioplasty, and diabetes between 1986 and 2008 (Model 2). Next, we adjusted for physical activity or total sedentary time assessed at the time point immediately before diagnosis (Model 3). Then, 2008 physical activity and total sedentary

time were mutually adjusted for to test for independence (Model 4) and we conducted sensitivity analyses adjusting for PSA recurrence and receipt of adjuvant therapy, independently, in addition to variables in Model 3 (Model 5 and 6). Finally, we ran Model 3 excluding all men with a PSA recurrence. When examining sexual and urinary subscales, Models 2 to 5 controlled for sexual and urinary dysfunction medication use, respectively. In addition, vigorous and non-vigorous activities were mutually adjusted for, and all other activity and walking time were controlled for when examining weightlifting and walking pace. Linear trends were examined using the median of each physical activity category/quartile as a continuous variable.

A priori, we examined interactions by age at diagnosis (<70, ≥70), time since treatment (<5, 5 to <10, ≥10 years), Gleason score (<7, ≥7), treatment type (limited to radical prostatectomy, radiation and hormone therapy), PSA recurrence (yes/no), BMI (<25, ≥25), and comorbidities (yes/no). Based on these results, subgroup analyses were conducted for vitality/hormonal functioning and total activity and walking (the predominant non-vigorous activity), and urinary incontinence and weight lifting. Interactions between physical activity and potential effect modifiers were assessed by entering cross products of activity with continuous variables or dummy variables for categorical variables in multivariate models. These multivariate models adjusted for covariates described above in Model 4. Furthermore, because the hormone/vitality subscale was somewhat heterogeneous, we conducted trend tests for each item (hot flashes, breast tenderness/enlargement, feeling depressed. lack of energy, and change in body weight) in relation to total activity and walking.

Given that men who were included in the present analyses did not differ from those who were excluded in terms of age at diagnosis, time since treatment, stage, PSA at diagnosis, primary treatment, Gleason score, BMI, and EPIC-26 subscale scores, we assumed data were missing at random.. The Tukey-Kramer method was applied to all comparisons to correct for any potential error as a result of multiple comparisons. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC). A priori, effect sizes (i.e. standardized mean difference between groups) were calculated using Cohen's *d* [38] for differences between the highest and lowest activity groups for relationships where the trend was significant for Model 3 in Tables 2 and 3 to determine the magnitude of the observed effects. Effects are defined as "small" (*d*= .2 to .4), "moderate" (*d*= .5 to .7) or "large" (*d* ≥ .8) [38].

Results

Age-standardized characteristics are presented in Table 1. Men in the highest (vs. lowest) activity category were younger in 2008 and at diagnosis, were more recently diagnosed, had a lower BMI, and had fewer comorbidities. In addition, men with higher activity were more likely to have treatment with radical prostatectomy, be taking sexual functioning enhancement medication, and had a lower proportion of PSA recurrence. Average daily sedentary time was similar across activity groups although those in the highest activity groups also reported the most sedentary behaviors. Among individuals in the highest 2008 physical activity category the majority (85.8%) reported ≥5 hours of pre-diagnosis activity compared to 26.2% in the lowest category of 2008 activity. Median weekly total activity and

walking time were 5.5 hours (interquartile range (IQR)=2.0, 9.0) and 3.0 hours (IQR=0.2, 5.5), respectively and 70.4% of the sample participated in ≥3 hours per week of total physical activity. Median daily sitting time was 3.9 hours (IQR=2.1, 6.1).

Physical Activity and HRQOL

Relationships between each type of activity and EPIC-26 subscale are presented in Table 2. Greater total activity category was associated (*p-trend,*<0.05) with higher scores on bowel and vitality/hormonal HRQOL subscales. After adjustment for covariates and pre-diagnosis physical activity, only vitality/hormonal functioning subscale relationships remained statistically significant. Men who reported exercising ≥3 hours/week had significantly higher subscale scores compared to men who exercised <1 hour/week (*p-trend,*<0.0001). The effect size for the highest (≥10 hours/week) versus lowest categories (<1 hour/week) of exercise was *d*=0.20 after controlling for covariates. Results were largely unchanged when controlling for sedentary time, PSA recurrence, adjuvant therapy and when restricting analyses to men without a PSA recurrence (results not shown).

Each increasing vigorous, non-vigorous, and walking duration category was associated only with improvements in the vitality/hormonal subscale (*p-trend* vigorous,0.02; *p-trend* non-vigorous,<0.0001; *p-trend* walking,<0.0001). After adjustment for covariates and pre-diagnosis activity, trends for non-vigorous and walking activity remained statistically significant, although the magnitude of associations was reduced, while vigorous activity was no longer significant. Prostate cancer survivors reporting ≥5 hours/week of non-vigorous activity had higher hormone/vitality scores (*p-trend,*<0.0001) than those reporting <1 hour. Men reporting ≥3 hours/week of walking had higher hormone/vitality functioning compared to men walking <1 hour (*p-trend,*0.0001). The effect sizes for the highest (≥10 hours/week) versus lowest categories (<1 hour/week) of non-vigorous activity and walking were *d*=0.16 and *d*= 0.17, respectively, after controlling for covariates. Furthermore, compared to men who walked at an easy pace, those who walked at a normal/average or brisk pace had improved urinary irritation/obstruction (87.9 vs. 90.1, *p*=0.03 and 87.9 vs. 90.5, *p*=0.03, respectively) and hormone/vitality (86.6 vs. 89.8, *p*=0.0003 and 86.6 vs. 90.8, *p* <0.0001, respectively) scores. Men who walked at a brisk pace also had better urinary incontinence (85.8 vs. 80.1, *p*=0.01) and sexual functioning (37.3 vs. 29.1, p=0.001) scores compared to men who walked at an easy pace, independent of walking duration. Finally, men who walked ≥90 minutes at a normal to very brisk pace reported better hormone/vitality scores (88.5 vs. 90.3, *p*=0.001) than those who walked <90 minutes per week at an easy pace (data not shown). Results for weight-lifting were mixed. More weight lifting was statistically significantly associated with worse urinary incontinence symptoms (*p-trend,*0.02) in multivariate models. The effect size for the highest category (≥3 hours/week) versus lowest categories (none) of weight lifting was d=0.07 after controlling for covariates.

Sedentary Time and HRQOL

Sedentary time was not significantly related to any EPIC-26 subscales after adjusting for covariates, pre- diagnosis sedentary time, physical activity, or PSA recurrence (Table 3).

Subgroup Analyses

For the hormone/vitality subscale items, increased total and walking activity were significantly related to the following being less problematic: feeling depressed (*p-trend*,<0.0001 for both), lack of energy (*p-trend*,<0.0001 for both) and change in body weight (*p-trend*,0.004 and 0.04, respectively) but unrelated to hot flashes or breast tenderness/enlargement.

We examined various subgroups separately, and evaluated effect modification by these factors on the relation of total activity with the hormonal/vitality subscale (Table 4). Significant trends were observed for most of the subgroups studied, with some categories of physical activity being significantly different from the reference category (see bolded mean values, Table 4). Men who were more active and ≥5 years post-treatment reported better hormone/vitality functioning, while no statistically significant increases were observed in men within 5 years of diagnosis (*p-int*,0.03). In addition, higher physical activity was associated with a greater increase in hormone/vitality scores in men with Gleason scores ≥7 compared to those with scores <7 (*p-int*,0.04) and in those who reported comorbid conditions (*p-int*,0.02). There was no evidence of effect modification for the relationship between total activity and any other disease or demographic factor or for the relations of walking and hormone/vitality functioning or weight lifting and urinary incontinence (data not shown).

Discussion

After controlling for covariates pre-diagnosis physical activity, and sedentary time, our findings indicate that higher duration of total, non-vigorous and walking activity - especially brisk walking - were associated with better hormone/vitality functioning but not bowel, urinary, or sexual functioning. The effects sizes between the highest and lowest activity categories were small (d=0.16–0.20), but the magnitude of the differences approached clinical significance (0.5 times the standard deviation; [39]). Weight-lifting results were mostly null. However, more weight lifting was associated with worse urinary incontinence although the difference between activity levels was likely not clinically meaningful and the effect size between the highest and lowest categories was very small d=0.07 [39]. Subgroup analyses indicated that time since treatment, Gleason score and presence of comorbid conditions may modify the relationship between total activity and hormone/vitality functioning.

Our results demonstrating a relationship between physical activity and hormone/vitality functioning are consistent with other studies in this area [10, 33]. Our subgroup analyses revealed indicate that the relationship between physical activity and for hormone/vitality functioning may be even stronger in longer-term survivors and those who have chronic conditions and were diagnosed with more advanced disease indicating that targeting programs and treatments at these groups may be particularly beneficial for improving prostate cancer-specific HRQOL. In addition, we found that differences in this subscale were largely driven by depression, fatigue, and body weight. Few studies have explicitly examined the mechanisms underlying the relationship between physical activity and HRQOL. However, potential mechanisms include enhanced insulin/insulin-like growth

factor [40] and sex hormone regulation [41], reductions in inflammation [42] and adiposity [41], and increased psychosocial functioning (e.g., self-efficacy, self-esteem, decreased anxiety; [43]) and neurochemicals that regulate mood [e.g., Brain-derived neurotropic factor (BDNF) [44].

Findings regarding the inverse relationship between weight lifting and urinary incontinence are biologically plausible as weight lifting increases intra-abdominal pressure [45] which may, in turn, increase urinary incontinence [46], particularly during weight lifting. However, only 22.9% of men reported >1 hour of weight lifting and details on the type of weight lifting were not available. Thus, we are hesitant to draw any strong conclusions from these data. We were somewhat surprised that physical activity was unrelated to any other HRQOL subscale given that physical activity has been associated with improvements in bowel functioning[47] and sexual functioning [16] in the general population and prostate cancer patients. One potential explanation for these findings is that, since average time since treatment was about 8.5 years, these subscales may contain items that are neither relevant nor salient to these men as longer-term survivors. Alternatively, the effects of physical activity may be domain specific. Future research is warranted to explore these relationships further.

It is important to note that the data from this study suggests that engaging in ≤3 hours per week of walking is associated with improved hormone functioning/vitality but also that even 90 minutes of normal/brisk walking per week may be beneficial. These data indicate that while exceeding physical activity recommendations may result in favorable HRQOL outcomes, benefits may also occur at lower levels of activity. This is particularly promising as this lower level of exercise may be more feasible for the older prostate cancer survivor population. Furthermore, lower intensity activity has been associated with other health benefits including reduced functional decline, disability, chronic disease prevalence, body mass index (BMI), waist circumference, depression, and fatigue and improved cardiovascular health and QOL in older adults [48, 49] and cancer survivors[19, 20]. Future studies should seek to replicate or refute our findings and further explore the relationships between lower doses of physical activity and other relevant health and quality of life outcomes in prostate cancer survivors.

Contrary to our hypothesis, sedentary time was not related to prostate cancer-specific HRQOL. However, it is important to note that the median sedentary time in this sample, 3.9 hours, was 2 hours less than self-reported general population estimates of 6.0 hours/day [50], and HRQOL profiles in this sample were relatively favorable. Thus, sedentary time may have been too low and HRQOL too high to observe any effects in this sample. As increased sedentary behavior has been associated with a host of deleterious side effects in the general population [21], future research is warranted to examine the relationship between sedentary time and general and disease-specific HRQOL and other health outcomes in prostate cancer survivors.

Our study has several limitations. First, we are unable to fully determine causality direction because we did not have a similar HRQOL measure prior to physical activity assessment. Hence, we cannot rule out the possibility that prostate cancer-specific HRQOL influences

physical activity. Some vitality/hormone subscale components, including “feeling depressed” and “lack of energy” may influence exercise behavior; however, physical activity has been shown to reduce depressive symptoms [50] and fatigue [18] in prostate cancer patients. Furthermore, because our measures of physical activity and HRQOL were taken two years apart, changes in activity could have occurred that were sufficient to impact HRQOL but were not captured in the present analyses. Future studies should evaluate how changes in physical activity and sedentary behavior influence general and disease-specific HRQOL over time using multiple assessments. Second, the study sample was mostly White and consisted of health professionals who may report HRQOL differently; thus, it is important to confirm these findings in other, more diverse samples. Additionally, although we did not use a standard comorbidity index (e.g. Charlson Comorbidity Index), adjustment for the presence of many chronic conditions included in these indices did not affect our multivariate estimates, so additional residual confounding due to other diseases is likely to be minor. Finally, physical activity and sedentary time were measured using self-report and therefore there will be some non-differential measurement error in our prospective physical activity and sedentary behavior assessment. Future studies should explore these relationships using objective measures.

Our study also had several strengths. To the best of our knowledge, this is the first prospective study to examine relationships between different types of physical activity, sedentary time, and disease-specific HRQOL in prostate cancer survivors. In addition, there was adequate variability in physical activity and sedentary time in this cohort to examine these exposures. Furthermore, we were able to control for pre-diagnosis behavior and to examine whether different types of physical activity differentially influenced HRQOL domains. Finally, our study population included a wide range of disease and treatment characteristics, suggesting findings could be relevant to many prostate cancer survivors.

Conclusions

Increased total, non-vigorous, and walking activity is associated with improvement in hormone/vitality functioning in prostate cancer survivors in the Health Professionals Follow-up Study. These findings suggest the potential importance of lower intensity activities and walking, activities that may be easier for older men to engage in, for improving HRQOL. Thus, encouraging men to engage in walking and lower intensity activities after prostate cancer diagnosis may help improve disease-specific HRQOL outcomes.

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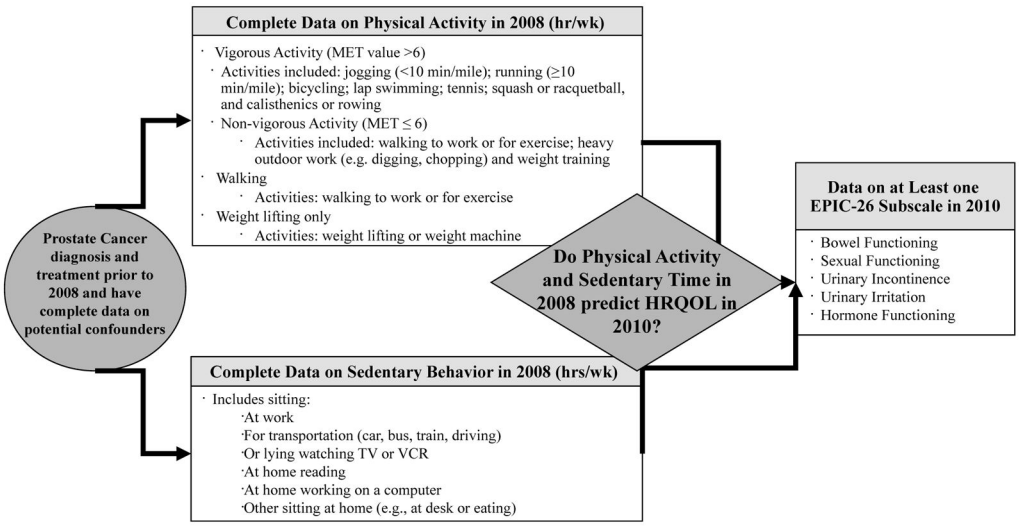

Figure 1.
Study Design and Measures

Table 1

Sample demographic and disease characteristics by weekly physical activity*

	Total Weekly Physical Activity (hours)				
	<1 (n= 272)	**1 to <3 (n= 295)**	**3 to <5 (n= 346)**	**5-<10 (n= 601)**	**≥10 (n= 403)**
Age in 2008 (*M*, SD)	78.1 (7.6)	75.6 (7.5)	74.9 (7.1)	74.5 (6.9)	74.2 (6.7)
Age at Diagnosis (*M*, SD)	70.7 (7.4)	68.4 (7.1)	68.3 (7.0)	67.7 (6.9)	67.7 (6.7)
Time Since Treatment in Months (*M*, SD)	113.3 (51.6)	108.2 (55.8)	100.2 (50.0)	101.8 (52.4)	97.6 (49.3)
Stage of Disease (%)					
T1	62.6	64.7	68.8	68.5	64.8
T2	35.9	33.7	30.1	30.4	33.3
T3/T4	1.5	1.7	1.1	1.1	1.9
Gleason Score (%)					
≤6	65.9	65.8	69.1	66.9	64.9
7	29.3	26.5	23.8	26.3	27.8
>7	4.8	7.7	7.0	6.7	7.2
PSA at Diagnosis (%)					
<4	17.1	11.8	14.2	13.7	12.7
4 to <10	60.4	64.4	67.0	65.3	66.1
10 to <20	14.9	19.4	14.2	17.4	12.2
≥20	5.4	4.0	4.3	3.0	7.5
Missing	2.3	0.4	0.3	0.6	1.5
Primary Treatment (%)					
Radical Prostatectomy	49.6	49.7	50.4	53.7	54.5
Radiation Therapy	37.2	38.5	36.1	34.7	35.2
Hormonal Therapy	3.8	2.7	2.8	2.5	2.6
Active Surveillance/None	6.7	5.5	7.0	6.0	4.7
Other	0.8	0.9	1.4	1.2	0.8
Missing	2.0	2.7	2.4	1.9	2.4
PSA Recurrence (%)	18.7	17.9	17.9	21.8	15.7

	Total Weekly Physical Activity (hours)				
	<1 (n= 272)	**1 to <3 (n= 295)**	**3 to <5 (n= 346)**	**5-<10 (n= 601)**	**≥10 (n= 403)**
Body Mass Index (*M*, SD)	26.9 (4.0)	26.2 (3.5)	25.9 (3.0)	25.9 (3.5)	25.3 (2.9)
Presence of comorbidities (%)**	41.3	40.0	33.7	33.0	34.4
Sexual Functioning Medications	7.1	8.3	8.1	8.3	10.9
Urinary Medications (%)	1.7	1.9	1.4	0.5	1.6
EPIC-26 Subscale scores (*M*, SD)***					
Bowel Functioning	92.6 (12.1)	91.1 (13.3)	91.0 (13.6)	92.7 (11.2)	93.2 (11.6)
Urinary Incontinence	75.9 (27.0)	77.4 (24.3)	79.2 (24.2)	78.8 (24.4)	79.7 (23.2)
Urinary Irritation/Obstruction	90.4 (12.9)	90.2 (12.9)	90.2 (12.6)	91.3 (11.0)	91.4 (11.3)
Sexual Functioning	29.3 (28.2)	29.3 (26.5)	35.3 (29.6)	32.8 (28.6)	34.7 (28.5)
Vitality/Hormonal Functioning	87.9 (15.1)	89.1 (13.8)	91.7 (10.9)	92.0 (12.0)	93.8 (10.3)
Sedentary Time (hrs/day; *M*, SD)	4.0 (3.3)	4.0 (2.8)	4.2 (2.6)	4.5 (2.5)	4.8 (2.5)
Pre-diagnosis Physical Activity (hrs/wk;%)					
<1 hour	36.8	13.7	9.8	4.8	1.9
1-<3 hours	26.5	28.7	25.1	14.1	6.7
3-<5 hours	10.6	18.3	20.2	17.9	5.6
5-<10 hours	18.9	25.1	28.6	41.1	36.2
≥10 hours	7.3	14.2	16.3	22.1	49.6

M=Mean; SD=Standard Deviation; PSA=Prostate-Specific Antigen; EPIC-26=Expanded Prostate Index Composite-26 item

*All descriptive characteristics (*M*, SD) are age-standardized values. The 2008 (time point immediately prior to the 2010 HRQOL assessment) physical activity assessment was used as the exposure for this analysis.

**Presence of comorbidities considered yes if participant reported any of the following between 1986- 2008: myocardial infarction, stroke, emphysema/chronic obstructive pulmonary disease, Parkinson's disease, coronary artery bypass or coronary angioplasty, and diabetes

***Higher scores indicate better HRQOL (i.e. less symptomology).

Table 2

Physical activity and health-related quality of life in prostate cancer survivors*

	Total Weekly Physical Activity Time (hours)					
EPIC-26 Subscale	**<1**	**1 to <3**	**3 to <5**	**5 to <10**	**≥10**	***p* trend**
Bowel Functioning (n= 1862)	n= 252	n= 285	n= 333	n= 593	n= 399	
Model 1	92.4	91.3	90.9	92.7	93.1	**0.04**
Model 2	91.3	90.3	89.6	91.3	91.8	0.07
Model 3	91.5	90.3	89.6	91.1	91.7	0.14
Urinary Incontinence (n= 1861)	n= 254	n= 287	n= 333	n= 591	n= 396	
Model 1	77.6	77.9	79.1	78.8	79.2	0.43
Model 2	80.4	80.7	81.8	81.9	82.2	0.35
Model 3	80.9	80.7	81.7	81.6	81.6	0.71
Urinary Irritation/Obstruction (n= 1810)	n= 247	n= 271	n= 322	n= 583	n= 387	
Model 1	90.1	90.4	90.3	91.4	91.4	0.09
Model 2	88.2	88.4	88.0	88.9	89.0	0.25
Model 3	88.4	88.2	87.8	88.7	88.8	0.40
Sexual Functioning (n= 1819)	n= 250	n= 277	n= 328	n= 573	n= 391	
Model 1	30.1	30.0	35.0	32.6	34.1	0.09
Model 2	29.3	29.1	33.5	31.4	32.3	0.22
Model 3	29.2	29.1	33.6	31.7	32.5	0.24
Vitality/Hormonal Functioning (n= 1866)	n= 259	n= 285	n= 335	n= 596	n= 391	
Model 1	88.3	89.2	**91.6**	**92.0**	**93.7**	**<0.0001**
Model 2	86.2	86.7	**88.8**	**89.2**	**90.7**	**<0.0001**
Model 3	86.3	86.7	**88.9**	**89.4**	**90.9**	**<0.0001**
	Total Weekly Vigorous Physical Activity Time (hours)					
	<1	**1 to <3**	**3 to <5**	**≥5**		***p* trend**
Bowel Functioning (n= 1862)	n= 1105	n= 347	n= 214	n= 196		
Model 1	92.0	92.4	93.0	91.6		0.95
Model 2	91.0	91.1	91.4	90.4		0.67

	Total Weekly Physical Activity Time (hours)					
EPIC-26 Subscale	**<1**	**1 to <3**	**3 to <5**	**5 to <10**	**≥10**	***p* trend**
Model 3	91.3	91.4	91.7	90.4		0.49
Urinary Incontinence (n= 1861)	n= 1107	n= 347	n= 215	n= 192		
Model 1	78.9	78.6	78.1	79.5		0.90
Model 2	81.7	81.1	81.5	82.1		0.91
Model 3	82.5	81.5	81.8	82.3		0.79
Urinary Irritation/Obstruction (n= 1810)	n= 1072	n= 335	n= 214	n= 189		
Model 1	90.5	91.0	92.1	90.5		0.56
Model 2	88.4	88.8	89.5	88.1		0.96
Model 3	88.4	88.7	89.4	88.0		0.97
Sexual Functioning (n= 1819)	n= 1078	n= 338	n= 212	n= 191		
Model 1	32.1	31.4	36.2	33.3		0.26
Model 2	31.3	29.8	34.6	31.7		0.50
Model 3	32.3	30.2	35.0	31.7		0.91
Vitality/Hormonal Functioning (n= 1866)	n= 1112	n= 345	n= 218	n= 191		
Model 1	90.9	91.5	93.0	92.6		**0.02**
Model 2	88.4	88.7	89.9	89.7		0.09
Model 3	88.3	88.8	89.9	89.7		0.08
	Total Weekly Non-vigorous Physical Activity Time (hours)					
	<1	**1 to 3**	**3 to <5**	**5 to <10**	**≥10**	***p* trend**
Bowel Functioning (n= 1862)	n= 361	n= 343	n= 373	n= 544	n= 241	
Model 1	92.3	91.3	91.4	93.3	93.0	0.09
Model 2	91.0	90.3	90.0	91.8	91.8	0.10
Model 3	91.4	90.5	90.1	92.0	92.0	0.13
Urinary Incontinence (n= 1861)	n= 364	n= 345	n= 371	n= 539	n= 242	
Model 1	77.3	79.7	78.7	78.2	79.9	0.41
Model 2	80.1	82.0	81.7	81.3	82.7	0.34
Model 3	80.3	82.1	81.7	81.4	82.9	0.38
Urinary Irritation/Obstruction (n= 1810)	n= 350	n= 333	n= 358	n= 535	n= 234	

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	Total Weekly Physical Activity Time (hours)					
EPIC-26 Subscale	**<1**	**1 to <3**	**3 to <5**	**5 to <10**	**≥10**	***p* trend**
Model 1	90.7	90.8	90.3	92.0	91.1	0.42
Model 2	88.7	88.6	87.9	89.5	88.7	0.59
Model 3	88.9	88.7	87.9	89.5	88.9	0.58
Sexual Functioning (n= 1819)	n= 358	n= 331	n= 366	n= 527	n= 237	
Model 1	31.1	33.0	34.3	34.1	33.6	0.37
Model 2	30.0	31.4	33.2	33.0	31.7	0.53
Model 3	29.2	30.8	32.8	32.8	31.8	0.35
Vitality/Hormonal Functioning (n= 1866)	n= 370	n= 343	n= 371	n= 543	n= 239	
Model 1	89.5	91.5	**91.8**	**92.8**	**94.4**	**<0.0001**
Model 2	87.0	88.7	89.0	**89.8**	**91.4**	**<0.0001**
Model 3	87.2	88.7	89.0	**89.9**	**91.5**	**<0.0001**
	Total Weekly Walking Time (hours)					
	<1	**1 to 3**	**3 to <5**	**5 to <10**	**≥10**	***p* trend**
Bowel Functioning (n= 1862)	n= 571	n= 318	n= 327	n= 510	n= 136	
Model 1	92.0	91.3	91.7	93.0	93.4	0.07
Model 2	91.9	90.1	90.2	91.6	92.5	0.05
Model 3	90.9	90.0	90.0	91.4	92.2	0.14
Urinary Incontinence (n= 1861)	n= 572	n= 321	n= 324	n= 508	n= 136	
Model 1	78.4	78.7	79.3	77.6	82.1	0.25
Model 2	81.1	81.1	82.2	80.7	84.0	0.31
Model 3	82.1	81.6	82.5	80.9	84.0	0.60
Urinary Irritation/Obstruction (n= 1810)	n= 553	n= 308	n= 314	n= 502	n= 133	
Model 1	90.8	90.0	90.7	91.8	89.9	0.99
Model 2	89.0	87.7	88.4	89.5	88.0	0.92
Model 3	88.8	87.3	88.0	89.0	87.2	0.50
Sexual Functioning (n= 1819)	n= 554	n= 311	n= 324	n= 495	n= 135	
Model 1	31.1	32.5	34.5	32.7	34.2	0.23
Model 2	29.8	31.1	33.3	31.6	32.0	0.35

	Total Weekly Physical Activity Time (hours)					
EPIC-26 Subscale	**<1**	**1 to <3**	**3 to <5**	**5 to <10**	**≥10**	***p* trend**
Model 3	28.5	30.2	32.7	31.2	31.5	0.24
Vitality/Hormonal Functioning (n= 1866)	n= 576	n= 322	n= 324	n= 508	n= 136	
Model 1	89.5	91.4	**92.5**	**91.9**	**94.0**	**<0.0001**
Model 2	87.0	88.5	**89.5**	**89.0**	**91.1**	**0.0003**
Model 3	86.2	87.6	**88.8**	**88.3**	**90.4**	**0.0007**
	Total Weight-lifting Time (hours)					
	None	**<1**	**1 to <3**	**≥3**		***p* trend**
Bowel Functioning (n= 1862)	n= 1198	n= 236	n= 263	n= 165		
Model 1	92.0	93.4	92.4	90.9		0.42
Model 2	90.7	92.1	91.4	89.6		0.37
Model 3	89.5	91.3	90.7	89.2		0.86
Urinary Incontinence (n= 1861)	n= 1194	n= 236	n= 267	n= 164		
Model 1	79.3	77.4	78.2	75.1		**0.04**
Model 2	82.3	79.9	80.1	78.1		**0.02**
Model 3	83.2	80.7	80.4	78.0		**0.02**
Urinary Irritation/Obstruction (n= 1810)	n= 1158	n= 231	n= 261	n= 160		
Model 1	91.1	89.8	90.6	89.4		0.09
Model 2	88.8	87.5	88.5	87.0		0.07
Model 3	88.2	87.0	87.9	86.7		0.20
Sexual Functioning (n= 1819)	n= 1167	n= 234	n= 260	n= 158		
Model 1	32.2	33.0	33.4	33.1		0.62
Model 2	31.3	31.2	30.9	31.9		0.85
Model 3	31.9	31.9	31.2	31.6		0.89
Vitality/Hormonal Functioning (n= 1866)	n= 1205	n= 236	n= 264	n= 161		
Model 1	91.4	89.6	91.4	91.4		0.99
Model 2	88.7	**86.6**	88.6	88.5		0.78
Model 3	88.2	86.6	88.7	88.5		0.73

*The 2008 (time point immediately prior to the 2010 HRQOL assessment) physical activity assessment was used as the exposure for this analysis. All values represent adjusted mean values with higher scores reflecting better HRQOL (i.e. less symptomology). Model 1: Adjusted for age at diagnosis and time since treatment; Model 2: Adjusted for age at diagnosis, time since treatment or diagnosis,

presence of comorbidities, stage of disease, Gleason score, treatment type, PSA at diagnosis, 2008 body mass index; Model 3: Adjusted for all variables in Model 2 and pre-diagnosis physical activity. Models examining non-vigorous physical activity or vigorous physical activity are mutually adjusted for the other. All models examining weightlifting control for all other activity. All models examining urinary or sexual functioning adjusted for use of respective medications. Values in bold indicate a significant difference from the reference category. Data on 95% confidence intervals for point estimates are available upon request.

Table 3

Sedentary time and health-related quality of life in prostate cancer survivors*

	Total Sedentary Time Quartiles (hours/day)				
EPIC-26 Subscale	**Quartile 1 0 to <2.1 (n= 240)**	**Quartile 2 2.1 to <3.9 (n= 561)**	**Quartile 3 3.9 to <6.1 (n= 382)**	**Quartile 4 ≥6.1 (n= 734)**	***p* trend**
Bowel Functioning (n= 1862)					
Model 1	92.5	92.8	92.5	91.0	0.05
Model 2	91.3	91.5	91.1	90.0	0.08
Model 3	91.2	91.5	91.2	90.3	0.24
Urinary Incontinence (n= 1861)					
Model 1	77.7	79.0	80.4	77.2	0.87
Model 2	80.6	82.1	83.6	79.5	0.57
Model 3	80.3	82.2	84.1	80.6	0.73
Urinary Irritation/Obstruction (n=1810)					
Model 1	90.8	91.7	91.0	89.8	0.10
Model 2	88.7	89.4	88.7	88.0	0.20
Model 3	88.4	89.4	89.1	88.7	0.93
Sexual Functioning (n=1819)					
Model 1	32.2	34.0	32.0	32.4	0.74
Model 2	30.8	32.6	31.2	31.4	0.99
Model 3	30.8	32.6	31.3	31.5	0.92
Vitality/Hormonal Functioning (n= 1866)					
Model 1	90.8	**93.2**	91.0	90.3	0.10
Model 2	88.4	**90.4**	88.6	87.9	0.18
Model 3	88.4	90.2	88.5	87.9	0.19

*The 2008 (time point immediately prior to the 2010 HRQOL assessment) sedentary time assessment was used as the exposure for this analysis. All values represent adjusted mean values with higher scores reflecting better HRQOL (i.e. less symptomology). Model 1: Adjusted for age at diagnosis and time since treatment; Model 2: Adjusted for age at diagnosis, time since treatment, presence of comorbidities, stage of disease, Gleason score, treatment type, PSA at diagnosis; 2008 body mass index; Model 3: Adjusted for all variables in Model 2 and total pre-diagnosis sedentary time. Values in bold indicate a significant difference from the reference category.

Table 4

Total physical activity and hormone/vitality functioning by subgroups*

		Total Weekly Walking Time (hours)						
		<1	**1 to <3**	**3 to <5**	**5 to <10**	**≥10**	***p* trend for stratification**	***p* for interaction variable**
Age at diagnosis								
<70 (n=1073)	***M***	83.0	84.8	**87.3**	**87.7**	**88.8**	**0.0003**	0.49
≥70 (n=793)	***M***	86.8	85.8	87.6	88.0	90.3	**0.009**	
Time since treatment in years								
<5 (n=478)	***M***	83.1	85.3	86.8	85.3	87.3	0.19	**0.03**
5 to <10 (n=707)	***M***	90.4	90.6	94.0	93.7	94.1	**0.04**	
≥10 (n=681)	***M***	80.4	80.3	80.6	83.8	**86.1**	**0.0002**	
Gleason score								
<7 (n=1245)	***M***	88.5	88.9	89.7	90.9	91.0	**0.03**	**0.04**
≥7 (n=621)	***M***	84.9	85.1	**90.1**	88.9	**93.3**	**<0.0001**	
Treatment Type								
Radical Prostatectomy (n=981)	***M***	87.6	89.5	**91.8**	**91.4**	**93.4**	**0.0006**	0.88
Radiation (n=669)	***M***	89.5	87.5	89.6	90.3	91.4	0.06	
PSA recurrence								
No (n=1510)	***M***	88.8	88.7	**91.5**	**91.9**	**92.8**	**<0.0001**	0.98
Yes (n=356)	***M***	80.6	84.1	83.4	84.0	86.7	0.09	
BMI								
<25 (n=763)	***M***	87.0	86.4	88.7	89.0	90.3	**0.01**	0.80
≥25 (n=1103)	***M***	85.2	86.6	**88.6**	**89.1**	**91.1**	**<0.0001**	
Presence of Comorbidities**								
No (n=1207)	***M***	90.0	89.6	91.1	91.2	92.3	**0.03**	**0.02**
Yes (n=659)	***M***	80.0	82.4	**85.5**	**86.7**	**89.5**	**<0.0001**	

PSA= Prostate-Specific Antigen; BMI= Body Mass Index

*2008 physical activity assessment was used as the exposure for this analysis (time point immediately prior to the 2010 HRQOL assessment). All values represent adjusted mean values with higher scores reflecting better HRQOL (i.e. less symptomology). Models are adjusted for all covariates other than variable stratified on including time since treatment, BMI, age at diagnosis, presence of comorbidities,

stage of disease, Gleason score, PSA, and pre-diagnosis physical activity. The reference category for all models is <1 hour per week. Values in bold indicate significance between group and reference category at $p < 0.05$.

** Presence of comorbidities considered yes if participant reported any of the following over the study period: myocardial infarction, stroke, emphysema/chronic obstructive pulmonary disease, Parkinson's disease, coronary artery bypass or coronary angioplasty, and diabetes.