



# Approach and avoidance coping: Diurnal cortisol rhythm in prostate cancer survivors



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**Abstract** Psychological coping responses likely modulate the negative physiological consequences of cancer-related demands. This longitudinal, observational study examined how approach- and avoidance-oriented strategies for coping with cancer are associated with diurnal cortisol rhythm in prostate cancer (PC) survivors. Sixty-six men ( $M$  age = 65.76;  $SD$  = 9.04) who had undergone radical prostatectomy or radiation therapy for localized PC within the prior two years reported their use of approach and avoidance coping via questionnaire at study entry (T1). Participants provided saliva samples (3 times per day over 3 days) for diurnal cortisol assessment at T1 and again 4 months later (T2). When controlling for relevant biobehavioral covariates, cancer-related avoidance-oriented coping was associated with flatter cortisol slopes at T1 ( $B$  = .34,  $p$  = .03) and at T2 ( $B$  = .30,  $p$  = .02). Approach-oriented coping was not associated with cortisol slopes. Post-hoc analyses revealed a significant interaction between avoidant coping and time since completion of cancer treatment on T2 cortisol slope ( $B$  = −.05,  $p$  = .04). Men who used relatively more avoidance-oriented coping who were further in time from treatment

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demonstrated a flatter cortisol slope. High avoidance-oriented coping is associated with dysregulation of cortisol responses, which may be an important target for reducing stress during PC survivorship.

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Coping constitutes cognitive and behavioral efforts to manage demands of circumstances an individual appraises as stressful (Lazarus and Folkman, 1984). The stressors experienced with cancer diagnosis and treatment are associated with a variety of physical and psychological outcomes in cancer survivors across the disease trajectory (Stanton, 2006). Coping responses, often construed as either approach-oriented (e.g., active planning, emotional expression) or avoidance-oriented (e.g., disengagement), modulate the negative consequences of cancer-related and general life stressors and alter quality of life (Low et al., 2006). Few studies have sought to identify the possibility that specific strategies for coping with cancer-related stress can shape neuroendocrine mechanisms (e.g., diurnal cortisol) (e.g., Diaz et al., 2014), which can contribute to adverse cancer outcomes (Armaiz-Pena et al., 2013).

Aberrant diurnal cortisol patterns have been linked to a number of health outcomes in cancer patients, including disease progression and early mortality (e.g., Cohen et al., 2012; Sephton et al., 2013; see also Armaiz-Pena et al., 2013). Findings in breast cancer patients suggest that diurnal cortisol rhythm may be shaped by individual coping strategies (Diaz et al., 2014). However, no study has examined these associations in men with prostate cancer (PC). Thus, it is unclear if men who are better able to cope with cancer sequelae exhibit healthier cortisol patterns. The present study examined how approach- and avoidant-oriented coping strategies are related to diurnal cortisol rhythm in PC survivors. It was hypothesized that greater use of avoidance- and less use of approach-oriented coping would be associated with flatter diurnal cortisol slopes. Such findings would emphasize the negative impact of PC diagnosis and treatment, and given findings that flatter cortisol slope predict worse outcomes, also highlight modifiable cognitive-behavioral intervention targets.

## 1. Method

### 1.1. Participants and procedures

Men who completed radical prostatectomy or radiation therapy for localized PC within the prior two years took part in a larger study on "health-related quality of life after PC." Sixty-six English-speaking, non-smoking men were recruited via physician/clinic referrals ( $n=4$ ), community outreach ( $n=12$ ), advertisement ( $n=3$ ), and an institutional tumor registry database ( $n=47$ ) (see Table 1). Participants were excluded for presence of medical conditions or medications, including steroids, that could confound cortisol evaluation.

This study utilized a longitudinal observational design. After providing written informed consent, participants completed questionnaires in person at study entry (T1) and again 4 months later (T2). At T1 and T2 participants provided saliva samples (3 times per day over 3 days beginning on

Tuesday) for measurement of cortisol output as described below. Men received \$50 compensation. All procedures were approved by the authors' Institutional Review Board.

### 1.2. Measures

*Cancer-specific coping* was assessed by the Brief COPE (Carver, 1997), a 28-item self-report inventory, and the Emotional Approach Coping Scales (Stanton et al., 2000). Patients rated their coping behaviors in response to their experience of cancer on a 4-point response scale. A composite measure of approach-oriented coping was constructed with the active coping, planning, acceptance, support seeking, emotional expression, and emotional processing subscales; the avoidance-oriented coping composite was constructed from the behavioral disengagement, denial, and mental disengagement subscales. The composite scale scores represent the mean of included items (approach  $\alpha = .82$ ; avoidance  $\alpha = .79$ ).

*Diurnal cortisol* was assessed with saliva samples collected at home using Salivette collection tubes (Sarstedt, Inc.). Participants collected saliva upon awakening (morning), 8 h post-awakening (afternoon), and at bedtime for three consecutive days. They were instructed not to eat, drink, or brush teeth for at least 20 min before sampling. Each day, participants self-reported relevant health behaviors (e.g., caffeine intake, tobacco use) and compliance with collection instructions. Participants were instructed to call or text a voicemail line after each sample collection to ensure compliance. Average sample collection times were: waking: 6:17 am ( $SD=1:01$ ); 8 h post-waking: 2:42 pm ( $SD=1:40$ ); bedtime: 11:34 pm ( $SD=1:45$ ). Participants refrigerated samples until returning them via express mail. Salivettes were stored in a  $-20^{\circ}\text{C}$  freezer until analysis. Concentrations of salivary free cortisol were measured in duplicate using a commercially available chemiluminescence-immunoassay at the TUD Biopsychology Laboratory in Dresden, Germany. Assay sensitivity was measured to be  $.015\text{ }\mu\text{g/dL}$ . The lower detection limit is  $.41\text{ nmol/L}$ , and inter-assay and intra-assay coefficients of variance are  $<10\%$ .

Participants self-reported demographic and disease-related variables. They also completed a modified version of the Impact of Events Scale-Intrusion subscale (Horowitz, 1987) as a measure of cancer-specific distress ( $\alpha = .89$ ).

### 1.3. Data analyses

Hierarchical linear modeling (HLM) allows for the analysis of nested data (i.e., the average cortisol output at three time points nested within participant). HLM provides analysis of change over time on an individual basis (i.e., cortisol levels across the day) (Bryk and Raudenbush, 1992). Observations of cortisol at T1 and T2 were predicted in separate models

**Table 1** Participant characteristics ( $N=66$ ).

Characteristic		Characteristic	
M age	65.76 ( $SD=9.04$ )	Job status	
Ethnicity		Full-time employment	35.4%
White (non-Hispanic)	84.8%	Part-time employment	10.8%
African American/Black	10.6%	Retired	47.7%
Hispanic/Latino	3.1%	Unemployed/disability	6.1%
Native American	1.5%	Relationship status	
Education		Married/partnered	89.4%
High school	10.7%	Widowed/divorced	7.5%
Some post-high school	21.2%	Single, never married	3.1%
2-year college degree	9.1%	Treatment	
4-year college degree	25.7%	Prostatectomy/surgery	71.2%
Advanced degree	33.3%	Radiation therapy	31.8%
Annual household income		Hormone therapy	9.1%
\$15,000 or less	3.1%	M months since treatment	15.63 ( $SD=7.53$ )
\$15,001–45,000	9.2%	M Gleason sum	5.7 ( $SD=1.39$ )
\$45,001–75,000	26.2%		
\$75,001–100,000	21.5%		
\$100,001 or more	40.0%		

Note: Several participants reported receipt of more than one treatment type. Only 2 participants reported current receipt of hormone therapy at time of participation.

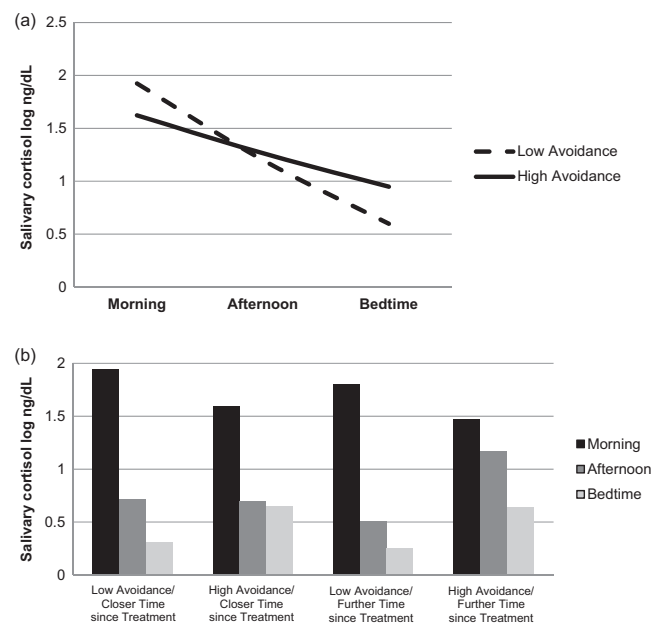
in HLM (HLM 7.0 statistical software program, SSI Inc.). The slope of the diurnal change in cortisol levels was calculated by regressing cortisol values on time of day for each collection day. Cortisol data were log-transformed to control for skewness. Cortisol observation times were entered as Level 1 units in the analyses. Coping variables and relevant controls were entered at Level 2.

## 2. Results

Relationships with relevant biobehavioral (e.g., body mass index, sleep quality) and disease-specific variables (e.g., treatment type) were examined to identify possible covariates. Only body mass index and age were related to cortisol and so were entered as covariates in subsequent models. Also, no significant covariate by coping interactions were found. Men reported greater use of approach-oriented ( $M=2.67$ ;  $SD=.71$ ) versus avoidance ( $M=1.34$ ;  $SD=.38$ ) coping. Daily cortisol output (determined as average across 3 collection days) was 1.37 ( $SD=.69$ ) at T1 and 1.45 ( $SD=.76$ ) at T2.

HLM revealed that higher levels of avoidance coping were associated with flatter cortisol slopes at T1 ( $B=.34$ ,  $p=.03$ ) and T2 ( $B=.30$ ,  $p=.02$ ). Approach-oriented coping was not significantly associated with either T1 ( $B=-.04$ ,  $p=.63$ ) or T2 ( $B=.05$ ,  $p=.52$ ) slopes. The observed cortisol pattern is depicted in Fig. 1a. Post-hoc analyses controlling for cancer-related distress did not significantly change the nature of observed relationships of avoidance and cortisol and no evidence for a distress by avoidance interaction was found.

To consider the possibility that the association of avoidance and cortisol slope varied across the survivorship trajectory, post-hoc analyses including an avoidance coping by time since treatment (in months) interaction term



**Fig. 1** (a) Illustrates diurnal cortisol patterns at high (above the median) and low (below the median) levels of avoidance-oriented coping (median = 1.25). High avoidance was associated with lower morning cortisol and higher cortisol output at bedtime. (b) Illustrates diurnal cortisol patterns at high (above the median) and low (below the median) levels of avoidance-oriented coping and time since cancer treatment (median = 14.5). The combination of high avoidance and greater time since treatment reflected a flatter slope characterized by lower morning cortisol levels and less cortisol decline by bedtime compared to other groupings.

were conducted. Results revealed a significant interaction for T2 slopes ( $B = -.05$ ,  $p = .04$ ). The observed cortisol pattern is depicted in Fig. 1b. As shown, the combination of high avoidance and greater time since treatment represented the most aberrant cortisol rhythm.

### 3. Discussion

This study examined the hypothesis that approach and avoidance coping strategies would be related to alterations in diurnal cortisol rhythms. As predicted, PC survivors using higher levels of avoidance-oriented coping had significantly flatter cortisol slope at both T1 and across time at T2 than those reporting relatively lower avoidance. Approach-oriented coping was unrelated to cortisol slope. Visual inspection of the observed slopes suggests that men engaging in relatively high avoidance exhibited a less rapid decline in cortisol in the evening hours. Avoiding stressors, such as denying the presence of cancer when cancer-related stressors are present, might prolong physiological stress responses across the day.

Post-hoc analyses suggested that these results might be driven by individuals who over-rely on avoidance-oriented coping as time since cancer diagnosis progresses. These individuals may be more likely to be managing unrelenting cancer-related stressors (e.g., prolonged physical side effects). Avoidance of such persistent stressors, particularly when used habitually, might contribute to the maintenance, rather than the mitigation, of stressors. Future work should assess the nature of cancer-related stressors across the recovery trajectory.

The lack of association of approach-oriented coping and cortisol was surprising especially given that such associations have been found in samples of healthy older adults (O'Donnell et al., 2008). Future studies with larger samples should attempt to consider the physiological responses associated with specific approach-oriented strategies (e.g., problem-solving vs. emotional expression). The aggregated measure in this study might represent a host of responses (Skinner et al., 2003).

The primary limitation of this study is the small sample size; findings require replication in a larger group of patients. Because the study was somewhat underpowered to detect effects, lack of statistically significant findings of approach coping should be interpreted with caution. We also relied on self-report for timing of sample collection. However, this is the first study to our knowledge to show an association between diurnal cortisol rhythm and coping strategies in PC survivors. Future work should further characterize related physiological processes that affect health. For instance, inflammatory processes which are sensitive to psychological coping (Hoyt et al., 2013) might be affected by diurnal cortisol rhythm. The degree to which cortisol is associated with physical and psychological outcomes in PC patients also deserves future attention. Finally, this study isolated the two-year period following treatment. However, a key issue will be to determine how these coping processes and associated stress responses unfold over a longer trajectory. Finally, we did not observe differences in cortisol between men who received radiation versus those who underwent surgery. Future studies should examine the

potential impact of treatment type on cortisol responses during or in closer proximity to active treatment.

Cortisol rhythms may be one mechanism by which coping affects outcomes in PC patients, particularly for avoidance-oriented coping strategies. Although previous research with women with cancer has demonstrated a relationship of cortisol and approach coping (Abercrombie et al., 2004), avoidance may be more salient in men's experience. More research is needed to examine these relationships across time and to identify intrapersonal or interpersonal factors that might condition the impact of avoidance on stress responses. Behavioral and other healthcare interventions that work to mitigate the use of denial of and disengagement from cancer-related stressors can positively alter endocrine function and potentially enhance psychological adjustment and physical health outcomes in prostate cancer patients.

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### Conflict of interest statement

The authors have no actual or potential financial and other conflicts of interest related to the submitted manuscript.

### Contributors

Authors Hoyt, Bower, Thomas, Irwin, and Stanton contributed to the design and implementation of the study. Author Marin-Chollom undertook the statistical analysis. All authors contributed to and have approved the final manuscript.

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