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Research paper

Effects of a randomized-controlled trial of cognitive behavioral stress management: Psychosocial adaptation and immune status in men with early-stage prostate cancer

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ABSTRACT

Objective: Targets of intervention in cognitive behavioral stress management (CBSM), such as benefit finding (BF) and perceived stress management skills (PSMS), may counteract stress-related changes that impact the immune system. This study tested whether BF, PSMS, and optimism influence the effects of CBSM on immune status in men with prostate cancer.

Methods: Men with prostate cancer were randomized to receive CBSM or a psychoeducation (PE) control comparison (NCT05486754). Life Orientation Test-Revised assessed baseline optimism. The Benefit Finding Scale and Measure of Current Status measured BF and PSMS after CBSM. T-cells and T-helper cells captured immune status change at baseline and 6-months post-CBSM. MPlus and SPSS (PROCESS) tested condition effects and moderated mediation, controlling for covariates.

Results: 256 primarily middle-aged, White Non-Hispanic or Hispanic men enrolled. PSMS mediated CBSM effects on T-cell and T-helper cell percentage, such that T-cell and T-helper cell percentages were reduced in men in CBSM versus PE via PSMS. Optimism moderated this mediation with the mediating effect of PSMS only observed among men with average optimism versus those with low or high optimism.

Conclusion: Baseline psychological characteristics, as well as limited specificity of immune measurement, could explain the conditional effects in this sample.

Trial Registration: NCT05486754

1. Introduction

Prostate cancer is the most common type of non-skin cancer diagnosed among men in the United States, and approximately 248,530 new cases will be diagnosed in 2022 [1]. Advancements in treatments and early detection have vastly improved survival rates [2]. As a result, many individuals with prostate cancer will survive their disease but often deal with negative aftereffects, including difficulties that can persist for months to years after treatment [3]. Physical and psychological symptoms and decrements in disease-specific quality of life, such as sexual and urinary dysfunction, fatigue, pain, fears of recurrence, sleep difficulties, and heightened anxiety and depressive symptoms, contribute to cancer-related stress and life stress for survivors of prostate cancer [4–6].

Stress related to a prostate cancer diagnosis or treatment-related side effects has downstream repercussions for psychological and physiological well-being [7]. Interpretation and experience of stressors activate the autonomic nervous system and a subsequent "fight or flight" response [7]. This physiological response is adaptive in acutely stressful situations. However, when individuals face chronic stress, this activation may act on the immune system [7]. Specifically, this stress response can alter T-cells, T-helper cells and natural killer (NK) cell function [8–10]. However, patients who are able to maximize accuracy of their perceptions of stressful events may be less likely to experience downstream immune dysregulation. Bower et al. (2009) proposed a hypothesis central to this cascade by suggesting that patients who reappraise

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their perceptions of stress as neutral or beneficial may be able to buffer these immune changes [11]. They define one form of re-appraisal, benefit finding, as noting positive aspects of inherently negative situations, like a cancer diagnosis, which may enhance coping behaviors and goals of an individual [11]. A patient's ability to consider benefit of stressful situations can reduce downstream negative health effects [11,12].

Cognitive behavioral stress management (CBSM) is a psychosocial intervention that targets skill-building to promote balanced appraisals and in turn, improve physiological adaptation [13–15]. Physiologic improvements after CBSM are well documented among several patient populations, and include immune system changes, most commonly related to improvements in total T-cell, T-helper and T-cytotoxic cell counts [13,16–18]. A prior study documented men with early-stage prostate cancer receiving CBSM showed greater benefit finding at post-CBSM follow-up, effects which were mediated by perceived stress management skill improvements [19]. However, while physiologic changes after CBSM are well-studied among other cancer populations (e.g., women with breast cancer [17,20,21]) no evidence exists among men with prostate cancer after CBSM.

Patients' presenting characteristics, strengths, and abilities may impact one's ability to find benefit in the cancer experience. Optimism has been identified as a trait predictor of benefit finding [14,22,23]. Optimistic patients may be more likely to reestablish positive beliefs about themselves and the world, thus maintaining a positive outlook during disease adaptation [14,23]. This suggests that patients presenting with greater optimism exhibit greater benefit finding. Yet, in prior studies with breast cancer survivors, women who entered the study with low levels of optimism reported the greatest gains in benefit finding up to one year after CBSM [14]. In contrast, women who presented with high levels of optimism reported gains in benefit finding only immediately following the CBSM intervention, which decreased by 3 and 9-months post-intervention [14]. These results warrant additional exploration of the relationship between benefit finding and baseline optimism among patients with other cancer types, such as men with prostate cancer.

This study aimed to address gaps in what is known about the mechanisms of a 10-week CBSM intervention on men with early-stage prostate cancer. We hypothesized that the effects of CBSM on immune status, T-cells and T-helper cells, would be mediated by post-intervention benefit finding. Perceived stress management skills were also assessed as a mediator to contextualize these findings within the previous literature among men with early-stage prostate cancer [19]. Furthermore, it was hypothesized that lower baseline optimism would predict greater increases in benefit finding and perceived stress management skills, and greater intervention-associated improvements in immunologic measures 6-months after intervention.

2. Materials and methods

2.1. Participants

This study is a secondary analysis of a randomized controlled trial of patients with early-stage prostate cancer conducted between 8/2000–5/2004 (NCT05486754). Eligible patients had undergone either a radical prostatectomy or radiation therapy (i.e., external beam or seed implant) for stage I or II prostate cancer in the preceding 18-months. Patients were recruited by convenience through community presentations, recruitment fliers, urology referrals and the Florida Cancer Data System, a HIPAA-compliant Florida Department of Health cancer registry. There were several inclusion criteria: 50 years of age or older; ability to speak, read, and write in English; having a ninth-grade reading level or greater; free of cognitive impairment that would interfere with the study; and no active psychiatric symptoms (previous three months). Additionally, patients were ineligible if they had a previous history of non-skin cancer or received adjuvant treatment, including hormone treatment, for prostate cancer.

2.2. Procedures and study design

Patients were approached and screened for eligibility. Study staff administered the Folstein Mini-Mental Status Examination [24], and patients who scored 23 or greater were included. Items from the Structured Clinical Interview for the Diagnostic Statistical Manual of Mental Disorders (SCID-IV) [25] determined current psychiatric status. If they met inclusion criteria, patients provided informed consent through an Institutional Review Board-approved consent form, enrolled, and completed the first assessment, which included a psychosocial battery and blood sample. Study staff assessors were blinded to participant condition, and assessments were completed in-person. All patients were subsequently randomized to receive either a 10-week CBSM intervention or a one-day psychoeducation (PE) seminar. The project manager executed parallel randomization through participant blocking dependent on size of cohort recruited to ensure at least 4–6 men comprised the intervention group at a time: 1:1 for >12 participants, 2:1 for 6–12 participants, and the flip of a coin for <6 participants. Patients in the PE group attended the seminar between the 5th and 6th weeks of the CBSM intervention. All patients completed a post-intervention follow-up assessment within three weeks and an assessment 6-months thereafter.

2.2.1. Experimental condition

CBSM was delivered in a manualized format over the course of 10-weeks. This intervention has been tailored for women with breast cancer and men with prostate cancer [15,26]. The program took place in groups of 3–8 patients weekly for 2-h. Sessions included 30 min of relaxation training and 90 min of didactic skill building, including identification of distorted thinking, rational thought replacement, coping effectiveness training, and interpersonal skills training. Patients were encouraged to interact with one another in a group setting to strengthen social bonds and facilitate support. All sessions were delivered by trained master's-level clinical psychology students or doctoral-level clinical psychologists under the supervision of the study principal investigator who monitored the delivery of the intervention for fidelity to prevent drift.

2.2.2. Control condition

Patients who were randomized to receive the PE control condition attended a one-day seminar for approximately four hours total. The seminar included an abbreviated version of the stress management skills provided in 10-week CBSM intervention. Patients in the control condition were provided with an identical intervention workbook and were instructed to practice skills and relaxation training interpedently. Seminar groups also consisted of 3–8 patients and were facilitated by trained master's-level students or doctoral-level psychologists.

2.3. Measures

2.3.1. Control variables

Sociodemographic and medical information, including age, education level, race/ethnicity, and type of treatment, were collected from the medical record and through patient self-report at the first study assessment. Prior research has found that such sociodemographic characteristics may impact outcomes related to CBSM, immune function, or response to psychosocial intervention receipt [17,19,27–30] so analyses accounted for such effects.

2.3.2. Benefit finding

The 17-item Benefit Finding Scale assessed benefit finding [14,23]. Patients indicated their level of agreement with statements related to positive perceptions because of their cancer on a scale of 1 (not at all) to 5 (extremely). The benefit finding scale has shown good reliability and

validity among patients with prostate cancer [31]. Within this sample, reliability was excellent at baseline and post-intervention (both alphas = 0.95).

2.3.3. Perceived stress management skills

The Measurement of Current Status-Subscale A (MOCS-A) by Carver (2006) measured perceived stress management skill mastery [32]. The MOCS-A captures perceived CBSM skill-specific abilities, including ability to relax at will, recognizing stress and tension in the body, and capacity to cope with stress. [32] Patients indicate their level of current ability to do various skills on a scale of 0 (I cannot do this at all) to 4 (I can do this extremely well) for 13 statements. In this study, reliability was high and ranged from 0.87 at baseline to 0.91 at post-intervention.

2.3.4. Optimism

The Life Orientation Test-Revised (LOT-R) was used to assess baseline optimism of patients. This 10-item measure has been used in many populations to determine level of general optimism [33,34]. Patients answered based on a five-point Likert scale from "I disagree a lot" to "I agree a lot." Baseline optimism reliability was adequate at an alpha-level of 0.693.

2.3.5. T-cell and T-helper cell count and percentage

T-cell (Total CD3+) and T-helper cell (CD3 + CD4+) raw counts and percentages were determined through peripheral blood mononuclear cell (PBMC) collection. Whole blood samples were analyzed using flow cytometry to estimate total blood values and specific T-cell phenotypes. This methodology is typical for T-cell and T-helper cell peripheral blood analysis [35].

2.4. Analytic plan

All data were assessed for normality and outliers. One individual reported a race/ethnicity of "Other" and self-identified as Asian American. This participant was omitted from the reported results since inclusion of a group with an $n = 1$ would have resulted in non-biased parameters, and all other groups controlling for race/ethnicity were specific identities (e.g., Hispanic, African American;/Black) of which this participant did not identify. Results with and without this participant did not differ. Total missing values ranged from 0 to 46.1% (greatest missingness among T-cell and T-helper cell percentage change score from baseline to 6-months post-intervention, $N = 157$ missing). Mediation and conditional process analyses consisted of condition randomized after baseline, the mediator of interest at post-intervention, and immune status at 6-months post-intervention. All tested mediators and immune status outcomes were calculated as change scores by subtracting the baseline value from the post-intervention value (for mediators) and from the 6-months post-intervention value (for immune outcomes) and included in analyses.

All analyses were conducted with intention to treat and utilized original participant randomization assignment. IBM SPSS (PROCESS macro, model 58) and Mplus software tested structural equation modeling and conditional process analysis for proposed hypotheses while controlling for covariates. Bootstrap sampling (5000 resamples) was used to estimate 95% confidence intervals to account for bias in the continuous moderator, optimism. Full information maximum likelihood was used to accommodate missing data, and pair-wise deletion was used for missing data in conditional process analyses. Condition group, treatment type, and racial/ethnic group were dummy coded and education, age, and months since treatment were included as continuous covariates. Because optimism was a continuous moderator, conditional indirect effects were assessed at three levels: one standard deviation above, one standard deviation below, and at the mean. If the 95% bootstrapped confidence interval crossed zero, the condition indirect effect did not exist at that level of optimism in the sample. If there was a significant interaction within either or both paths of a condition indirect effect, Johnson-Neyman analyses were conducted to assess the point along the continuous moderator at which the significant interaction exists [36]. If neither indirect path individually had a significant interaction, no Johnson-Neyman analyses were conducted.

Additional, post-hoc exploratory analyses would be considered to contextualize findings if a conditional process effect was detected. Due to the numerous tests conducted, we included a multiple comparisons test correction to all final models run. The SPSS PROCESS Macro (model 58) generated direct and indirect conditional process analyses using confidence intervals to determine significant relationships. Therefore, a false discovery rate could not be estimated without *p*-values of each analysis; therefore, a Bonferroni multiple comparisons approach was taken. The 95% confidence interval represented a p-value of 0.05, and with all hypothesized and exploratory analyses, we anticipated conducting at least five tests. So, as determined by Bonferroni correction, the 95% confidence interval was increased to a 99% confidence interval to account for these numerous tests (0.05/5 = 0.01; 0.01 represented by a 99% confidence interval). The 99% confidence interval is the only interval offered by the PROCESS Macro after 95%, so in the event that more or less than five tests would be conducted, the 99% confidence interval would still be used as a conservative approach to multiple comparisons.

3. Results

The sample consisted of 294 men, 256 of whom were randomized to either receive the PE control or the CBSM intervention and 38 were lost to follow-up (e.g., withdrawn, lost to follow-up). Participant flow characteristics can be found in previously published work [37] and in supplemental materials (Supplemental Fig. 1). Men were on average 15.56 months since diagnosis ($SD = 6.9$, range: 2–48) and 10.32 months since treatment ($SD = 4.5$, range: 1–24). The sample was primarily White Non-Hispanic (41.0%) or Hispanic (42.2%). The remainder of the sample identified as Black or African American (16.8%). Full participant characteristics are located in Table 1. Condition had no significant main effects on immune status. All estimated main effects with covariates may be found in Table 2.

Table 1
Participant baseline characteristics.

Characteristic M (SD); N (%)	CBSM Intervention ($N = 147$)	PE Control ($N = 109$)	Total ($N = 256$)
Age	65.97 (7.53)	64.56 (7.84)	65.37 (7.68)
Months since diagnosis	15.52 (7.36)	15.40 (6.34)	15.47 (6.93)
Months since treatment	10.07 (4.65)	10.53 (4.35)	10.26 (4.52)
Years of education	13.71 (3.41)	14.01 (3.31)	13.84 (3.36)
Race/ethnicity:			
Non-Hispanic White	62 (42.2%)	43 (39.5%)	105 (41.0%)
Hispanic	62 (72.9%)	46 (42.2%)	108 (42.2%)
Black/African American	23 (18.5%)	20 (18.3%)	43 (16.8%)
Procedure type:			
Surgery	66 (44.9%)	55 (50.5%)	121 (47.3%)
Radiation	81 (55.1%)	54 (49.5%)	135 (52.7%)
Income (thousands)	48.11 (47.39)	55.15 (54.36)	50.97 (50.26)
Baseline optimism	19.75 (3.54)	19.69 (3.40)	19.72 (3.54)
Baseline perceived stress management status	34.79 (8.58)	34.10 (9.74)	34.50 (9.08)
Baseline benefit finding	57.22 (15.99)	55.49 (17.31)	56.48 (16.55)

Table 2
Main effects of condition on immune status and proposed mediators.

		Condition	Age	Time Since Treatment	Education	Race/Ethnicity: Black	Race/Ethnicity: Hispanic	Procedure Type
T-cells	Count	−63.75 (43.76)	−4.79 (3.98)	−4.66 (4.41)	0.74 (6.86)	−45.58 (65.26)	63.80 (51.51)	64.79 (59.51)
	Percentage	0.60 (0.77)	−0.15 (0.07)**	0.11 (0.08)	0.07 (0.12)	−0.48 (1.14)	0.36 (0.90)	1.18 (1.09)
T-helper cells	Count	−28.74 (28.57)	−3.62 (2.60)	−1.57 (2.88)	−1.93 (4.48)	−35.64 (42.62)	6.87 (33.64)	58.27 (38.86)
	Percentage	0.68 (0.75)	−0.15 (0.07)**	0.09 (0.08)	−0.07 (0.12)	−0.18 (1.12)	−1.34 (0.89)	1.47 (1.03)
Benefit Finding		2.19 (1.57)	0.12 (0.14)	−0.00 (0.17)	−0.63 (0.25)**	−1.40 (2.27)	−7.00 (1.81)***	−2.10 (1.99)
Perceived Stress Management Skills		3.11 (1.12)***	0.17 (0.10)*	0.18 (0.12)	−0.12 (0.18)	−0.42 (1.60)	1.10 (1.29)	−3.26 (1.41)**

Note: *B* (SE); unstandardized coefficients reported; *$p < .10$, **$p < .05$, ***$p < .01$. All dependent variables are change scores (baseline to post-intervention: benefit finding and perceived stress management skills; baseline to 6-months post-intervention: T-cells and T-helper cells).

3.1. Mediator analyses

Proposed mediators were included in structural equation models with covariates to assess the hypothesized mechanism of change (Table 2). Condition did not have a significant effect on benefit finding ($b = 2.19$, $SE = 1.57$, $p = .16$; Table 3). Perceived stress management skills were significantly predicted by condition ($b = 3.11$, $SE = 1.12$, $p < .01$), such that the CBSM intervention group had on average 3.11 units greater of perceived stress management abilities at the second timepoint than the PE control group.

Due to lack of condition effects, benefit finding was not included as a mediator in subsequent analyses. There was neither an indirect nor direct effect of condition on total T-cell count via perceived stress management skills. There was a negative indirect effect of condition on T-cell percentage via perceived stress management ($b = −0.54$, $SE = 0.25$, $p = .028$) and a trending positive direct condition effect ($b = 1.38$, $SE = 0.77$, $p = .07$) on T-cell percentage. T-helper cell count was neither directly nor indirectly predicted by condition via perceived stress management skills. However, condition had a significant direct effect and indirect effect on T-helper cell percentage via perceived stress management skills (direct: $b = 1.49$, $SE = 0.74$, $p = .045$; indirect: $b = −0.56$, $SE = 0.25$, $p = .026$). All simple mediation indirect and direct effects may be found in Table 3.

3.2. Moderated mediation analyses

Uncorrected conditional process (i.e., 95% CI) results may be found in Table 4. The indirect effect of condition on T-cell percentage via perceived stress management skills was moderated by optimism level, such that participants with average optimism had a negative indirect effect of condition on T-cell counts that did not exist among participants with high or low optimism (Table 4). There was no unconditional direct effect of condition on T-cell percentage. Neither path of the indirect effect was significant (condition x optimism interaction: $b = 0.14$, $SE = 0.44$, $p = .74$; perceived stress management skills x optimism interaction: $b = −0.02$, $SE = 0.01$, $p = .18$).

Table 3
Simple mediation effects of condition on immune statue via PSMS.

	Direct Effect		Indirect Effect	
	B	SE	B	SE
T-cells (Count)	−0.094	0.088	−0.020	0.019
T-cells (%)	0.152*	0.083	−0.059**	0.026
T-helper Cells (Count)	−0.047	0.089	−0.027	0.020
T-helper Cells (%)	0.165**	0.081	−0.062**	0.027

Note: PSMS = Perceived Stress Management Skill change score. Standardized coefficients reported; *p < .10, **p < .05, ***p < .01.

Table 4
Conditional direct and indirect effects of condition on T-cell and T-helper cell percentage.

Direct Effect: Condition to T-cell (percentage)

Optimism Level	B	Standard Error	95% Bootstrapped CI	99% Bootstrapped CI
-	1.37	0.83	[−0.27, 3.01]	[−0.80, 3.54]
Conditional Indirect Effect: Condition to T-cell (percentage) via *Perceived Stress Management Skills*				
−3.27	−0.52	0.44	[−1.57, 0.18]	[−2.23, 0.42]
0.00	−0.87	0.37	[−1.69, −0.23]	[−2.05, −0.07]
3.27	−1.27	0.58	[−2.47, −0.21]	[−2.94, 0.03]

Direct Effect: Condition to T-helper cell (percentage)

Optimism Level	B	Standard Error	95% Bootstrapped CI	99% Bootstrapped CI
–	1.02	0.78	[−0.53, 2.57]	[−1.03, 3.07]
Conditional Indirect Effect: Condition to T-helper cell (percentage) via *Perceived Stress Management Skills*				
−3.27	−0.53	0.38	[−1.40, 0.09]	[−1.73, 0.31]
0.00	−0.85	0.33	[−1.55, −0.24]	[−1.79, −0.06]
3.27	−1.22	0.54	[−2.34, −0.23]	[−2.72, 0.01]

There was a significant conditional indirect effect of condition on T-helper cell percentage via perceived stress management skills as a function of baseline optimism. Like T-cell percentage, participants who entered the study with average levels of optimism had a significant negative indirect effect of condition on T-helper cell percentage via perceived stress management versus those with high ro low optimism (Table 4). Although there was a significant conditional indirect effect, neither leg of the indirect effect exhibited a significant interaction with moderation (condition x optimism interaction: $b = 0.14$, $SE = 0.44$, $p = .74$; perceived stress management skills x optimism interaction: $b = −0.02$, $SE = 0.01$, $p = .18$). Neither path comprising the indirect effects on T-cells or T-helper cells was moderated individually, which eliminated the possibility of conducting Johnson-Neyman techniques in either model to identify at which level of optimism these effects existed.

3.3. Exploratory analyses

Unplanned, post-hoc analyses were conducted, as follows, to consider the context of the results found in hypothesized analyses. At baseline, T-cell count, T-helper cell count were positively correlated with optimism ($r(185) = 0.165$, $p = .024$; $r(185) = 0.152$, $p = .038$). No immune variables were correlated with perceived stress management skills at baseline.

Based on previous work among patients with breast and prostate cancer, there may be additional moderators existing in this sample to explain the negative effects found. Men who receive radiation treatments for prostate cancer may experience different psychosocial consequences and symptom burden than men who receive surgery [38]. We reran moderated mediation analyses with procedure type as the moderator. Here, we found a significant uncorrected negative conditional indirect effect of condition on T-cell percentage for men who underwent surgery but not for men who received radiation (surgery: $b = -0.99$, $SE = 0.48$, bootstrapped 95% CI [−1.91, −0.001]; radiation: $b = -0.47$, $SE = 0.57$, bootstrapped 95% CI [−1.89, 0.32]). However, when corrected using a 99% CI, neither procedure type exhibited indirect effects of condition on immune status via perceived stress management skills.

Another potential moderator of these effects considered was perceived stress, as measured by the Perceived Stress Scale [39]. Perceived stress has previously been related to physical and emotional well-being and health-related quality of life in men with prostate cancer [40,41]. Additionally, greater baseline distress has been linked with heightened response to CBSM versus those with lower distress among women with breast cancer [42]. We tested perceived stress at baseline as a moderator of the relationship between condition and T-cell percentage. A significant conditional indirect effect of condition on T-cell percentage existed through perceived stress management skills, such that men with average levels of perceived stress exhibited a significant indirect effect versus those with low or high perceived stress (−1 SD: $b = -0.99$, $SE = 0.57$, bootstrapped 99% CI [−2.70, 0.41], M: $b = -0.90$, $SE = 0.35$, bootstrapped 99% CI [−1.90, −0.13, +1 SD: $b = -0.69$, $SE = 0.38$, bootstrapped 99% CI [−1.87, 0.17]).

4. Discussion

The current study examined the effects of a 10-week, group-based CBSM intervention on T-cells and T-helper cells among men with early-stage prostate cancer. Prior research has found CBSM-related physiological improvements by way of psychological benefit [13,16,17], which was retested in this sample. No main effects of condition on immune status existed. However further analyses revealed that the intervention did have an indirect effect on T cell counts at 6-month follow-up via changes in pre-post intervention levels of perceived stress managament skills, but only in those with average levels of optimism or perceived stress at baseline.

While previous studies found significant improvements in benefit finding among patients with cancer who receive CBSM [17,19,43], there was no condition effect on benefit finding in this sample. Compared to existing levels in this population, benefit finding was particularly high among this sample at baseline [31]. These high baseline levels could have reduced the ability to detect CBSM effects on benefit finding. Perceived stress management skills improved in the hypothesized direction when assessed for main condition effects as a mediator. These results are consistent with research on CBSM across cancer types [44–47] However, counter to hypothesized results, increases in perceived stress management skills contributed to a reduction in T-cell and T-helper cells.

While counter to hypothesized analyses, there are several possible explanations of a reduction in T-cell and T-helper cell percentages after stress management. Similar decreases in immune activities have been found in a previous stress management intervention trial, in which T-cell blastogenesis decreased among patients with breast cancer who received 18 1.5-h stress management sessions [48]. Additionally, the T-helper cell measurements from this sample included all types of T and T-helper cells, which vary in role. T-helper cells consist of Th1 and Th2 lymphocytes [49]. Th1 cells produce cancer-fighting components, such as tumor necrosis factor and interferon-gamma, whereas Th2 cells are known to promote malignant tumor growth [50]. Therefore, while an increase in Th1 cells may represent productive cancer surveillance, an increase in Th2 T-helper cells may represent advancing tumor growth or pro-cancer mechanisms. While Th1-specific cytokines have been found to increase after CBSM among women with breast cancer [21], such nuances of T-helper cell measurement were not included in the outcomes of this study. T-cells were also measured without specificity of T-cell type, which is important due to the complex role of T-regulatory (T-reg) cells in the immune system [51]. T-reg cells are one of several types of T-cells that can, similarly to Th2 cells, suppress cancer-fighting mechanisms by other immune cells. Additional research is required to isolate and understand outcomes of the immune system relevant to pro and anti-cancer activities within T-cells and T-helper cells and among men with prostate cancer who received CBSM.

4.1. Limitations and considerations

There are several considerations and limitations of the current study. The sample was comprised of a majority non-Hispanic White or Hispanic, well-educated, and socio-economically advantaged men from a large metropolitan area of south Florida. While potentially representative of other urban areas of the United States, this sample did not primarily reflect the population where the study was conducted, which may impact generalizability of conclusions. Additionally, the current sample had a large range of missing data, up to approximately 46%. This study was completed in the early 2000s and may not entirely represent the current state of detection and treatment of prostate cancer. Since conducted, the detection and treatment of prostate cancer has vastly improved. These improvements may alter how a psychological intervention, like CBSM, is operationalized by patients with prostate cancer. For instance, among men with very early detection of disease, there is an opportunity for cognitive reappraisal during the uncertain time of watchful waiting (i.e., active surveillance) [52]. Moreover, modern advancements in technology would aid the delivery of CBSM for use over telehealth video conferencing and smart phone app development. These modalities may additionally provide greater accessibility to this intervention, particularly for individuals far from academic medical centers.

4.2. Clinical implications

The results of this study highlight the importance of presenting patient characteristics in the delivery and receipt of psychosocial interventions, like stress management. For those presenting with average levels of optimism or perceived stress, patients may be more open or receptive to these types of interventions. A component of CBSM is to identify unrealistic thoughts, which in this case, may pertain to unrealistically negative cognitions and, inadvertently, to overly positive/optimistic cognitions. Participants with either especially high or low levels of optimism may, in turn, feel a greater challenge to identify and restructure these thoughts. These patients may benefit from additional tailoring, such as more practice or time dedicated in CBSM for cognitive restructuring, to better facilitate this skill. A similar reason may underlie those presenting with average perceived stress who exhibited an effect; individuals facing extremely high or low stress may be either 1) too overwhelmed to engage in CBSM or 2) feel content with their current level of stress. Additionally, future iterations of CBSM may consist of an abbreviated treatment version. 5-week intervention versions of CBSM components have been shown efficacious in improving psychological and physiological measures in women undergoing treatment for breast cancer [53–55]. Future research should explore the efficacy of abbreviated CBSM for physiologic adaptation among men with prostate cancer and if men with varying levels of baseline optimism or perceived stress differ.

4.3. Conclusions

CBSM significantly improved perceived stress management skills,

which were associated with subsequent reductions in T-cell and T-helper cells. This study is the first to test perceived stress management skills as a predictor of physiologic outcomes among men with prostate cancer, and there are several reasons that could underly these counterintuitive effects. Baseline characteristics, like optimism and perceived stress, should be considered in patients presenting for psychosocial treatments, like CBSM, and impact downstream immune regulation.

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CRediT authorship contribution statement

Emily A. Walsh: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Michael H. Antoni:** Funding acquisition, Conceptualization, Supervision, Writing – review & editing. **Paula J. Popok:** Writing – review & editing. **Patricia I. Moreno:** Writing – review & editing. **Frank J. Penedo:** Conceptualization, Project administration, Supervision, Writing – review & editing.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.genhosppsych.2022.10.012.

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