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ORIGINAL ARTICLE

Who benefits from an eHealth-based stress management intervention in advanced prostate cancer? Results from a randomized controlled trial

Roberto M. Benzo[1] | Patricia I. Moreno[2] | Blanca Noriega-Esquives[2] | Amy K. Otto[2] | Frank J. Penedo[1,3]

[1]Department of Psychology, University of Miami, Miami, Florida, USA

[2]Department of Public Health Sciences, University of Miami Miller School of Medicine, Miami, Florida, USA

[3]Department of Medicine, University of Miami Miller School of Medicine, Miami, Florida, USA

Correspondence
Frank J. Penedo, Department of Medicine, University of Miami Miller School of Medicine, 5665 Ponce de Leon Boulevard, Flipse Building, 5th Floor, Miami, FL 33146, USA.
Email: frank.penedo@miami.edu

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Abstract

Objective: Conduct a secondary analysis to examine the effects of a tablet-delivered, group-based cognitive-behavioral stress management (CBSM) intervention for reducing symptom burden among men with advanced prostate cancer (APC) and elevated baseline levels of symptom burden.

Methods: A total of 192 men with APC were randomized to either a CBSM or a health promotion condition and followed for one year. Six analytical samples were included in our study, each including participants who reported elevated levels of burden for the corresponding outcome at baseline. Outcomes included five domains of symptom-related quality of life (urinary incontinence $n = 98$; urinary irritation $n = 61$; bowel function $n = 43$; sexual function $n = 177$; and hormonal function $n = 149$) and depression ($n = 31$). Repeated measures mixed models were used to detect within- and between-group changes in outcomes.

Results: Regardless of condition, participants with elevated symptom burden or mild-to-severe depression showed short-term (6-month) improvements in urinary irritation, bowel function, hormonal function, and depression scores. Only participants in the CBSM condition showed short-term (6-month) improvements in urinary incontinence, and long-term (12-month) improvements in urinary irritation, bowel function, hormonal function, and depression scores.

Conclusions: Our findings suggest that targeting a web-based CBSM intervention to recipients most likely to benefit (elevated levels of symptom burden) can improve several domains of symptom-related quality of life and depressive symptoms in men with APC.

KEYWORDS
cognitive behavioral therapy, depression, erectile dysfunction, patient reported outcome measures, prostatic neoplasms, psycho-oncology, quality of life, telemedicine, urinary incontinence

1 | INTRODUCTION

Prostate cancer is the most frequently diagnosed cancer and the second leading cause of cancer death among men in the US.[1] Men with prostate cancer may experience symptoms such as difficulty passing urine, pain, and sexual dysfunction, which in turn may cause distress, anxiety, or depression, and ultimately impair their health-related quality of life (HRQOL).[2] Men with advanced prostate cancer (APC) have poorer prognosis, experience greater prostate-specific symptom burden, and poorer functional well-being than men with localized prostate cancer.[3] For example, the prevalence of depression is 1.5– to 2-fold higher among men with APC compared to localized disease.[4] Although several psychosocial interventions have been developed to reduce psychosocial and physical symptoms associated to prostate cancer, most have been tested in men with localized disease[2]; thus, evaluation of psychosocial interventions for individuals with APC remain limited.

Psychosocial interventions such as cognitive-behavioral stress management (CBSM) have been linked to improved emotional well-being, HRQOL, and sexual functioning outcomes in men with localized prostate cancer.[5,6] Cognitive-behavioral stress management combines aspects of cognitive-behavioral therapy (CBT; e.g., cognitive reframing, enhanced adaptive skills) and stress management skills (e.g., progressive muscle relaxation). Given the higher levels of psychosocial burden exhibited by men with APC compared to those with localized cancer, our group recently compared a 10-week web-based CBSM intervention adapted for men with APC to a 10-week health promotion (HP) control condition.[7] Regardless of condition, authors did not see evidence of an intervention effect and were unable to demonstrate a difference between groups in symptom-related quality of life and depression.[8]

Pre-intervention symptom burden has been shown to moderate the efficacy of psychosocial treatment for cancer patients. Schneider et al., found that pre-intervention distress significantly moderated intervention effects, reporting that the effects on anxiety and depression were often negligible when pre-intervention distress levels were low and pronounced when it was high.[9] Similarly, in a meta-analysis published by Heron-Speirs et al. reported that both studies recruiting patients with elevated baseline distress and those with an untreated control group produce higher effects.[10] Thus, we hypothesize that the lack of significant changes within groups were due to high baseline levels in HRQOL which likely diminished the opportunity for improvement (ceiling effect). We believe this may have also been true for certain prostate cancer-specific symptom burden domains (urinary, bowel, hormonal) as well as depression.

Via a subgroup secondary analysis of men experiencing pre-intervention elevated symptom burden, the present study was conducted to detect any intervention effects on symptom-related quality of life (QOL) and depression. Specifically, our study aimed to compare the effects of CBSM intervention versus HP program on symptom-related QOL domains (via EPIC-26) and depression among a subset of participants with mild-to-severe symptom burden. Based on our previous findings,[7] we hypothesized (1) regardless of condition, participants will report improvements in symptom burden at 6-month; and (2) only participants in the CBSM condition will report improvements in symptom burden at 12-month.

2 | METHODS

This study includes a series of secondary data analysis on subsamples of the analytical sample (n = 192) obtained from a previously conducted study.[7] In this study the authors examined the impact of CBSM and HP on various domains of symptom-related QOL life (urinary incontinence, urinary irritation, bowel function, sexual function, and hormonal function) and depression, among a subsample of participants who reported increased levels of symptom burden at baseline.

2.1 | Subjects

The study CONSORT diagram, details about recruitment, and descriptions of study conditions can be found in our previous publication which includes findings of our primary aims.[7] The eligibility criteria included men who were 50 years of age or older, fluent in English at the sixth grade level or higher, initially diagnosed with stage-III or -IV prostate cancer and had undergone androgen deprivation therapy (ADT). Men were excluded if they had undergone treatment for any other cancer in the previous five years, received inpatient psychiatric treatment for mental illness within the past six months, reported active substance or alcohol dependence, were diagnosed with an acute or chronic immune system condition, reported an anticipated life expectancy <12-month, or received a score <20 on the Mini Mental State Examination.[11]

2.2 | Procedures

Institutional review board approval was received prior to enrollment, and the protocol is available in more detail at ClinicalTrials.gov (NCT03149185).[7] All participants provided informed consent. Participants attended in-person visits at baseline (T1), 6- (T2), and 12-month (T3) post-baseline where they completed a battery of psychosocial assessments, and clinical information was obtained from participants' medical records. Participants were randomized (1:1) to either a CBSM or a HP condition.

2.3 | Study conditions

Both conditions were group-based, manualized, and delivered weekly over 10-week via a Health Insurance Portable Accountability Act - compliant web-based platform.[12] Participants received a workbook, a study tablet, and headphones prior to their first group session. All

participants accessed the weekly group sessions and study-related content on the tablet provided. Sessions were facilitated by masters- or doctoral-level therapists and recordings of online sessions were reviewed weekly with licensed clinical psychologists. During weekly sessions, participants had the opportunity to interact with group facilitators and fellow group members. Participants were asked to review the weekly didactic material and expert videos on the program's website, and those randomized to the CBSM condition, were also asked to practice the relaxation exercises. Men in CBSM did not have access to the HP intervention content or workbook and vice versa. Treatment attendance and attrition, and descriptions of study conditions, can be found in the original publication.[7]

The CBSM condition is a combination of cognitive-behavioral stress- and self-management skills with relaxation skills training aimed to improve health-related quality of life and reduce symptom burden delivered once a week over a 10-week period.

The HP condition is a combination of didactic health-related presentations of both general health and information specific to living with advanced prostate cancer, which was also delivered weekly over a 10-week period. The content in the HP condition did not include any stress- or self-management skills presented in the CBSM condition but rather didactic presentations of guidelines for nutrition, physical activity, treatment compliance, health information seeking, and other relevant topics. See Supplemental Table 1 for additional details of the content included in the CBSM and HP conditions.

2.4 | Measures

Age, body mass index (BMI), stage of disease (stage-III vs. stage-IV), and time since diagnosis were collected at baseline via medical chart review. Income, race, ethnicity, and presence of any comorbidities were collected at baseline via self-report. Comorbidities were combined into a weighted index score using the weighting scheme from the Charlson Comorbidity Index, where a higher score is indicative of poorer health status.[13]

Symptom-related QOL was measured using the 26-item Expanded Prostate Cancer Index Composite (EPIC-26) short-form version.[14] The EPIC-26 contains five symptom domains (urinary incontinence, urinary irritation, sexual, bowel, and hormonal), each is scored from 0 (worst) to 100 (best) and can be tracked over time to understand symptom burden, functional outcomes, and the impact of self-management strategies. EPIC-26 is a brief, valid and reliable subjective measure of health quality among prostate cancer patient.[14]

Depression was measured using the Patient Reported Outcome Measurement Information System (PROMIS)-Depression Item Bank computer adaptive test.[15] PROMIS assessments are T-scored so that a mean score of 50 with a standard deviation of 10 represents the average U.S. population score, and higher scores represent higher levels of depression. The measure has been well validated for use in cancer samples.[16,17]

2.5 | Sample Selection

This study included six sub-samples of participants with elevated levels of symptom-related QOL or depression. We used the previous literature to inform our pre-determined thresholds used to identify those with elevated burden,[18,19] so that we can further delineate the effects of each study condition on symptom-related QOL domains and depression levels individually. Five of the subsamples were determined by scoring from the EPIC-26, one sample for each of the five domains, and the remaining sample was derived from the PROMIS-Depression instrument. For each domain of the EPIC-26, we included only those participants who reported a mild-to-severe symptom burden risk, defined as having a score ≤80 at baseline. Our threshold was informed by a study conducted by Laviana et al. who translated the scores of EPIC-26 domains by probability of outcomes, showing that participants who scored ≤80 presented greater symptom burden in each domain, compared to those who score >80.[18] For example, at a score of 81–100 on urinary incontinence an estimated 93% of men reporting rarely or never leaking, compared to 6% at a score of 80-61. For this reason, we converted our EPIC-50 measure used in the original study,[20] to the EPIC-26 so that our selected threshold (domain score of ≤80) used to identify those with increase symptom burden was supported by previous literature.[14] For the depression analysis, we included only those who reported at least a mild level of depression, denoted as a PROMIS T-score ≥55.[19]

2.6 | Data Analysis

We chose this approach to detect within- and between-group changes in outcomes, given the statistical advantages of allowing for missing observations within-subject and for time to be treated as either categorical or continuous.[21] Two-level multilevel models were used to conduct analyses comparing the effects of CBSM and HP on EPIC-26 domain scores (urinary incontinence, urinary irritation, bowel function, sexual function, and hormonal function) and depression scores over time in Stata version 14.2 (StataCorp LLC). These models tested for between and within group differences in EPIC-26 domains and depression scores at, or between, each time point (T1-T3).

Analyses controlled for cancer-specific covariates, including stage of disease (stage-III vs. stage-IV), cancer treatment (surgery, radiation, chemotherapy, and ADT), and time since diagnosis. Men who received a radical retropubic prostatectomy did so prior to baseline. Treatment with radiation, chemotherapy, and/or ADT varied by individual and across time points. Therefore, the main effect of prostatectomy was a non-time-varying Level 2 covariate and main effects for radiation, chemotherapy, and ADT were included as time-varying Level 1 covariates. Analyses also controlled for key covariates that are known to influence health, including age, BMI, comorbidities, socioeconomic status (income), race, ethnicity, and time between baseline and intervention completion. The following

covariates were continuous and grand-mean centered to aid interpretation: age, years since diagnosis, BMI, Charlson Comorbidity Index, time from baseline to intervention completion.[13] Categorical variables included income (≥35k = 1, <35k = 0), race, metastasis, ADT, radiation, chemotherapy, prostatectomy. Final models included both a random intercept and slope for time at Level 1.

3 | RESULTS

A description of sociodemographic and medical-related information for the overall sample, and each analytical sample, are presented in Table 1. Descriptive statistics of outcomes (overall and by condition) and corresponding sample size at each timepoint can be found in Table 2.

3.1 | Intervention effects on EPIC domains

Table 3 shows the effects of CBSM and HP interventions on each symptom-related QOL domain and depression score.

3.1.1 | Urinary Incontinence

There was no Condition × Time interaction ($p = 0.4$) in urinary incontinence or between-group differences at any timepoint (T1: $p = 0.2$; T2: $p = 0.1$; T3: $p = 0.9$). However, urinary incontinence improved (increased) from baseline to 6-month for participants in the CBSM condition (see Figure 1A; $B = 7.58$, Standard Error (SE) = 3.59, $p = 0.035$).

3.1.2 | Urinary Irritation

No Condition × Time interaction ($p = 0.8$) was identified in urinary irritation or between-group differences at any timepoint (T1: $p = 0.9$; T2: $p = 0.9$; T3: $p = 0.6$). Urinary irritation, however, improved from baseline to 6-month for participants in both conditions (see Figure 1B; $B = 7.51$, SE = 2.28, $p = 0.023$ for CBSM; $B = 8.69$, SE = 3.22, $p = 0.007$ for HP). For the CBSM group, this improvement was maintained long-term, as evidenced by the significant improvement from baseline to 12 months ($B = 9.03$, SE = 4.46, $p = 0.043$).

3.1.3 | Bowel Function

There was no Condition × Time interaction ($p = 0.5$) in bowel function or between-group differences at any timepoint (T1: $p = 0.2$; T2: $p = 0.5$; T3: $p = 0.09$). Bowel function improved from baseline to 6-month for participants in both conditions (see Figure 1C; $B = 14.66$, SE = 4.87, $p = 0.003$ for CBSM; $B = 16.46$, SE = 3.39, $p < 0.001$ for HP). We observed a marginally significant decrease (impairment) in bowel function from 6- to 12-month among participants in the HP condition ($B = -8.16$, SE = 4.16, $p = 0.05$). Improvement in bowel function was maintained from baseline to 12-month in the CBSM group ($B = 14.66$, SE = 5.97, $p = 0.014$).

3.1.4 | Sexual Function

No Condition × Time interaction ($p = 0.5$) was identified in sexual function or between-group differences at 12-month (T3: $p = 0.4$). Participants in the HP condition reported higher levels of sexual function at baseline and 6-month compared to participants in the CBSM condition (see Figure 1D; $B = -5.73$, SE = 2.47, $p = 0.021$ at baseline; $B = -5.81$, SE = 2.74, $p = 0.034$ at 6-month). There were no changes in sexual function across time for participants in either condition.

3.1.5 | Hormonal Function

There was no Condition × Time interaction ($p > 0.9$) *in* hormonal function or between-group differences at any timepoint (T1: $p = 0.8$; T2: $p > 0.9$; T3: $p > 0.9$). Hormonal function increased (improved) from baseline to 6-month in both conditions (see Figure 1E; $B = 5.41$, SE = 2.35, $p = 0.021$, for CBSM; $B = 4.55$, SE = 2.04, $p = 0.042$ for HP). Improvement in hormonal function was maintained from baseline to 12 months for participants in both conditions ($B = 7.02$, SE = 2.48, $p = 0.005$ for CBSM; $B = 6.40$, SE = 2.35, $p = 0.007$ for HP).

3.2 | Intervention effects on depression

3.2.1 | Depression

There was no Condition × Time interaction ($p = 0.2$) in depression scores or between-group differences at 6- or 12-month (T2: $p = 0.8$; T3: $p = 0.8$). Participants in the CBSM condition reported higher levels of depression at baseline, compared to participants in the HP condition ($B = 3.62$, SE = 1.71, $p = 0.035$). Depression scores decreased (improved) from baseline to 6-month in both conditions (see Figure 1F; $B = -8.76$, SE = 1.67, $p < 0.001$ for CBSM; $B = -4.61$, SE = 1.87, $p = 0.014$ for HP); however, only those in the CBSM condition showed significantly lower scores at 12-month compared to baseline ($B = -7.05$, SE = 2.47, $p < 0.001$).

4 | DISCUSSION

The present study compared the within- and between-group effects of a 10-week web-based CBSM intervention with a HP control condition in men with APC.[7] This work extends the literature by evaluating the effects of both a CBSM and a HP intervention among a subsample of prostate cancer survivors with elevated burden in

TABLE 1 Sample characteristics for original dataset and six analytical samples

		Urinary incontinence		Urinary irritation		Bowel function		Sexual function		Hormonal function		Depression	
	Overall (n = 192)	CBSM (n = 47)	HP (n = 51)	CBSM (n = 28)	HP (n = 33)	CBSM (n = 16)	HP (n = 27)	CBSM (n = 89)	HP (n = 88)	CBSM (n = 78)	HP (n = 71)	CBSM (n = 16)	HP (n = 15)
Age, mean (SD)	68.84 (8.87)	67.04 (7.55)	69.08 (8.79)	68.75 (9.57)	69.03 (8.71)	62.81 (5.49)	67.41 (7.68)	68.71 (8.64)	68.94 (9.42)	68.04 (8.71)	68.38 (9.27)	65.00 (7.79)	68.93 (9.20)
BMI (SD)	28.82 (5.09)	29.17 (5.67)	29.42 (5.18)	30.06 (6.33)	29.50 (6.10)	29.87 (5.67)	28.93 (5.52)	29.37 (5.38)	28.62 (4.94)	29.03 (4.98)	29.00 (4.81)	29.41 (5.70)	29.70 (5.23)
Family annual income ≥ $35,000, n (%)	125 (65.1)	34 (72.3)	32 (62.7)	20 (71.4)	19 (57.6)	8 (50)	18 (66.7)	65 (73.0)	56 (63.6)	51 (65.4)	51 (71.8)	13 (81.2)	12 (80.0)
Race: White, n (%)	113 (58.9)	28 (59.6)	32 (62.7)	22 (78.6)	13 (39.4)	6 (37.5)	20 (74.1)	54 (60.7)	54 (61.4)	37 (47.4)	48 (67.6)	12 (75.0)	11 (73.3)
Metastatic (stage IV), n (%)	81 (42.2)	17 (36.2)	14 (27.5)	15 (53.6)	13 (39.4)	6 (37.5)	13 (48.1)	34 (38.2)	39 (44.3)	30 (38.5)	36 (50.7)	6 (37.5)	7 (46.7)
# Sessions completed, mean (SD)	7.69 (2.97)	7.21 (3.43)	8.16 (2.63)	7.71 (3.39)	8.06 (2.62)	7.75 (2.91)	7.52 (3.32)	7.47 (3.14)	7.70 (2.93)	7.45 (3.22)	8.03 (2.64)	7.06 (3.75)	7.67 (3.18)
ADT 12-month prior to baseline, n (%)	131 (68.2)	29 (61.7)	40 (78.4)	16 (57.1)	24 (72.7)	11 (68.8)	23 (85.2)	57 (64.0)	67 (76.1)	46 (59.0)	58 (81.7)	11 (68.8)	14 (93.3)
Radiation therapy 6-month prior to baseline, n (%)	39 (20.3)	11 (23.4)	10 (19.6)	8 (28.6)	10 (30.3)	4 (25)	8 (29.6)	19 (21.3)	19 (21.6)	17 (21.8)	17 (23.9)	‘2 (12.5)	4 (26.7)
Chemotherapy 6-month prior to baseline, n (%)	9 (4.7)	2 (4.3)	2 (3.9)	1 (3.6)	2 (6.1)	1 (6.3)	4 (14.8)	3 (3.4)	6 (6.8)	3 (3.8)	5 (7.0)	1 (6.3)	1 (6.7)
Prostatectomy 6-month prior to baseline, n (%)	98 (51.0)	30 (63.8)	36 (70.6)	13 (46.4)	17 (51.5)	6 (37.5)	13 (48.1)	44 (49.4)	49 (55.7)	33 (42.3)	43 (60.6)	9 (56.3)	10 (66.7)
Years since diagnosis, mean (SD)	4.70 (5.28)	3.91 (4.08)	5.70 (6.09)	4.48 (6.05)	4.82 (4.83)	2.45 (1.63)	4.70 (5.07)	4.61 (5.24)	5.29 (5.59)	3.83 (4.41)	4.87 (4.99)	3.76 (3.47)	5.78 (5.26)
Charlson comorbidity index, mean (SD)	1.39 (1.38)	1.63 (1.42)	1.42 (1.25)	1.67 (1.52)	1.47 (1.39)	1.94 (1.48)	1.81 (1.67)	1.39 (1.25)	1.41 (1.52)	1.37 (1.29)	1.42 (1.50)	1.56 (1.50)	1.87 (2.00)
Months from baseline to group completion, mean (SD)	3.35 (1.13)	3.34 (1.06)	3.49 (1.16)	3.38 (1.30)	3.18 (1.04)	3.33 (1.11)	3.48 (1.19)	3.28 (1.06)	3.39 (1.20)	3.31 (1.13)	3.37 (1.22)	3.93 (1.28)	3.47 (1.51)

Note: There were no statistically significant differences across groups on baseline sociodemographic or medical covariates. Groupings by symptom burden are based on number of participants with ≤ 80 on EPIC or ≥ 55 on PROMIS Depression.

Abbreviations: ADT, androgen deprivation therapy; CBSM, Cognitive Behavioral Stress Management; EPIC, Expanded Prostate Cancer Index Composite; HP, Health Promotion; PROMIS, Patient Reported Outcome Measurement Information System; SD, standard deviation.

TABLE 2 Descriptive Statistics for Domains of EPIC-26 and Depression at Baseline, 6 and 12 months

	Baseline			6 months			12 months		
	Overall	**CBSM**	**HP**	**Overall**	**CBSM**	**HP**	**Overall**	**CBSM**	**HP**
EPIC-26	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Urinary incontinence	53.14 (21.17)	55.90 (20.50)	50.59 (21.66)	59.54 (26.42)	62.86 (26.88)	56.52 (25.93)	54.78 (26.42)	55.96 (24.66)	53.69 (28.22)
Sample size, n	98	47	51	84	40	44	77	37	40
Urinary irritation	64.75 (11.30)	64.73 (10.52)	64.77 (12.08)	73.41 (11.78)	71.88 (14.39)	74.77 (8.92)	73.91 (17.54)	75.85 (18.23)	72.14 (17.29)
Sample size, n	61	28	33	51	24	27	46	22	24
Bowel function	65.89 (13.49)	68.49 (9.00)	64.35 (15.52)	80.24 (18.31)	78.82 (21.06)	80.98 (17.17)	78.60 (19.09)	81.25 (21.58)	76.93 (17.76)
Sample size, n	43	16	27	35	12	23	31	12	19
Sexual function	18.38 (17.24)	15.39 (14.21)	21.41 (19.45)	16.51 (14.41)	14.28 (14.04)	18.91 (14.51)	17.08 (17.05)	16.30 (16.70)	17.97 (17.53)
Sample size, n	177	89	88	145	75	70	134	71	63
Hormonal function	62.42 (16.03)	61.83 (17.22)	62.96 (14.95)	67.73 (17.15)	68.15 (17.44)	67.73 (17.01)	70.81 (16.14)	70.70 (15.93)	70.90 (16.47)
Sample size, n	149	71	78	131	62	69	118	57	61
PROMIS	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Depression	59.51 (4.71)	60.84 (5.23)	58.08 (3.74)	53.46 (8.63)	52.92 (9.82)	54.21 (7.08)	53.71 (8.47)	55.74 (9.50)	49.94 (4.58)
Sample size, n	31	16	15	24	14	10	20	13	7

Abbreviations: CBSM, Cognitive Behavioral Stress Management; EPIC, Expanded Prostate Cancer Index Composite; HP, Health Promotion; PROMIS, Patient Reported Outcome Measurement Information System; SD, standard deviation.

TABLE 3 Effect of intervention and covariates on EPIC-26 domains and PROMIS depression in two-level mixed models

Instrument	*EPIC-26*															*PROMIS*		
	Urinary incontinence			*Urinary irritation*			*Bowel*			*Sexual*			*Hormonal*			*Depression*		
Domain	*Coef. (SE)*	*Z*	*p*	*Coef. (SE)*	*Z*	*p*	*Coef. (SE)*	*Z*	*p*	*Coef. (SE)*	*Z*	*p*	*Coef. (SE)*	*Z*	*p*	*Coef. (SE)*	*Z*	*p*
Intercept	60.71 (8.39)	7.24	0.000	63.27 (5.69)	5.69	0.000	90.53 (7.33)	12.36	0.000	26.74 (4.69)	5.70	0.000	73.11 (4.71)	15.51	0.000	50.5 (3.90)	12.94	0.000
Intervention																		
CBSM versus HP	6.47 (4.75)	1.36	0.173	0.50 (2.95)	0.17	0.865	5.17 (4.09)	1.26	0.206	−5.72 (2.47)	−2.31	0.021	−0.70 (2.80)	−0.25	0.803	3.62 (1.72)	2.11	0.035
Time																		
6 months versus Baseline	6.22 (3.25)	1.91	0.056	8.68 (3.22)	2.69	0.007	16.46 (3.39)	4.86	0.000	−0.97 (1.70)	−0.57	0.569	4.55 (2.24)	2.04	0.042	−4.61 (1.87)	−2.46	0.014
12 months versus Baseline	6.75 (3.88)	1.74	0.082	7.02 (4.25)	1.65	0.098	8.30 (4.68)	1.77	0.076	−3.01 (2.10)	−1.43	0.152	6.40 (2.35)	2.72	0.007	−4.57 (2.92)	−1.56	0.118
Intervention*Time																		
CBSM																		
6 months versus Baseline	7.58 (3.59)	2.11	0.035	7.51 (3.30)	2.28	0.023	14.66 (4.87)	3.01	0.003	−1.05 (1.70)	−0.62	0.537	5.41 (2.35)	2.30	0.021	−8.76 (1.67)	−5.25	0.000
12 months versus 6 months.	−6.66 (3.85)	−1.73	0.084	1.52 (3.70)	0.41	0.056	0.00 (4.97)	0.00	1.00	1.02 (1.81)	0.56	0.572	1.61 (2.52)	0.64	0.524	1.71 (1.81)	0.95	0.345
HP																		
6 months versus Baseline	6.22 (3.25)	1.91	0.056	8.69 (3.22)	2.69	0.007	16.46 (3.39)	4.86	0.000	−0.97 (1.70)	−0.57	0.569	4.55 (2.24)	2.04	0.042	−4.61 (1.87)	−2.46	0.014
12 months versus 6 months.	0.53 (3.57)	0.15	0.882	−1.67 (3.59)	−0.46	0.642	−8.16 (4.16)	−1.96	0.050	−2.04 (1.90)	−1.07	0.283	1.85 (2.42)	0.76	0.445	0.04 (2.26)	0.02	0.987
CBSM versus HP																		
at Baseline	6.46 (4.75)	1.36	0.173	0.50 (2.95)	0.17	0.865	5.17 (4.09)	1.26	0.206	−5.73 (2.47)	−2.31	0.021	−0.70 (2.80)	−0.25	0.803	3.62 (1.71)	2.11	0.035
at 6 months.	7.82 (5.21)	1.50	0.133	−0.68 (3.75)	−0.18	0.856	3.37 (5.30)	0.64	0.525	−5.81 (2.74)	−2.12	0.034	0.16 (2.96)	0.05	0.957	−0.53 (2.61)	−0.20	0.839
at 12 months.	−0.03 (0.03)	−1.00	0.316	2.51 (5.48)	0.46	0.647	11.53 (6.82)	1.69	0.091	−2.74 (3.20)	−0.86	0.391	−0.08 (3.10)	−0.03	0.979	1.14 (3.81)	0.30	0.765
Age	−0.43 (0.28)	−1.54	0.123	0.00 (0.14)	0.00	0.997	0.73 (0.23)	3.13	0.002	−0.13 (0.14)	−0.92	0.357	0.47 (0.14)	3.41	0.001	−0.52 (0.14)	−3.63	0.000
BMI	−0.03 (0.42)	−0.08	0.937	0.14 (0.22)	0.64	0.524	0.03 (0.37)	0.09	0.930	0.02 (0.24)	0.08	0.938	−0.37 (0.23)	−1.62	0.105	0.69 (0.21)	3.25	0.001
Income (≥35k vs. <35k)	1.18 (5.78)	0.20	0.838	−4.36 (3.73)	−1.17	0.242	−4.20 (4.18)	−1.01	0.315	1.85 (2.98)	0.62	0.534	−5.19 (2.95)	−1.76	0.078	−4.05 (3.55)	−1.14	0.254
Race (white vs. Black/Other)	2.63 (4.87)	0.54	0.590	0.77 (3.10)	0.25	0.803	5.87 (4.17)	1.41	0.159	−5.54 (2.64)	−2.10	0.036	−0.60 (2.57)	−0.23	0.816	8.53 (2.88)	2.96	0.003
Metastasis (yes vs. no)	−3.58 (4.69)	−0.76	0.445	7.56 (2.60)	2.90	0.004	−2.73 (4.04)	−0.68	0.500	−2.63 (2.58)	−1.02	0.308	−0.15 (2.50)	−0.06	0.951	−0.50 (1.78)	−0.28	0.779
ADT (yes vs. no)	4.39 (3.97)	1.11	0.269	3.98 (2.37)	1.68	0.093	−6.45 (2.87)	−2.25	0.025	−0.11 (2.07)	−0.05	0.956	−0.81 (2.01)	−0.40	0.688	−0.45 (1.71)	−0.26	0.791
Radiation (yes vs. no)	5.11 (3.21)	1.59	0.112	0.19 (2.53)	0.07	0.941	−1.37 (3.59)	−0.39	0.703	−0.90 (1.64)	−0.55	0.582	−3.74 (2.03)	−1.84	0.065	−0.90 (1.54)	−0.58	0.560
Chemotherapy (yes vs. no)	−4.77 (10.22)	−0.47	0.641	−4.61 (6.92)	−0.67	0.505	11.67 (5.89)	1.98	0.048	1.80 (5.21)	0.35	0.730	8.05 (4.75)	1.70	0.090	−6.87 (3.04)	−2.26	0.024
Prostatectomy (yes vs. no)	−25.44 (5.56)	−4.58	0.000	5.76 (3.01)	1.92	0.505	−11.32 (4.19)	−2.70	0.007	−4.66 (2.93)	−1.59	0.112	4.63 (2.92)	1.59	0.113	2.20 (2.33)	0.94	0.346
Years since diagnosis	0.58 (0.47)	1.22	0.222	−0.42 (0.35)	−1.22	0.223	0.94 (0.42)	2.23	0.026	0.02 (0.26)	0.08	0.937	−0.02 (0.28)	−0.07	0.947	0.42 (0.20)	2.08	0.037
Charlson comorbidities index	−2.49 (1.72)	−1.45	0.146	−0.64 (1.02)	−0.62	0.533	−1.93 (1.10)	−1.76	0.079	−0.87 (0.88)	−0.99	0.324	−1.98 (0.83)	−2.39	0.017	2.68 (0.70)	3.80	0.000
Time from baseline to intervention completion	−0.10 (1.86)	−0.06	0.956	−1.59 (1.26)	−1.27	0.205	−3.40 (1.53)	−2.22	0.026	−0.13 (1.11)	−0.12	0.908	−2.41 (1.05)	−2.31	0.021	0.17 (0.61)	0.29	0.775

Note: Reference categories in binary variables are listed second.

Abbreviations: ADT, androgen deprivation therapy; BMI, body mass index; CBSM, Cognitive Behavioral Stress Management; Coef, coefficient; EPIC, Expanded Prostate Cancer Index Composite; HP, Health Promotion; PROMIS, Patient Reported Outcome Measurement Information System; SD, standard deviation; SE, standard error.

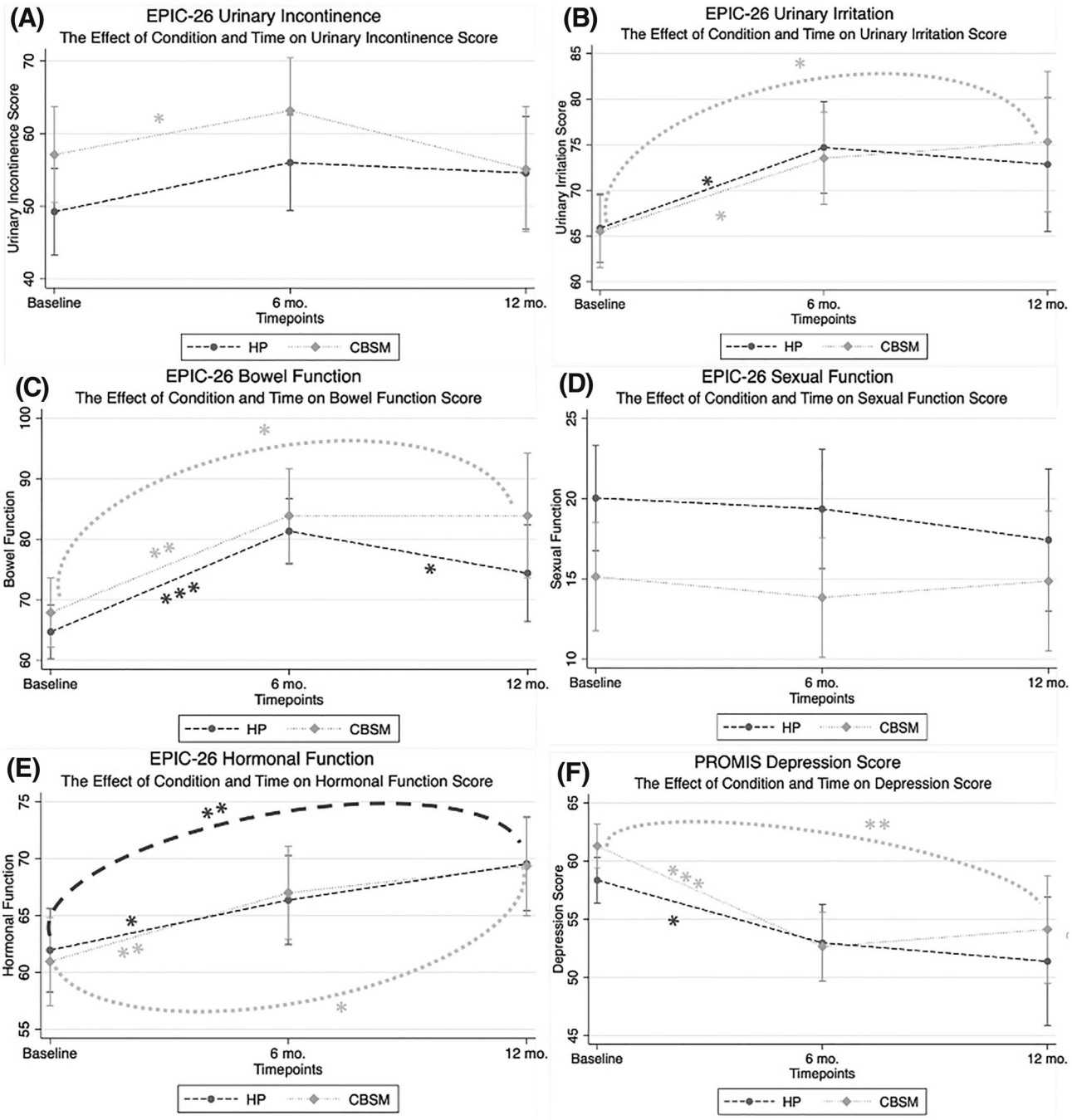

FIGURE 1 Groupings by symptom burden are based on the number of participants with 80 on the EPIC-26 or 55 on the PROMIS Depression measures. A higher score on the EPIC-26 domains is indicative of less symptom burden, whereas a higher score on the PROMIS Depression score is indicative of greater depressive symptoms. Measures were collected at three time points: baseline, 6-month, and 12 months. CBSM, Cognitive Behavioral Stress Management; EPIC, Expanded Prostate Cancer Index Composite; HP, Health Promotion; PROMIS, Patient Reported Outcome Measurement Information System

symptom-related QOL and depression. In contrast to the previously published findings, we found that both CBSM and HP conditions led to significant improvements over time in various domains of symptom-related quality of life and depression scores, but only among men entering the study with greater symptom burden and depressive symptoms.

Our findings showed that both interventions resulted in significant short-term (6-month) improvements. To improve our interpretation of findings we compared changes in each domain to established minimally important differences for each domain in the EPIC-26.[22] Skolarus et al. applied two established methods to identify a range minimal important differences for each domain of the EPIC-26: 6–9 units for urinary incontinence; 5–7 units for urinary irritation; 4–6 units for bowel function, 10–12 units for sexual function; and 4–6 units for hormonal function.[22] Both conditions resulted in improvements from baseline to 6-month that met the threshold for minimally important differences in

urinary irritation (7.15-units in CBSM; 10.00-units in HP), bowel function (10.33-units in CBSM; 16.63-units in HP), and hormonal function (6.32-units in CBSM; 4.7-units in HP).[22] These findings suggest that both conditions can produce specific symptom burden improvements among advanced prostate cancer survivors (specifically, in urinary bother, bowel function, and hormonal function). It is possible that improvements in both groups were due to similarities in intervention content across conditions. For example, both groups received information to enhance understanding of advanced prostate cancer, including information on managing hormone-related side effects, accessing health information, and the importance of follow-up care. Future research using a Multiphase Optimization Strategy approach, could be used to better delineate the effects of the components included in each intervention.[23]

Only participants in the CBSM condition improved in urinary incontinence from baseline to 6-month (6.96-units), which met the threshold for a minimally important difference.[22] This finding suggests that CBSM-based interventions may lead to psychological benefits that positively impact urinary incontinence, that cannot be improved by promotion of health behaviors alone. There are numerous studies that have shown psychological factors such as low self-esteem, depression, anger, and stress often occur in individuals with urinary incontinence.[24] However, it is unknown if these psychological factors contribute to the occurrence of urinary incontinence or even play a causative role. More studies that control for changes in health behaviors are needed to elucidate the mechanisms that drive differential improvements in symptom burden among advanced prostate cancer survivors.

Regardless of condition, participants reported significant improvement in hormonal function from baseline to 12-month (7.96-units HP; 8.87-units CBSM); whereas only those in the CBSM condition reported improvements in urinary bother and bowel function from baseline to 12-month. There are a couple of hypotheses that could explain why we observed improvements over time in both conditions. First, we believe that the "attention" provided to participants (90 min in CBSM and 60 min in HP condition) by the study staff could have played a role in the improvement of symptoms over time in both conditions. Second, participation bias (e.g., participant's desire to reduce their stress) may also in part explain why individuals in both conditions improved outcomes. Lastly, we also hypothesize that improvement in hormonal function across conditions could be attributed to overlapping content presented (e.g., education component, attention, social support). On the other hand, long-term improvements in urinary irritation (11.12-units) and bowel function (12.76-units) in the CBSM condition could be attributed to the direct effects that CBT or relaxation related skills have on these domains. This is consistent with previous work that shows CBT as a possible method for reducing urinary incontinence among women,[25] and a review that concluded CBT as an effective therapy in alleviating the physical and psychological symptoms of irritable bowel syndrome such as abdominal pain, bloating, and altered bowel habits.[26] More research is needed to elucidate and disentangle the effects of CBSM interventions on symptom-related quality of life among advanced prostate cancer survivors.

Our findings showed that independent of condition, participants exhibited significant reductions in depression scores from baseline to 6-month (−7.9-units CBSM; −3.87-units HP); however, only those in the CBSM condition showed long-term (12-month) reductions in depression (−5.1-units). This finding contrasts those published in a review by Parahoo et al., who concluded that there is no clear evidence to suggest that psychosocial interventions are associated with improvements in depression among men with prostate cancer, mainly due to very low-quality evidence available.[2] On the other hand, authors found that individual-based interventions significantly reduced depression levels compared to control groups.[2] We believe these findings are of significance given that a T-score of 3-4 points is a reasonable minimally important difference for PROMIS depression scales.[27] Thus, our data suggest that either a lifestyle or psychosocial intervention can lead to clinically significant reductions in depression at short-term (6-month), but that only CBSM may produce longer-lasting effects (12-month). Again, the short-term improvements in depression among all participants could have been due to the similarities in content of each condition (e.g., disease-related education, contact with a support group). However, only participants in CBSM showed long-lasting improvements, which is likely due to the acquisition of cognitive behavioral stress and self-management skills along with relaxation skills training.[28]

4.1 | Clinical implications

Aligned with previous publications,[9,10,18] our findings support the assessment of health-related quality of life (e.g., EPIC-26 and depression) in clinical practice to identify patients with elevated levels of cancer-specific symptom burden, placing them at risk for negative health outcomes. Cancer survivors with a high symptom burden may benefit from referrals to cancer support services (e.g., psychiatry, support groups, social worker) to identify strategies tailored to reduce symptoms and improve their quality of life. To overcome the time-constrained clinical environment, electronic health record (EHR) integrated assessments of patient reported outcomes could improve value-based care, minimize provider burden, and maximize the use of services offered at various cancer centers. One example of this approach implemented at the University of Miami, called My Wellness Check (MWC), is an EHR-integrated symptom and needs screening (symptoms, barriers to care, and nutritional needs).[29] My Wellness Check enables a referral system to cancer support services when unmet needs are identified. The authors reported MWC is an acceptable and feasible approach for assessing patients' unmet needs and triaging them to appropriate cancer support services.[29] More research focused on implementation of health-related quality of life assessments in clinical settings to identify patients who could benefit from symptom management interventions is warranted.

4.2 | Study limitations

There are several strengths of this study. First, we tried to overcome the problem of ceiling effects in our prior work by reanalyzing the data using subsamples of advanced prostate cancer survivors who showed greater levels of symptom burden and depression. This approach allowed us to further compare the effects of intervention type on prostate cancer specific symptom burden and depression. Second, we compared our findings with minimally important differences published in the literature, which allowed us to identify clinically meaningful changes. There are also several limitations to note. First, as a secondary analysis focusing on subsamples with elevated symptom burden greatly reduced our sample size and statistical power to detect differences. Screening participants to include only those with elevated pre-intervention levels of symptom burden may improve effectiveness of psychosocial interventions. Second, in contrast to the stress management skills self-efficacy measure included in the original study, there was no health promotion skills self-efficacy measure. Thus, limiting our ability to understand what skills participants developed in the HP condition, and what effect they may have had on the outcomes. Third, the control HP condition group meetings were 30-min shorter in duration compared to the CBSM, which could contribute to differential benefits in outcomes. Lastly, while our results report the effectiveness of the intervention, we do not yet fully understand the mechanisms and health benefits associated with this intervention. Future studies should consider including a semi-structured interview with a subgroup of participants to identify other benefits that were not measured (e.g., hope, resilience, etc.)

5 | CONCLUSIONS

This study is unique in that we explored the effects of a psychosocial intervention among men with APC who reported elevated pre-intervention levels of symptom burden, and the pre-determined threshold of burden was guided by scientific literature. Our findings suggest that targeting a web-based CBSM intervention to men with APC and elevated symptom burden at baseline, can lead to improvements in symptom-related QOL and depression. Health promotion interventions also led to health-related benefits among men with APC; however, more research is needed to elucidate the individual effects of HP and CBSM interventions on symptom burden in men with APC.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

The data are currently used for other studies and manuscript development. The data that support the study may be available upon request with permission from the researchers who collected the data.

ORCID

Roberto M. Benzo https://orcid.org/0000-0001-8634-6472

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