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Prostate Cancer

A Comprehensive 6-mo Prostate Cancer Patient Empowerment Program Decreases Psychological Distress Among Men Undergoing Curative Prostate Cancer Treatment: A Randomized Clinical Trial

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Abstract

Background: Although survival rates for newly diagnosed prostate cancer patients are very high, most of them will likely suffer significant treatment-related side effects, depression, or anxiety, affecting their quality of life.
Objective: The aim of this study was to examine the effects of a 6-mo online home-based physical, mental, and social support intervention, the Prostate Cancer Patient Empowerment Program (PC-PEP), on preventing psychological distress among men undergoing curative prostate cancer treatment.
Design, setting, and participants: In a crossover randomized clinical trial of 128 men aged 50–82 yr scheduled for curative prostate cancer surgery or radiotherapy (± hormone treatment), 66 received the 6-mo PC-PEP intervention and 62 were randomized to a waitlist-control arm and received the standard of care for 6 mo, and then PC-PEP to the end of the year. The PC-PEP intervention consisted of daily e-mails with video instructions providing education, patient activation, and empowerment on healthy living including physical and mental health, dietary recommendations, social support, physical and pelvic floor fitness, stress reduction using a biofeedback device, social connection and intimacy, and social support.
Outcome measurements and statistical analysis: The primary outcome was nonspecific psychological distress (clinical cutoff $\geq$20) measured at baseline, and at 6 and 12 mo using the Kessler Psychological Distress Scale (K10).
Results and limitations: At 6 mo, patients in the waitlist-control group had 3.59 (95% confidence interval: 1.12–11.51) times higher odds for nonspecific psychological distress and need for psychological treatment than men who received the PC-PEP intervention.

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At 12 mo, the wait-list control group that received the intervention at 6 mo had higher psychological distress than the early group.
Conclusions: PC-PEP delivered early following diagnosis significantly prevented the burden of psychological distress in men undergoing curative prostate cancer treatment compared with standard of care, or late (6 mo later) intervention.
Patient summary: In this report, we looked at the effectiveness of a program (Prostate Cancer Patient Empowerment Program: PC-PEP) developed with patients' engagement on the mental distress of patients awaiting curative treatment for their prostate cancer. The PC-PEP program lasted for 6 mo, and it prescribed, described, and demonstrated daily aerobic and strength training, kegels (pelvic floor training to help with urinary and sexual function), dietary changes that have been shown to be helpful in the prevention of prostate cancer and prostate cancer progression, stress reduction using a biofeedback device, as well as social and emotional support. All patients in the PC-PEP program were invited to a monthly video conference with the leads of the program who appeared in the 6 mo of daily videos prescribing the activities the patients were asked to watch and follow. The leads were a prostate cancer oncologist and a scientist in prostate cancer quality of life research. Half of the patients in this study received PC-PEP daily for the first 6 mo and were re-assessed at the end of the year. The other half received standard of care for 6 month and then received the intervention to the end of the year. The results of the study show that, at 6 mo, this intervention was effective at reducing the mental distress that accompanies a prostate cancer diagnosis and treatment compared with the standard of care. Mental distress was significantly reduced when the intervention was received early, compared with that received late (6 mo after scheduled curative treatment). We conclude that multi-faceted patient education and empowerment programming of this kind that is developed with patient engagement from the start is crucial to the care of patients diagnosed with prostate cancer and should be implemented in the standard of care. While treatment for prostate cancer is highly successful, side effects that accompany most treatments significantly affect the quality of life of patients. Here, we describe PC-PEP, a patient education and activation program that is cost effective, highly enforced by patients, and successful at reducing the impact of prostate cancer active treatment–related side effects on their psychological state. To learn more about this project, please visit www.pcpep.org. The program is now being tested in a phase 4 implementation trial throughout Canada and internationally (New Zealand), and is being expanded and tested for other types of cancer.

1. Introduction

In 2020, worldwide, there were an estimated 1.4 million newly diagnosed cases of prostate cancer (7% of all cancers) and 375000 deaths [1]. Unlike most forms of cancer, however, survival rates for newly diagnosed cases of prostate cancer are very high [2]. Yet 90% of these patients will likely suffer significant treatment-related side effects, including urinary problems, erectile dysfunction, feeling isolated, and many others, which can profoundly affect their quality of life [2–5]. A recent meta-analysis (n = 655 149) found that men with a lifetime history of prostate cancer were almost twice more likely to experience significant depression, anxiety, or both (17%) than same-age males who never had a prostate cancer diagnosis (9%) [6]. In a recent analysis from Denmark (n = 54 766), 18 yr after diagnosis, men with a history of prostate cancer diagnosis had higher hazard ratios for depression than men who never had prostate cancer, with the highest difference found in the first 2 yr after diagnosis [7]. Prostate cancer survivors with co-occurring depression have low adherence to active forms of treatment and higher health care utilization compared with men treated for prostate cancer without co-occurring depression [8].

Yet there is a paucity of randomized clinical trials assessing interventions aimed at reducing mental distress in prostate cancer patients. To our knowledge, few comprehensive interventions exist to fully address the side effects and survivorship needs that prostate cancer patients have, and most are limited in scope with regard to which of these aspects they address [9,10]. The Prostate Cancer Patient Empowerment Program (PC-PEP) is a home-based comprehensive intervention aimed at fully addressing the educational, physical, and psychosocial needs of prostate cancer patients before, during, and after treatment, with the primary objective of improving their mental health [11]. A 28-d pilot study assessed PC-PEP's feasibility and safety, and demonstrated mental and physical health improvements, and high program compliance rates [11]. However, the pilot did not have a control group, included many long-term survivors, and was of short duration, bringing into question the program's effectiveness in helping patients maintain these health improvements long term. To address these concerns, we expanded PC-PEP into a

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6-mo format and tested its effectiveness in a crossover randomized clinical trial. The trial's entrance point was right after scheduling of curative surgery or radiotherapy (± hormone treatment). The treatment group received the PC-PEP intervention for the first 6 mo and the waitlist group for the second 6 mo of the trial. We hypothesized that a significantly lower percentage of men scheduled for curative prostate cancer treatment who received the PC-PEP intervention would screen positive for nonspecific psychological distress and need for clinical treatment at 6 mo compared with men in the usual care (waitlist control). Secondary analyses were conducted to determine whether the proportion of distress for men who received the intervention at baseline differed from men who received it at 6 mo. Exploratory analyses further examined the patterns of mean sum score differences for psychological distress and its subscales (depression and anxiety).

2. Patients and methods

In this single-site, university, tertiary care, crossover randomized clinical trial, 171 men interested in participating in the study were assessed for eligibility following referral by their urologist or radiation oncologist, or self-referral from poster advertisements provided to all major oncology clinics throughout Nova Scotia, Canada. All patients had biopsy-proven prostate adenocarcinoma and were recruited from December 2019 to January 2021. The study protocol is attached in the Supplementary material. The inclusion criteria were the following: adult men scheduled for potentially curative prostate cancer treatment with either radical prostatectomy (robotic assisted or laparoscopic/open) or primary or salvage radiation therapy (external beam or brachytherapy) ± hormone therapy; having primary treatment completed within 6 mo after trial randomization; deemed safe to participate in a low to moderate exercise program; being able to read English; willing to travel to Halifax, Nova Scotia, at baseline, 6 mo, and 12 mo for in-person physical assessments; and having access to daily e-mail and Internet. Interested participants signed an institutional Nova Scotia Health Authority–approved (1024822) protocol-specific informed consent form (ClinicalTrials.gov NCT03660085).

The study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline (Supplementary material). Of the 171 patients assessed for eligibility, 140 were randomized, one withdrew consent immediately, and 11 did not receive curative treatment within 6 mo and were excluded (Fig. 1). Patients were randomized (1:1) to either the PC-PEP intervention or the control waitlist (standard of care) for the first 6 mo. A computer-generated fixed block randomization intervention allocation scheme described by Zelen [12] was used to balance the presence or absence of clinical mental distress (Kessler Psychological Distress Scale [K10]; scores $\geq$20 or <20, respectively), hormone therapy status, and type of curative treatment (surgery, radiotherapy, or salvage radiotherapy after prostatectomy). The randomization allocation table was kept in a password-protected Excel file and was available only to the principal investigator (PI) who was not involved in the consent or assessments process. Patients, clinicians, and research staff were blinded to the randomization process. After the patient completed all prerandomization assessments, the PI assigned the patient to either the intervention or the control group based on the table of the randomization allocation sequence (Supplementary material). Of the 128 eligible men who completed the trial, 66 were randomized to PC-PEP and 62 to waitlist control. At 6 mo, the waitlist control received the PC-PEP intervention, while the patients in the intervention group continued to have access to the PC-PEP materials and live online monthly video conferences. All patients completed a health-related quality of life survey online at baseline, 6 mo, and 12 mo, which included assessment of the primary outcome and prognostic covariates. Biometric data were measured during in-person assessments, while medical chart review was obtained at the end of the trial (stage of cancer at randomization, prescribed hormone therapy, treatment modality, and absence of cancer recurrence at 6 and 12 mo after randomization).

2.1. Exposure

Details of the PC-PEP intervention are described in the study protocol (Supplementary material) and at PCPEP.org [11]. Briefly, participants received a daily email for 6 mo containing a 3–5-min video (from coauthors G.I. and R.D.H.R.), which provided education, encouragement, and prescribed physical, mental, and social activities for that day, and additional video links demonstrating each component, patterned into a weekly schedule. Men were encouraged to exercise daily (with resistance strength 2 d/wk using provided elastic exercise bands), engage in pelvic floor exercises three times daily (facilitated by optional text alerts), and engage in a relaxation technique daily using a stress reduction biofeedback device (HeartMath) [13,14] device. The strength and pelvic floor muscle training routines advanced in difficulty over 6 mo. Strength routines were customized based on patients' fitness level. Healthy diet (high on fruits and vegetables), healthy habit formation (eg, sleep hygiene and vitamin D intake), intimacy and sexuality education addressing erectile dysfunction, communication techniques, and relationship recommendations were provided through the daily videos. Men were provided strategies for increased social support and were encouraged to connect often and more deeply with their loved ones. Optional social support included calling two coparticipants weekly and joining a live monthly Zoom videoconference of all participants in the intervention.

2.2. Outcomes

The primary outcome was nonspecific psychological distress measured by the K10, at baseline, 6 mo, and 12 mo [15,16]. The K10 is a ten-item screening measure (scores ranging from 10 to 50) used commonly in research and clinical practice to detect nonspecific psychological distress within the past 30 d [17]. Its two subscales measure depression (items 1, 4, 7, 8, 9, and 10) and anxiety (items 2, 3, 5, and 6). Scores $\geq$20 indicate presence (coded 1) and scores <20 indicate absence of significant distress and need for clinical treatment [18]. The K10 has very good psychometric properties and is considered one of the best screening tools for internalizing disorders [19,20]. Internal consistency of the K10 as measured by Chronbach α in our sample was excellent (0.85, 0.94, and 0.97 at baseline, 6 mo, and 12 mo, respectively.)

2.3. Prognostic covariates

Variables such as patient age (years) [21–23], Charlson Comorbidity Index [24], days between randomization and start of treatment [4], treatment modality (surgery-coded 1, primary radiotherapy/salvage radiotherapy–coded 2) [25], relationship status (1—yes, 0—no) [26], and prescribed medication for depression, anxiety, or both (1—present; 0—absent) [4,22] are known to significantly affect mental health outcomes in this population and were planned a priori to be added to the primary analysis as covariates [2–4,6,18–28].

2.3.1. Sample size calculation

With a two-sided test, α = 0.05, power = 0.80, and an anticipated incidence of screening positive for mental distress ($\geq$20) at 6 mo among 30% (control) versus 10% (intervention) of patients, a sample size of 124 participants was calculated to be necessary to detect a minimum meaningful effect [29].

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CONSORT
TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram

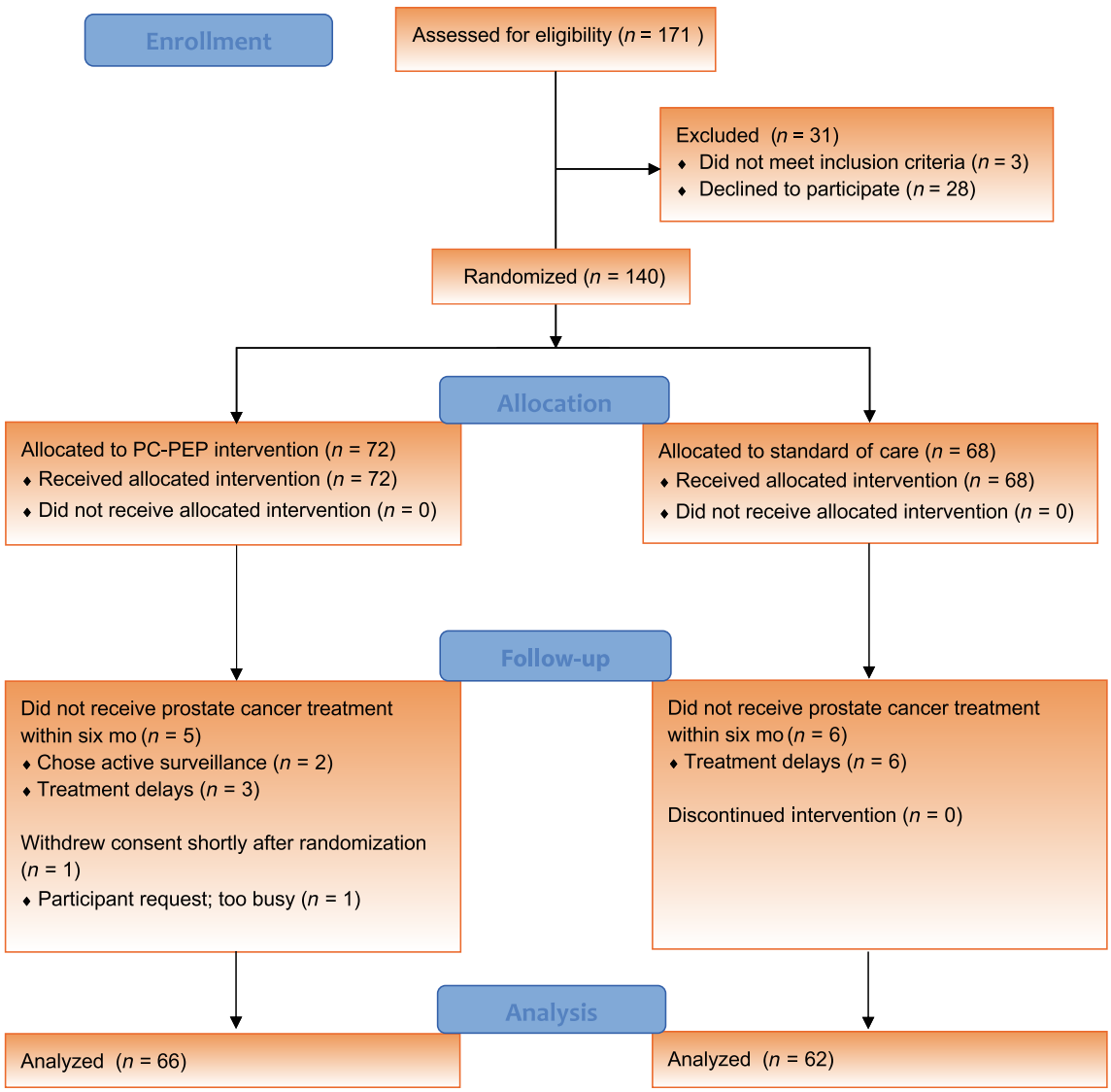

Fig. 1 – CONSORT 2010 flow diagram. CONSORT = Consolidated Standards of Reporting Trials; PC-PEP = Prostate Cancer Patient Empowerment Program.

2.4. Statistical analysis

Multiple logistic regression was used to examine clinical relevance in the dichotomous psychological distress outcome at 6-mo follow-up, with group (PC-PEP vs waitlist control), controlling for baseline psychological distress, and prognostic covariates [27,28]. A secondary analysis, analogous to that described above, was conducted to determine whether change in psychological distress (at 6 and 12 mo for the early and late groups, respectively) differed between the groups receiving intervention early vs late. A paired sample *t* test was performed to compare psychological distress in the waitlist-control group between 6 and 12 mo. Exploratory two-level linear modeling was used to model the continuous distress outcome and its subscales (anxiety and depression), and assess the fixed effects of the group defined as PC-PEP versus control (A) and the group defined as early versus late PC-PEP (B), with time (baseline and 6 mo), group × time, and covariates. Pairwise comparisons examined estimated marginal mean differences. Significance levels for all analyses were set at two-sided $p < 0.05$. Analyses were conducted using IBM SPSS, Armonk (NY, USA) statistical software version 27.0 [30].

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Table 1 – Sample characteristics at baseline between the Prostate Cancer Patient Empowerment Program (PC-PEP) intervention and waitlist-control groups, among 128 prostate cancer patients undergoing curative-intent treatment in Nova Scotia, Canada

	PC-PEP intervention (n = 66)	Waitlist control (n = 62)
Age (yr)	66, 66 (60–70)	62, 68 (61–72)
Body mass index	66, 29 (24–34)	62, 27 (23–31)
Household income at baseline, >30 000 CAD/past year	54, 82%	52, 84%
Race, White	60, 91%	61, 98%
Education, university or above	31, 47%	37, 60%
Employed (part of full time)	22, 33%	23, 37%
Relationship status (married/currently in a relationship)	59, 89%	61, 98%
Screening positive for nonspecific psychological distress and need for clinical treatment (K10 ≥20)	9, 18%	11, 14%
Stage of cancer		
Risk category (RP or primary RT ± HT) [a]		
Low	1, 1.5%	2, 3.2%
Intermediate	42, 75%	40, 67%
High	13, 23%	18, 30%
PSA (ng/ml) at time of RT (salvage group only)	10, 0.11 (0.065–0.16)	2, 0.28 (0.18–0.37)
Post-COVID [b] enrolment	51, 77%	50, 81%
Prescribed ADT	27, 41%	21, 34%
Treatment modality		
Radical prostatectomy	29, 44 %	33, 53%
Radiation therapy [c]	27, 41%	27, 44%
Radiation therapy (salvage) [c]	10, 15%	2, 3.2%
Charlson Comorbidity Index	66, 2 (2–3)	62, 3 (2–3)
Self-identified as cigarette smoker	5, 7.6%	3, 4.8%
Time between randomization and treatment (d)	66, 61 (34–99)	62, 73 (29–101)
Intake of prescribed medication for depression, anxiety, or both at the time of entering the trial	12, 18%	7, 11%
Absence of cancer recurrence at 6 mo after randomization	63, 96%	58, 94%

ADT = androgen deprivation therapy; HT = hormone therapy; K10 = Kessler Psychological Distress Scale; PRO = patient-reported outcome; PSA = prostate-specific antigen; RP = radical prostatectomy; RT = radiation therapy.
Summary statistics are presented as n, median and interquartile range, or n (%) for categorical data.
There were no statistically significant differences between the two arms at baseline for any of the PROs, sociodemographic, or medical covariates.
[a] National Comprehensive Cancer Network.
[b] The COVID pandemic restrictions began in the Canadian Maritime Provinces Nova Scotia, New Brunswick, and Prince Edward Island on March 16, 2020.
[c] The radiation therapy and salvage radiation groups were pooled together to allow for meaningful comparisons.

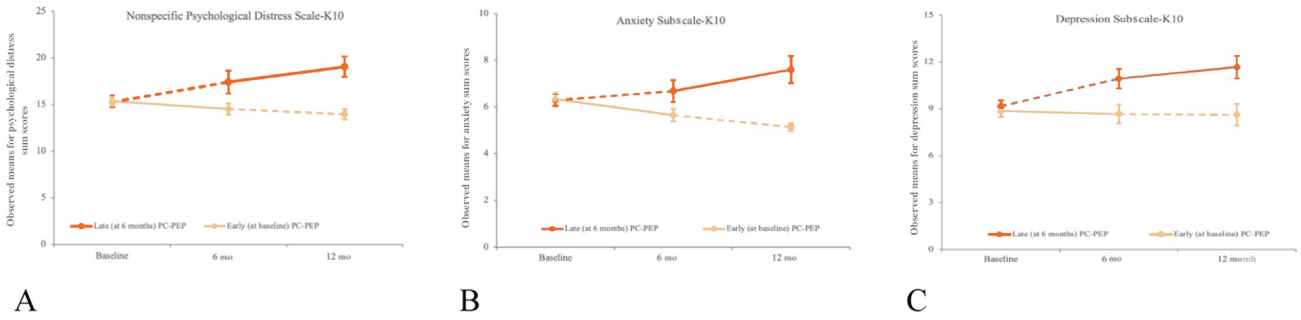

Fig. 2 – Observed K10 nonspecific psychological distress, K10 depression, and K10 anxiety for the early versus late intervention groups at baseline, 6 mo, and 12 mo among 128 curative prostate cancer patients treated in Nova Scotia, Canada. K10 = Kessler Psychological Distress Scale; PC-PEP = Prostate Cancer Patient Empowerment Program.

3. Results

No attrition, or adverse or serious adverse events were observed during the trial. Preintervention characteristics for the PC-PEP and control arms were comparable (Table 1). Figure 2 displays the observed means and standard errors for each time point for the PC-PEP versus waitlist-control group.

At 6 mo, 23% of men in the control group and 14% in the intervention group screened positive (≥20) for psychological distress and need for clinical treatment compared with men in the control group (14% and 18%, at baseline, respectively). A multiple logistic regression with group (intervention vs waitlist control) as a predictor, controlling for prognostic covariates and baseline distress sum scores, revealed that at 6 mo participants in the control group had 3.59 (95% confidence interval [CI]: 1.12, 11.51; absolute risk difference:16%, p = 0.031) times higher adjusted odds for psychological distress and need for clinical treatment than the PC-PEP participants (Table 2). A model fitting early versus late (delivered at 6-mo) intervention, controlling for prognostic covariates and preintervention distress sum

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Table 2 – Multiple logistic regression assessing nonspecific clinical psychological distress and need for treatment (≥20 on K10) at 6 mo by group (PC-PEP vs waitlist control) and at intervention completion by group (early/baseline vs late/6-mo timing of PC-PEP intervention delivery), while controlling for prognostic covariates among 128 prostate cancer patients undergoing curative-intent treatment in Nova Scotia, Canada

	aOR (95% CI)	*p* value
Presence of psychological distress and need for clinical treatment at 6 mo		
Full cohort analysis [a] (*N* = 128)		0.001
Group		
PC-PEP intervention	1.0 Reference	
Waitlist control	3.59 (1.12–11.51)	0.031
Psychological distress (K10) baseline	1.20 (1.08–1.34)	<0.001
Partial cohort analysis [a] (*N* = 116; 12 salvage radiation patients removed from the analysis)		<0.001
Group		
PC-PEP intervention	1.0 Reference	
Waitlist control	3.55 (1.02–12.36)	0.047
Psychological distress (K10) baseline	1.23 (1.09–1.38)	<0.001
Presence of psychological distress and need for clinical treatment after PC-PEP intervention		
Full cohort analysis [b] (*N* = 128)		<0.001
Group		
Early intervention (PC-PEP received at baseline)	1.0 Reference	
Late waitlist control (PC-PEP received at 6 mo)	4.41 (1.35, 14.41)	0.014
Psychological distress (K10) baseline	6.44 (2.01–20.68)	0.002
Partial cohort analysis [b] (*N* = 116; 12 salvage radiation patients removed from the analysis)		<0.001
Group		
Early intervention (PC-PEP received at baseline)	1.0 Reference	
Late waitlist Control (PC-PEP received at 6 mo)	4.20 (1.23, 14.33)	0.022
Psychological distress (K10) baseline	6.54 (1.98–21.58)	0.002

aOR = adjusted odds ratio; CI = confidence interval; K10 = Kessler Psychological Distress Scale; PC-PEP = Prostate Cancer Patient Empowerment Program.
[a] Analyses are controlled for sum scores for psychological distress at baseline.
[b] Analyses are controlled for sum scores for psychological distress at baseline for the early group and sum scores for psychological distress at 6 mo for the late waitlist control group.
All analyses include the following prognostic covariates: age, treatment modality (surgery vs radiation), relationship status (not in a relationship vs currently in a relationship), Charlson Comorbidity Index, prescribed medication for depression or anxiety or both (yes vs no), and days between randomization and treatment.

scores, revealed that postintervention men in the waitlist-control group had 4.41 (95% CI: 1.35, 4.41; absolute risk difference: 26%, $p = 0.014$) times higher adjusted odds for screening positive for psychological distress and need for clinical treatment than men in the early intervention group (Table 2). A paired *t* test assessing psychological distress in the waitlist-control group between 6 mo (mean [M] = 17.4; standard deviation [SD] = 9.5) and 12 mo (M = 19.0; SD = 11.4) revealed no statistically significant difference (t [61] = −1.267, $p = 0.2$).

Exploratory two-level linear modeling analyses revealed a statistically significant difference between groups (PC-PEP vs waitlist control) over time for psychological distress ($p = 0.028$) and depression ($p = 0.027$), but not for anxiety sum scores ($p = 0.057$; Table 3). Pairwise comparisons indicate that at 6 mo, the estimated marginal mean difference for psychological distress and depression was less among men in the PC-PEP group than among those in the waitlist-control group (−3.5 [95% CI: −5.7, −1.3], $p = 0.002$, and −2.2 [95% CI: −3.6, 0.8], $p = 0.002$, respectively). Fitting the early versus late/6-mo delivery of the intervention (Table 3) revealed a statistically significant difference between groups (early vs late) over time (before to after intervention) for anxiety ($p = 0.005$), but not for psychological distress ($p = 0.088$) or depression ($p = 0.3$). Pairwise comparisons show that after intervention, the estimated mean difference for anxiety was less for men who received the intervention early than for those who received the intervention late (−2.3 [95% CI: −3.4, −1.1]).

Table 4 displays exit evaluations of the intervention by group at the end of the 6-mo intervention.

4. Discussion

In this waitlist crossover controlled randomized trial, PC-PEP, a comprehensive 6-mo home-based online program promoting healthy physical, mental, and social behaviors, led to significant average and clinically relevant decreases in nonspecific distress and need for clinical psychological treatment in men scheduled for curative prostate cancer treatment compared with control at 6 mo, and similarly benefited both surgery only and primary radiation ± hormone therapy patients. No adverse events were reported. Mental health benefits for patients who received PC-PEP early compared with those who received it late (waitlist control) were maintained in percentage of psychological distress. Results point to the likely importance of providing access to PC-PEP as early as possible after diagnosis. This latter point is substantiated by research showing that patients are particularly distressed early on around diagnosis and, then they improve at 1–2 yr after diagnosis, only to become distressed again at 24 mo to later years in survivorship [2–4,7,9].

The rising incidence of prostate cancer, its long natural history, and high rates of treatment-related side effects have created a silent epidemic of poor mental health among prostate cancer survivors [2,3,6,7]. The vital importance of multifaceted interventions aimed at addressing the psychosocial and emotional effects of the prostate cancer diagnosis has previously been documented, but limited progress has been made in the adoption of such interventions in the standard of prostate cancer care [9,31–33]. A recent system-

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Table 3 – Results of the two-level linear model analysis fitting psychological distress and its depression and anxiety subscales among prostate cancer patients evaluating differences between groups (PC-PEP vs waitlist control, and early/baseline vs late/6-mo timing of PC-PEP intervention delivery) by time

Level	Parameter estimate	95% Confidence interval		*p* value
		Lower	Upper	
	Nonspecific psychological distress and need for clinical treatment sum scores			
PC-PEP vs waitlist control				
Group (PC-PEP vs control)	−3.5			
Time (baseline vs 6 mo)	−0.8	−2.7	1.0	
Time × group (PC-PEP)	−3.0	−5.6	−0.3	0.028
	Depression sum scores			
Group (PC-PEP vs control)	−2.2			
Time (baseline vs 6 mo)	−0.15	−1.3	1.0	
Time × group (PC-PEP)	−1.9	−3.5	−0.2	0.027
	Anxiety sum scores			
Group (PEP vs control)	−1.2			
Time (baseline vs 6 mo)	−0.7	−1.5	−0.1	
Time × group (PC-PEP)	−1.1	−2.2	0	0.057
Early/baseline vs late/6-mo timing of PC-PEP intervention delivery				
	Nonspecific psychological distress and need for clinical treatment sum scores			
Group (early/baseline vs late/6-mo PC-PEP)	−5.4			
Time (before vs after intervention)	−0.8	−2.8	1.1	
Time × group (early/baseline PC-PEP)	−2.5	−5.3	0.4	0.088
	Depression sum scores			
Group (early/baseline vs late/6-mo PC-PEP)	−3.1			
Time (before vs after intervention)	−0.2	−1.4	1.1	
Time × group (early/baseline PC-PEP)	−0.9	−2.7	0.9	0.3
	Anxiety sum scores			
Group (early/baseline vs late/6-mo PC-PEP)	−2.3			
Time (before vs after intervention)	−0.7	−1.5	0.1	
Time × group (early/baseline PC-PEP)	−1.6	−2.7	−0.5	0.005

PC-PEP = Prostate Cancer Patient Empowerment Program.
Control and late/6-mo timed intervention were treated as reference groups. Models included age, treatment modality, relationship status (not in a relationship vs currently in a relationship), Charlson Comorbidity Index, prescribed medication for depression or anxiety or both (yes vs no), and days between randomization and treatment.

atic review identified 22 randomized trials that assessed the effectiveness of psychosocial and patient education interventions in reducing distress, depression, and anxiety among prostate cancer patients, compared to usual care [9]. Of the 22 trials, three combined approaches and were the only ones that were successful in improving all three mental health outcomes compared with studies evaluating either approach alone [9]. Our study extends this literature [11,34]. To our knowledge, this is the longest (6 mo) intervention to provide prostate cancer patients with daily prescribed healthy living instructions, and is the first randomized clinical trial to assess the effects of early (as soon as curative treatment is scheduled) versus late (6 mo later) delivery of a multifaceted prostate cancer patient education and empowerment intervention in improving psychological distress, depression, and anxiety.

Patient activation is likely a contributing factor in the effectiveness of the program. Specifically, the daily video messages activated the role patients have in their own care (eg, exercising, eating healthier, and seeking social support) and delineated it from the role of the medical system. Indeed, evidence supports encouraging patients to take an active role in their care along with the care the medical system provides [35–39]. Another contributing factor may be patients' perceived professional competency of the leads. Specifically, the daily video messages were created and presented by an oncologist and scientist in prostate cancer quality of life research. Indeed, advice provided by a clinician can be a strong impetuous for patients' changing unhealthy behaviors [35–39], although behavioral change is an extremely complex phenomenon with many factors acting simultaneously [40].

This study is not without limitations. The intervention was time and effort intensive (70+ min of prescribed activities daily), and the percentage of all newly diagnosed patients interested in such an intense empowerment program may be low. The trial design may have worsened the mental health of the men randomized to the waitlist-control group by delaying their access to the intervention to a time when men are usually at the peak of experiencing treatment side effects. A phase 4 trial is assessing this hypothesis. An analysis of secondary outcomes included in the trial, which include weekly engagement with the various aspects of the program and urologic function, is underway.

This study has many strengths. The PC-PEP intervention is home based, appears safe, and can be administered from a distance. The experience of conducting this trial during the global pandemic, and its lack of attrition, speaks to the benefits of online programming. Many older men living in rural Canada were willing and able to participate in the program. Most patients remained engaged in the program, and many have taken leading research citizens roles in the program's outreach [35,36].

Lastly, the potential for PC-PEP to help reduce health care costs merits consideration. Overall, PC-PEP is cheap to administer (~200CAD per patient) and is expanding to other geographic regions (pcpep.org) as well as other types of cancer. The eligibility criteria for the implementation trial (in progress) assessing generalizability includes the full

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Table 4 – Exit evaluations at the end of the 6-mo completion of the PC-PEP program among the 128 prostate cancer patients enrolled in the trial

	PC-PEP (n = 66) Completed at 6 mo Responses ranged from 0 (not at all) to 10 (extremely/ highest rating)			Control (n = 62) Completed at 12 mo Responses ranged from 0 (not at all) to 10 (extremely/ highest rating)		
	N	Mean	SD	*N*	Mean	SD
Participants' perceived competence of the PC-PEP Research and Clinical Team	66	9.59	0.84	62	9.23	1.23
Participants' rated likelihood of recommending PC-PEP to men who have been diagnosed with prostate cancer	66	9.38	1.55	62	8.81	2.20
Participants' perceived importance of implementing PC-PEP to the standard of care of patients diagnosed with prostate cancer, from day 1 of diagnosis	66	9.12	1.51	62	8.87	2.02
Participants' interest in the PC-PEP after the training session	66	8.79	1.71	62	8.54	1.96
Participants' perceived usefulness of the training sessions at baseline	66	8.86	1.59	62	8.48	1.98
Participants' interest in the PC-PEP intervention at recruitment	66	8.56	1.83	62	8.60	2.13
Participants' perceived usefulness of the PC-PEP intervention	66	8.45	2.08	62	8.08	2.48
Participants' perceived accessibility and quick response to inquiries during the duration of the trial from the PC-PEP research team and staff	66	8.20	2.23	62	7.94	2.30
Participants' perceived usefulness of the program's pelvic floor (kegels) training videos	66	8.18	2.58	62	7.68	2.97
Participants' perceived usefulness of the program's strength and aerobic exercise videos and materials	66	7.92	2.45	62	8.05	2.43
Participants' perceived usefulness of the program's dietary advice materials (educational videos and daily messages)	66	7.80	2.84	62	7.61	2.52
Participants' perceived improved life-style benefits at the end of 6 mo compared with the start of the program (baseline)	66	7.77	2.39	62	7.31	3.04
Participants' perceived usefulness of the program's videos and online collection of educational materials	66	7.77	2.99	62	7.39	2.99
Participants' perceived usefulness of the program to their partner (if applicable) during the 6 mo	66	7.53	3.03	62	6.50	3.75
Participants' perceived usefulness of the program's daily videos with education and empowerment messages	66	7.56	3.31	62	7.48	2.94
Participants' perceived usefulness of the program's intimacy and connection education materials (videos and daily messages)	66	7.23	3.07	62	6.77	3.23
Participants' perceived usefulness of the program's pelvic floor (kegels) daily texts reminders (optional program component)	64	7.19	3.27	59	7.02	3.59
Participants' perceived usefulness of the program's monthly video/Zoom conference (if attended)	61	6.95	3.27	59	6.39	3.82
Participants' perceived usefulness of the program's website	66	6.71	3.22	62	7.06	3.21
Participants' perceived usefulness of the program's stress reduction biofeedback device (HRV monitor)	66	6.46	3.21	62	6.48	3.25
Participants' perceived usefulness of the program's meditation videos	66	5.94	3.26	62	5.84	3.67
Participants' perceived usefulness of the program's Buddy system (connection with 2 co-participants attending and going through the program at the same time, and going through a similar prostate cancer treatment; optional program component)	60	5.27	3.71	52	5.81	4.30
Participants' perceived usefulness of the program's Mentor system (connection with patients who already went through the program; optional program component)	66	4.93	3.30	62	5.42	4.26
		n	%		*n*	%
In-person (vs online, due to COVID-19 testing restrictions) training for the program	66	41	62	62	38	61
Interest in continuing with the program after the 6 mo	66	37	56	62	32	52
Participants' interest to become a mentor for the PC-PEP intervention	66	17	26	62	9	15
Participants' interest to become a research citizen for the PC-PEP intervention	66	23	35	62	16	26
Participants who have been tested for COVID-19 during the trial	66	27	41	62	44	71

PC-PEP = Prostate Cancer Patient Empowerment Program; SD = standard deviation.

range of patients from those on active surveillance through early metastatic disease.

5. Conclusions

While it is incumbent on clinicians to screen for and address mental health issues that are common among prostate cancer patients, the optimal mechanism through which this should be accomplished remains unclear. PC-PEP does not appear to burden the clinicians, nurses, or regular delivery of care, and if provided early after diagnosis, may help prevent high levels of psychological distress and associated health care costs. PC-PEP has the potential to reach individuals on a wider scale, and its blueprint may be considered a new approach to enhancing patient and public mental health.

Author contributions: Gabriela Ilie had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Ilie, Rutledge, Mason, MacDonald, Kephart.
Acquisition of data: Ilie, Rutledge, Mason, Rendon, MacDonald, Kucharczyk, Bowes, Bailey, Bell, Lawen, Wilke, Massaro, Ha.
Analysis and interpretation of data: Ilie, Rutledge, MacDonald, Rendon, Mason, Bowes, Kucharczyk.
Drafting of the manuscript: Ilie, Rutledge, MacDonald.
Critical revision of the manuscript for important intellectual content: Ilie, Rutledge, Mason, Rendon, MacDonald, Kucharczyk, Bowes, Bailey, Bell, Lawen, Wilke, Massaro, Ha, Zahavich, Kephart.
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Obtaining funding: Ilie, Mason, Rutledge, Bailey, Bell, Bowes, Patil, Lawen.
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Supervision: Ilie, Rutledge.
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Peer Review Summary

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