Urinary and sexual function do not mediate psychological distress reduction in the PC-PEP randomized controlled trial: A secondary mediation analysis

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ABSTRACT

Introduction: Psychological distress is common among men treated for localized prostate cancer and is often presumed to stem from treatment-related urinary and sexual sequelae. The Prostate Cancer-Patient Empowerment Program (PC-PEP), a six-month, comprehensive, digital intervention, reduces psychological distress and improves patient-reported urinary and sexual function. This secondary analysis tested whether improvements in urinary incontinence, urinary irritative/obstructive symptoms, or sexual function explain PC-PEP's effect on psychological distress.

Methods: In a randomized controlled trial, 128 men with localized prostate cancer were assigned to PC-PEP (n=66) or standard care (n=62) for six months. Psychological distress was measured using the

KEY MESSAGES

- The Prostate Cancer-Patient Empowerment Program (PC-PEP), an integrative, home-based digital intervention, significantly improved patient-reported urinary outcomes in the full cohort and produced additional postoperative improvements in sexual function.
- These improvements in urinary and sexual function did not mediate the reduction in psychological distress associated with PC-PEP, indicating that the program's mental health benefits arise through mechanisms other than symptom relief.
- Post-treatment prostate cancer care should therefore consider factors beyond urinary and sexual symptoms when addressing psychological distress.

Kessler psychological distress scale (K10), and urinary and sexual function were assessed using the expanded prostate cancer index composite (EPIC) at baseline and six months. Mediation models adjusted for age, relationship status, use of medications for anxiety or depression, Charlson comorbidity index, treatment modality, time from randomization to treatment, and baseline K10 and EPIC scores.
Results: PC-PEP produced significant improvements in urinary incontinence and urinary irritative/obstructive symptoms across the full cohort and attenuated postoperative declines in sexual function; however, none of these urinary or sexual outcomes mediated the program's effect on psychological distress.
Conclusions: While PC-PEP enhances key urinary and postoperative sexual outcomes, these functional gains do not account for its mental health benefits. This challenges the assumption that psychological distress in prostate cancer survivorship is predominantly driven by urinary or sexual sequelae and highlights the importance of addressing broader psychosocial and behavioral determinants of mental health in survivorship care.

INTRODUCTION

Localized prostate cancer carries an excellent prognosis, with contemporary series reporting five-year disease-specific survival exceeding 98%.[1-2] Given its high incidence and the proportion diagnosed at an early stage, survivorship outcomes have become a defining focus of clinical care.[3] Treatment-related adverse effects, including urinary incontinence, irritative/obstructive urinary symptoms, sexual dysfunction, bowel disturbances, and psychological distress, are major determinants of long-term functional morbidity.[4-5]

Large population-based cohorts consistently demonstrate that these functional impairments are both common and durable, with patterns that vary meaningfully by treatment modality. In a nationwide population cohort, urinary incontinence at one year was more common after robot-assisted radical prostatectomy than after radiotherapy, whereas irritative and obstructive urinary symptoms and bowel symptoms were more prominent after radiotherapy. Despite these modality-specific differences, erectile dysfunction remained highly prevalent across treatments and overall urinary bother was the same in both groups.[6] Five-year findings from the Prostate Cancer Outcomes Study similarly showed marked differences in urinary and bowel effects by treatment, with persistent incontinence after prostatectomy and higher rates of bowel urgency and painful hemorrhoids after radiotherapy.[7] Ten-year findings from the CEASAR study confirm that prostatectomy leads to more long-term urinary incontinence, sexual function becomes comparable across treatments, and bowel and hormone-related symptoms remain more pronounced after radiotherapy with androgen-deprivation therapy in higher-risk disease.[8] Alongside these functional sequelae, psychological distress, including symptoms of anxiety, depression, and overall psychological distress burden, is highly prevalent among prostate cancer survivors.[9-10] Distress can remain elevated for more than a decade after diagnosis and is associated with a 61%

increase in all-cause mortality among men with comorbid depression, with disproportionately higher risks for Hispanic, Black, and low-SES men and those receiving androgen-deprivation therapy (ADT).[9] Despite its clinical significance, distress frequently goes untreated. In a cohort of 37 388 men initiating ADT, 10.6% developed new-onset depression or anxiety, yet nearly half (47.7%) received no mental-health treatment, and fewer than 1% accessed psychotherapy.[11] Approximately one in five received benzodiazepines, agents that may exacerbate ADT-related vulnerabilities such as fatigue, cognitive slowing, and fall risk, while only one-third received selective serotonin reuptake inhibitors, the evidence-based first-line treatment for depression and anxiety.[11] The majority of prescriptions (72%) originated in primary care rather than oncology or psychiatry, highlighting the absence of an integrated mental-health pathway for men undergoing ADT.

Urinary and sexual dysfunction are often assumed to be the primary drivers of psychological distress in prostate cancer survivorship.[12–13] Yet large population-based studies show that even substantial modality-specific differences in urinary, bowel, and sexual function rarely correspond to differences in anxiety, depression, or global quality of life.[6–8] This mismatch suggests that functional recovery alone does not determine psychological trajectories and that broader psychosocial determinants are influential.[14] Accordingly, the central mechanistic question in this secondary analysis is whether functional recovery (urinary and sexual outcomes) explains the psychological distress reductions observed with PC-PEP.

Multicomponent survivorship interventions, including pelvic-floor muscle training, structured exercise, nutrition, cognitive-behavioral strategies, and peer support, have shown benefits across multiple domains.[15-21] Yet the mechanisms through which these interventions reduce psychological distress remain insufficiently defined, and recent scholarship has urged a departure from mind–body dualism toward mechanism-informed models grounded in biopsychosocial theory.[20-22]

The Prostate Cancer Patient Empowerment Program (PC-PEP) is a six-month, digitally delivered, multicomponent survivorship intervention grounded in a biopsychosocial framework. It incorporates daily pelvic-floor muscle training, structured exercise, stress-reduction practices, sleep and nutrition guidance, and weekly virtual peer-support and education sessions. Prior analyses from the randomized trial show that PC-PEP reduces psychological distress and improves urinary and sexual function.[27–29] A secondary analysis further found that psychological improvements were mediated by gains in self-efficacy and more adaptive illness perceptions.[30] These findings suggest that shifts in appraisal, coping confidence, and illness perception contribute meaningfully to PC-PEP's mental-health benefits.

However, these psychosocial mediators do not address a longstanding clinical assumption in urology that reductions in psychological distress arise primarily from improvements in treatment-related urinary or sexual sequelae. Whether improvements in urinary incontinence, urinary irritative/obstructive symptoms, or sexual function constitute additional mediators of PC-PEP's effects has not been established.

This secondary analysis tests whether improvements in patient-reported urinary incontinence, urinary irritative/obstructive symptoms, or sexual function mediate the effect of PC-PEP on

psychological distress at six months. We hypothesized that assignment to PC-PEP would improve urinary and sexual function and that these functional gains would, in turn, be associated with lower psychological distress. Clarifying whether functional recovery explains psychological benefit addresses a longstanding assumption in prostate cancer survivorship and informs the design and optimization of comprehensive survivorship interventions.[20-21,23,26-28]

METHODS

Study design and participants

We conducted a secondary analysis of the Prostate Cancer Patient Empowerment Program (PC-PEP) trial, a single-center, prospective, crossover randomized controlled trial conducted in Halifax, Nova Scotia, Canada. A complete description of PC-PEP, a 6-month, home-based, multicomponent health-promotion program is available elsewhere.[23] In brief, PC-PEP delivers daily email-based content including structured videos and instructions addressing physical activity (aerobic and resistance exercises), pelvic-floor muscle training, relaxation and mindfulness practices, nutrition guidance, and relationship and intimacy skills. Participants are encouraged to complete a standardized set of daily tasks, track their adherence, and engage in optional monthly group videoconferences to enhance accountability and peer support. Because participants crossed over after 6 months, mediation analyses were restricted to the initial randomized period to preserve internal validity.

From December 2019 to January 2021, participants were recruited through referrals from the Departments of Urology and Radiation Oncology at the Queen Elizabeth II Health Sciences Centre or through self-referral in response to advertisements placed in major oncology clinics across the province. Eligible participants were men aged ≥18 years with biopsy-confirmed prostate cancer who were scheduled to receive curative-intent treatment within 6 months of randomization (radical prostatectomy or radiotherapy, with or without androgen-deprivation therapy), capable of low- to moderate-intensity physical activity, able to speak and understand English, able to travel to Halifax for in-person assessments at baseline, 6 months, and 12 months, and with daily access to email. All participants provided written informed consent. The study was approved by the Nova Scotia Health Authority Research Ethics Board and registered at ClinicalTrials.gov (NCT03660085).

Of 171 men assessed for eligibility, 140 were randomized 1:1 to PC-PEP or waitlist control. Fixed-block randomization was used to balance psychological-distress level, treatment modality, and hormone-therapy status between groups. The randomization sequence was computer-generated, with allocation concealed. Post-randomization, 12 participants were excluded (1 withdrew consent, 11 did not receive curative treatment within 6 months). The analytic sample included 66 men assigned to PC-PEP and 62 to waitlist control (CONSORT Flow Diagram, Figure 1).

Group exposure: PC-PEP vs waitlist control

Program components have been described previously.[23] In brief, participants in the intervention arm received daily emails for 6 months containing educational content, motivational messaging, and video-based instructions delivered by coauthors GI and RR. Core program elements included relaxation and

stress-reduction techniques, nutritional guidance, aerobic and resistance physical activity, pelvic-floor muscle training, and guidance on relationships and intimacy. Participants also had the option to join monthly videoconferences and were encouraged to engage with peers as an additional source of social support. The exposure variable for the mediation analysis was assignment to PC-PEP versus waitlist control over the initial 6-month period.

Outcome: Non-specific psychological distress

Psychological distress at 6 months was measured using the Kessler Psychological Distress Scale (K10), a 10-item self-report instrument assessing anxiety and depressive symptoms over the prior month.[30] Each item is rated on a five-point Likert scale (1=*none of the time* to 5=*all of the time*), yielding a total score ranging from 10 to 50, with higher scores indicating greater distress. The K10 demonstrates strong psychometric performance among older adults and prostate cancer populations.[31-32]

Mediator variables

Potential mediators were patient-reported urinary and sexual function at 6 months, assessed using the Expanded Prostate Cancer Index Composite (EPIC).[33] EPIC evaluates urinary, bowel, sexual, and hormonal domains on 0–100 scales, with higher scores indicating better function.[34] Mediators included the urinary incontinence domain, urinary irritative/obstructive domain, and sexual domain.

Prognostic covariates

Covariates selected a priori based on prior literature included age (years),[35] Charlson Comorbidity Index score,[36] time from randomization to treatment start,[37] treatment modality (radical prostatectomy vs radiotherapy),[38] relationship status,[39] and use of clinician-prescribed medication for anxiety, depression, or both.[40]

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics version 29.0.2.0 and the PROCESS Macro version 5.0.[41] Baseline characteristics were summarized using descriptive statistics. Continuous variables were expressed as medians with interquartile ranges, and categorical variables as frequencies and percentages. Between-group differences at baseline were assessed using the Mann–Whitney U test for continuous variables and either the chi-square test or Fisher exact test for categorical variables. Two-sided p values less than .05 were considered statistically significant.

The primary analysis evaluated whether change in psychological distress differed between the PC-PEP and waitlist control groups from baseline to six months. Mixed-effects linear models with restricted maximum likelihood estimation included fixed effects for group assignment, time, and the group by time interaction, and a random intercept for each participant. Models were adjusted for prespecified prognostic variables that included age, Charlson Comorbidity Index score, relationship status, prescribed medication for depression, anxiety, or both, treatment modality, and days between randomization and initiation of active treatment. The group by time interaction estimated differential change in distress over time.

Parallel mixed-effects models examined changes in patient-reported urinary incontinence, urinary irritative or obstructive symptoms, and sexual function using the respective Expanded Prostate Cancer Index Composite domains. Because patterns of functional recovery differ by treatment modality, moderation analyses were prespecified to test whether intervention effects varied between men treated with radical prostatectomy and those treated with radiotherapy. These models included a group by time by treatment modality interaction. When moderation was present, results were presented separately within treatment subgroups.

Mediation analyses were conducted to determine whether changes in urinary incontinence, urinary irritative or obstructive symptoms, or sexual function at six months accounted for the effect of PC-PEP on psychological distress at six months. These analyses were prespecified secondary analyses of the PC-PEP randomized controlled trial, which was powered for the primary psychological distress outcome. These analyses used ordinary least-squares regression within the PROCESS Macro Model 4 framework.[42] Each model estimated the association between group assignment and the mediator and the association between the mediator and psychological distress after adjustment for group assignment. Models were adjusted for the same prognostic covariates used in the mixed-effects models as well as for baseline values of both the mediator and the Kessler Psychological Distress Scale,[43] thereby modelling the effect of change in mediator status over the intervention period. Indirect effects were estimated using bias-corrected bootstrap confidence intervals generated from ten thousand resamples. An indirect effect was considered statistically significant when the confidence interval did not include zero. Because functional improvements in sexual outcomes associated with PC-PEP have been observed primarily among surgical patients, a prespecified sensitivity mediation analysis was performed within the radical prostatectomy subgroup. Sensitivity results are presented in the Supplementary Materials.

RESULTS

Sample characteristics

A total of 128 men were randomized, with 66 allocated to the PC-PEP intervention and 62 to the waitlist control group. Baseline demographic and clinical characteristics were comparable between groups (Table 1). There were no statistically significant differences in age, Charlson Comorbidity Index, relationship status, antidepressant/anxiolytic medication use, treatment modality, time from randomization to treatment, or baseline K10 or EPIC domain scores (all $p > 0.05$).

Consistent with published findings from this randomized trial, PC-PEP significantly reduced psychological distress at six months compared with the waitlist control group and produced clinically meaningful improvements in urinary incontinence and irritative/obstructive symptoms, particularly among men treated with radical prostatectomy.[23,24] Sexual-function decline was attenuated among postoperative participants receiving the program. Full mixed-effects model estimates and subgroup analyses are presented in Supplementary Tables S1.

Mediation analysis

Mediation models examined whether changes in patient-reported urinary incontinence, urinary irritative/obstructive symptoms, or sexual function accounted for reductions in psychological distress at 6 months. The total effect of PC-PEP on psychological distress was statistically significant in the urinary incontinence model (b=–2.45; p=0.045) and the sexual function model (b=–2.47; p=0.044), and marginally non-significant in the urinary irritative/obstructive model (b=–2.34; p=0.055). Although PC-PEP had statistically significant direct effects on patient-reported urinary incontinence (b=13.84; p<0.001) and urinary irritative/obstructive symptoms (b=6.65; p=0.002), none of these changes significantly mediated reductions in psychological distress; all bootstrapped 95% confidence intervals for indirect effects included zero (Table 2, Figure 2). In the sexual-function model, the total and direct effects were numerically identical, reflecting the absence of an indirect pathway. For clarity, Figure 3 contrasts the *a priori* hypothesized mediation pathway (functional recovery mediating distress reduction) with the observed results from the present analyses (no mediation via urinary or sexual function).

Given prior evidence that improvements in sexual function were specific to postoperative men, a sensitivity mediation analysis was conducted in the prostatectomy subgroup (n=62). PC-PEP significantly improved sexual function in this subgroup (b=11.93; p=0.003), but no mediation effect was detected. Sensitivity analyses for urinary outcomes similarly showed that PC-PEP produced larger improvements in the surgery subgroup (urinary incontinence: b=28.41; p<0.001; urinary irritative/obstructive symptoms: b=13.61; p<0.001), yet none of these patient-reported urinary outcomes mediated changes in psychological distress (Supplementary Figure S1, and Table S2).

Taken together, these findings show that PC-PEP statistically improves patient-reported urinary continence and urinary irritative/obstructive symptoms in the full cohort, with postoperative participants experiencing additional gains in both urinary and sexual function. However, these changes did not statistically mediate the reductions in psychological distress observed in the intervention group.

DISCUSSION

This secondary analysis of the Prostate Cancer Patient Empowerment Program (PC-PEP) randomized crossover trial examined whether improvements in urinary incontinence, urinary irritative or obstructive symptoms, or sexual function mediated reductions in psychological distress at six months. Consistent with previous reports, PC-PEP significantly improved urinary outcomes and attenuated the decline in sexual function among postoperative patients, with the largest benefits observed after radical prostatectomy.[24] However, in this analysis, none of the changes in urinary or sexual function statistically mediated the reduction in psychological distress. Indirect effects were small and statistically not significant, indicating that functional recovery did not account for the mental-health benefits of the program (Figure 3).

The absence of mediation is clinically important because it challenges the assumption that urinary and sexual dysfunction are the primary determinants of psychological morbidity in prostate cancer survivorship.[6–8,12–13,14,48] These findings align with population-based evidence showing that treatment-related urinary, bowel, and sexual differences do not predict long-term psychological outcomes.[6–8] Although functional impairments and distress influence one another, these associations are

modest and insufficient to explain psychological trajectories.[12] Instead, distress is more strongly shaped by psychosocial determinants such as illness perceptions, self-efficacy, identity changes, communication challenges, and unmet supportive-care needs.[13,27,48]

These findings are consistent with broader literature showing that psychological distress in prostate cancer is shaped primarily by uncertainty, altered identity, and the meaning attached to the diagnosis itself. A major review by Chambers and colleagues concluded that distress is driven more by psychosocial factors and unmet needs than by urinary or sexual dysfunction.[27] The very labeling of the condition as cancer can profoundly influence mindset, affecting fear of recurrence, self-concept, and coping. Vyas and colleagues showed that illness perceptions and appraisals are among the strongest predictors of mental-health outcomes, exceeding the contribution of functional deficits.[13] Scandurra and colleagues similarly highlighted the importance of body image, identity disruption, and insufficient social support as predictors of anxiety and depression.[45] These convergent findings help explain why the mental-health benefits of PC-PEP occurred independently of changes in urinary or sexual symptoms.

From a population-health perspective, psychological distress can persist for more than a decade after diagnosis and is associated with increased all-cause mortality, with disproportionate risk among men of lower socioeconomic status, racialized communities, and those receiving androgen-deprivation therapy.[9,50] Despite this burden, nearly half of men who develop anxiety or depression during androgen-deprivation therapy receive no mental-health treatment, and fewer than one percent receive psychotherapy.[11] This underscores a substantial gap in survivorship pathways, where distress screening and psychosocial care remain insufficiently embedded in routine urologic and radiation oncology practice.

Structured survivorship programs may help address persistent gaps in psychosocial care.[23,26,48] PC-PEP is one such program and has been implemented across ten Canadian provinces, as well as in New Zealand and South Africa, with additional cultural adaptations underway.[23–26,48] Its fully digital, low-resource design allows integration into routine clinical workflows. A recent economic evaluation identified PC-PEP as a cost-saving strategy, with projected health-system savings of roughly CAD $660,000 per 1,000 participants.[49] By targeting multiple modifiable determinants of psychological health including physical activity, pelvic-floor training, stress regulation, nutrition, sleep, and opportunities for peer connection, the program aligns with a biopsychosocial approach to survivorship care.[23–26]

Since the launch of the Phase 4 implementation trial, more than 700 men have enrolled across ten Canadian provinces.[48] Recruitment has involved 29 named referring clinicians across urology, radiation oncology, and medical oncology, along with additional referring physicians identified in provincial datasets. Although the program offers one of the most comprehensive and sustained survivorship supports currently available, with six months of structured daily material and ongoing follow-up, implementation remains variable across regions. Greater integration of survivorship pathways and support from professional societies may help standardize referral processes and strengthen the incorporation of evidence-based psychosocial interventions into routine care.

These findings have direct implications for clinical practice. Improvements in continence and sexual function remain meaningful goals of care, but clinicians should not assume that symptomatic

improvement will resolve psychological distress. Routine distress screening should occur independently of functional status, given the persistent and sometimes severe psychological burden documented in large cohorts.[9,46,50] Structured programs such as PC-PEP provide an effective adjunct to standard rehabilitation because they address psychosocial determinants that traditional function-focused care does not target. Embedding such programs in survivorship pathways may help reduce the substantial under-treatment of mental-health needs among men with prostate cancer.[11]

Several limitations should be noted. This was a single-center study, which may limit generalizability. As a secondary analysis, the trial was powered a priori to detect clinically meaningful differences in psychological distress, the primary outcome of the randomized trial, rather than indirect effects in mediation models. Mediation analyses typically require larger samples to detect small-to-moderate indirect effects, and thus the present study may have been underpowered to identify subtle mediation pathways. Adherence to core program components, including pelvic-floor muscle training, was high, with no loss to follow-up and complete outcome data across participants.[24] Nevertheless, as a multicomponent behavioral intervention, the relative contribution of individual elements to psychological outcomes cannot be disentangled within the present mediation framework. Internal validity is strengthened by computer-generated randomization and concealed allocation. However, participation required motivation, digital access, and willingness to engage in a comprehensive survivorship program; therefore, findings may be most applicable to men who actively seek structured strategies to contribute to their recovery, potentially limiting generalizability to less engaged populations. Finally, the crossover design restricted analyses to the initial six-month period.
PC-PEP improves urinary and sexual outcomes, particularly after radical prostatectomy, yet these functional gains do not account for its effect on psychological distress. Reductions in distress appear to arise through psychosocial pathways such as enhanced self-efficacy, more adaptive illness perceptions, and strengthened coping capacity. These findings highlight that psychological recovery in prostate cancer survivorship cannot be achieved through functional rehabilitation alone. Embedding structured, mechanism-based behavioral and psychosocial interventions within standard survivorship care has the potential to improve patient well-being, address long-standing gaps in mental-health support, and enhance system-wide quality of care. Supplementary Materials: Table S1. Psychological Distress, Urinary Function, and Sexual Function Outcomes From the PC-PEP Randomized Crossover Trial; Table S2. Mediation Analysis of the Effect of PC-PEP vs Waitlist Control on Psychological Distress (Surgery Subgroup Only); Figure S1. Mediation Analysis of the Effect of PC-PEP on Psychological Distress by EPIC Sexual Function at 6 Months (Surgery Subgroup Only).

REFERENCES

1. American Cancer Society. Survival rates for prostate cancer. Available at: https://www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/survival-rates.html. Accessed 2025 Oct 30.
2. Canadian Cancer Society. Survival statistics for prostate cancer. Available at: https://cancer.ca/en/cancer-information/cancer-types/prostate/prognosis-and-survival/survival-statistics. Accessed 2025 Oct 30.
3. Raychaudhuri R, Lin DW, Montgomery RB. Prostate cancer: A review. *JAMA* 2025;333:1433-40. doi:10.1001/jama.2025.0228
4. Muise A, Pan MM, Rose B, et al. Functional outcomes after prostate cancer treatment: A comparison between single and multiple modalities. *Urol Oncol* 2023;41:104.e1-e9. doi:10.1016/j.urolonc.2022.07.014
5. Luckenbaugh AN, Wallis CJD, Huang LC, et al. Association between treatment for localized prostate cancer and mental health outcomes. *J Urol* 2022;207:1029-37. doi:10.1097/JU.0000000000002370
6. Corsini C, Bergengren O, Carlsson S, et al. Patient-reported side effects 1 year after radical prostatectomy or radiotherapy for prostate cancer: A register-based nationwide study. *Eur Urol Oncol* 2024;7:605-13. doi:10.1016/j.euo.2023.12.007
7. Potosky AL, Davis WW, Hoffman RM, et al. Five-year outcomes after prostatectomy or radiotherapy for prostate cancer: The prostate cancer outcomes study. *J Natl Cancer Inst* 2004;96:1358-67. doi:10.1093/jnci/djh259
8. Al Hussein Al Awamlh B, Wallis CJD, Penson DF, et al. Functional outcomes after localized prostate cancer treatment. *JAMA* 2024;331:302-17. doi:10.1001/jama.2023.26491
9. Hu S, Chang CP, Snyder J, et al. Mental health outcomes in a population-based cohort of patients with prostate cancer. *J Natl Cancer Inst* 2024;116:445-54. doi:10.1093/jnci/djad175
10. Fervaha G, Izard JP, Tripp DA, et al. Psychological morbidity associated with prostate cancer: Rates and predictors of depression in the RADICAL PC study. *Can Urol Assoc J* 2020;15:181-7. doi:10.5489/cuaj.6912
11. Tsao PA, Ross RD, Bohnert ASB, et al. Depression, anxiety and patterns of mental health care among men with prostate cancer receiving androgen deprivation therapy. *Oncologist* 2022;27:314-22. doi:10.1093/oncolo/oyab033
12. Orom H, Biddle C, Underwood W, et al. Worse urinary, sexual and bowel function cause emotional distress and vice versa in men treated for prostate cancer. *J Urol* 2018;199:1464-9. doi:10.1016/j.juro.2017.12.047
13. Vyas N, Brunckhorst O, Fanshawe JB, et al. Prognostic factors for mental wellbeing in prostate cancer: A systematic review and meta-analysis. *Psychooncology* 2023;32:1644-51. doi:10.1002/pon.6225
14. Xiang J, Dai L, Tan L, et al. Psychosocial experiences of prostate cancer survivors after treatment: a systematic review of qualitative studies. *Front Public Health* 2025;13:1625611. doi:10.3389/fpubh.2025.1625611
15. Geerkens MJM, Pouwels NSA, Beerlage HP. The effectiveness of lifestyle interventions to reduce side effects of androgen deprivation therapy for men with prostate cancer: A systematic review. *Qual Life Res* 2020;29:843-65. doi:10.1007/s11136-019-02361-z

16. Menichetti J, Villa S, Magnani T, et al. Lifestyle interventions to improve the quality of life of men with prostate cancer: A systematic review of randomized controlled trials. *Crit Rev Oncol Hematol* 2016;108:13-22. doi:10.1016/j.critrevonc.2016.10.007
17. Baumann FT, Reimer N, Gockeln T, et al. Supervised pelvic floor muscle exercise is more effective than unsupervised pelvic floor muscle exercise at improving urinary incontinence in prostate cancer patients following radical prostatectomy: A systematic review and meta-analysis. *Disabil Rehabil* 2022;44:5374-85. doi:10.1080/09638288.2021.1937717
18. Kang DW, Fairey AS, Boulé NG, et al. A randomized trial of the effects of exercise on anxiety, fear of cancer progression and quality of life in prostate cancer patients on active surveillance. *J Urol* 2022;207:814-22. doi:10.1097/JU.0000000000002334
19. Pieramico S, Castro R, Aguiar S, et al. A systematic review on the efficacy of CBT interventions for the mental and sexual health of survivors of prostate cancer. *Sex Med Rev* 2023;12:48-58. doi:10.1093/sxmrev/qead024
20. Salvy SJ. Psychological interventions in prostate cancer: A farewell to mind-body dualism. *Prostate Cancer Prostatic Dis* 2021;24:587-8. doi:10.1038/s41391-021-00350-3
21. Mundle R, Afenya E, Agarwal N. The effectiveness of psychological intervention for depression, anxiety and distress in prostate cancer: A systematic review. *Prostate Cancer Prostatic Dis* 2021;24:674-87. doi:10.1038/s41391-021-00342-3
22. Bolton D. A revitalized biopsychosocial model: Core theory, research paradigms and clinical implications. *Psychol Med* 2023;53:7504-11. doi:10.1017/s0033291723002660
23. Ilie G, Rendon R, Mason R, et al. A comprehensive six-month prostate cancer patient empowerment program decreases psychological distress among men undergoing curative prostate cancer treatment: A randomized clinical trial. *Eur Urol* 2023;83:561-70. doi:10.1016/j.eururo.2023.02.009
24. Lawen T, Ilie G, Mason R, et al. Six-month prostate cancer empowerment program improves urinary function: A randomized trial. *Cancers* 2024;16:50958. doi:10.3390/cancers16050958
25. MacNevin W, Ilie G, Rendon R, et al. PC-PEP, a comprehensive daily six-month home-based patient empowerment program, leads to weight loss in men with prostate cancer: A secondary analysis. *Curr Oncol* 2024;31:1667-78. doi:10.3390/curroncol31030127
26. MacDonald C, Ilie G, Kephart G, et al. Mediating effects of self-efficacy and illness perceptions on mental health in men with localized prostate cancer: A secondary analysis. *Cancers (Basel)* 2024;16:32352. doi:10.3390/cancers16132352
27. Chambers SK, Hyde MK, Smith DP, et al. New challenges in psycho-oncology research III: A systematic review of psychological interventions for prostate cancer survivors and partners. *Psychooncology* 2017;26:873-913. doi:10.1002/pon.4431
28. Cockle-Hearne J, Faithfull S. Self-management for men surviving prostate cancer: A review of behavioural and psychosocial interventions. *Psychooncology* 2010;19:909-22. doi:10.1002/pon.1657
29. Andrews G, Slade T. Interpreting scores on the Kessler Psychological Distress Scale (K10). *Aust N Z J Public Health* 2001;25:494-7. doi:10.1111/j.1467-842X.2001.tb00310.x
30. Vasiliadis HM, Chudzinski V, Gontijo-Guerra S, et al. Screening instruments for a population of older adults: The K10 and GAD-7. *Psychiatry Res* 2015;228:89-94. doi:10.1016/j.psychres.2015.04.019

31. Thakre MN, Sathe HS, Talapalliwar MR, et al. Psychometric properties of Kessler's Psychological Distress Scale (K10) in cancer patients. *Arch Ment Health* 2022;23:101-6. doi:10.4103/amh.amh104_21
32. MacNevin W, Lukic R, Ilie G, et al. Psychological distress in prostate cancer: Validation of the K10 scale using a crossover randomized clinical trial. *Can Urol Assoc J* 2025;Epub ahead of print. doi:10.5489/cuaj.9294
33. Chang P, Szymanski KM, Dunn RL, et al. Expanded prostate cancer index composite for clinical practice: Development and validation. *J Urol* 2011;186:865-72. doi:10.1016/j.juro.2011.04.085
34. Laviana AA, Hernandez A, Huang LC, et al. Interpretation of domain scores on the EPIC-how does the domain score translate into functional outcomes? *J Urol* 2019;202:1150-8. doi:10.1097/JU.0000000000000392
35. Kurian CJ, Leader AE, Thong MSY, et al. Examining relationships between age at diagnosis and health-related quality of life in prostate cancer survivors. *BMC Public Health* 2018;18:1060. doi:10.1186/s12889-018-5976-6
36. Wille S, Heidenreich A, von Knobloch R, et al. Impact of comorbidities on post-prostatectomy incontinence. *Urol Int* 2006;76:223-6. doi:10.1159/000091623
37. Sun M, Abdollah F, Hansen J, et al. Is a delay in radical prostatectomy safe in low-risk prostate cancer? *J Sex Med* 2012;9:2961-9. doi:10.1111/j.1743-6109.2012.02806.x
38. Lardas M, Liew M, van den Bergh RC, et al. Quality of life outcomes after primary treatment for localized prostate cancer: A systematic review. *Eur Urol* 2017;72:869-85. doi:10.1016/j.eururo.2017.06.035
39. Harju E, Rantanen A, Helminen M, et al. Marital relationship and health-related quality of life in prostate cancer patients and spouses: A longitudinal clinical study. *J Clin Nurs* 2018;27:2633-9. doi:10.1111/jocn.14343
40. Ilie G, Rutledge R, Sweeney E. Anxiety and depression symptoms in adult males in Atlantic Canada with or without prostate cancer. *Psychooncology* 2020;29:280-6. doi:10.1002/pon.5244
41. IBM Corp. IBM SPSS Statistics for Macintosh, version 29.0.2.0. Armonk, NY: IBM Corporation; 2022.
42. Hayes AF. Introduction to mediation, moderation and conditional process analysis. 3rd ed. New York, NY: *Guilford Press*; 2021.
43. European Medicines Agency. Guideline on adjustment for baseline covariates in clinical trials. EMA/CHMP/295050/2013. Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-adjustment-baseline-covariates-clinical-trials_en.pdf. Accessed 2025 Oct 22.
44. Wang L, Luo J, Li Y, et al. Social support, anxiety and depression in patients with prostate cancer: Complete mediation of self-efficacy. *Support Care Cancer* 2022;30:6851-8. doi:10.1007/s00520-022-07065-8
45. Scandurra C, Muzii B, La Rocca R, et al. Social support mediates the relationship between body image distress and depressive symptoms in prostate cancer patients. *Int J Environ Res Public Health* 2022;19:4825. doi:10.3390/ijerph19084825
46. Crump C, Stattin P, Brooks JD, et al. Long-term risks of depression and suicide among men with prostate cancer: A national cohort study. *Eur Urol* 2023;84:263-72. doi:10.1016/j.eururo.2023.04.026
47. Santaliz-Moreno I, Lewis-Thames MW, Khan S, et al. The hidden costs: A qualitative analysis exploring the experience of prostate cancer treatment-related side effects on sexual function and

urinary incontinence among Black survivors and their caregivers. *J Cancer Surviv* 2024;Epub ahead of print. doi:10.1007/s11764-024-01681-5
48. Prostate Cancer Patient Empowerment Program (PC-PEP). Halifax (NS): PC-PEP; c2019-2025. Available at: https://pcpep.org/. Accessed 2025 Nov 12.
49. Nuyens A, Ilie G, Rendon RA, et al. Evaluating the cost-effectiveness of the prostate cancer patient empowerment program: A comprehensive health economic analysis from a randomized controlled trial. *Can Urol Assoc J* 2025;19:E9222. doi:10.5489/cuaj.9222
50. Friberg AS, Brasso K, Larsen SB, et al. Risk of depression after diagnostic prostate cancer workup: A nationwide registry-based study. *Psychooncology* 2021;30:1939-47. doi:10.1002/pon.5766

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FIGURES AND TABLES

Figure 1. CONSORT 2010 participant flow diagram. CONSORT: Consolidated Standards of Reporting Trials; PC-PEP: Prostate Cancer-Patient Empowerment Program.

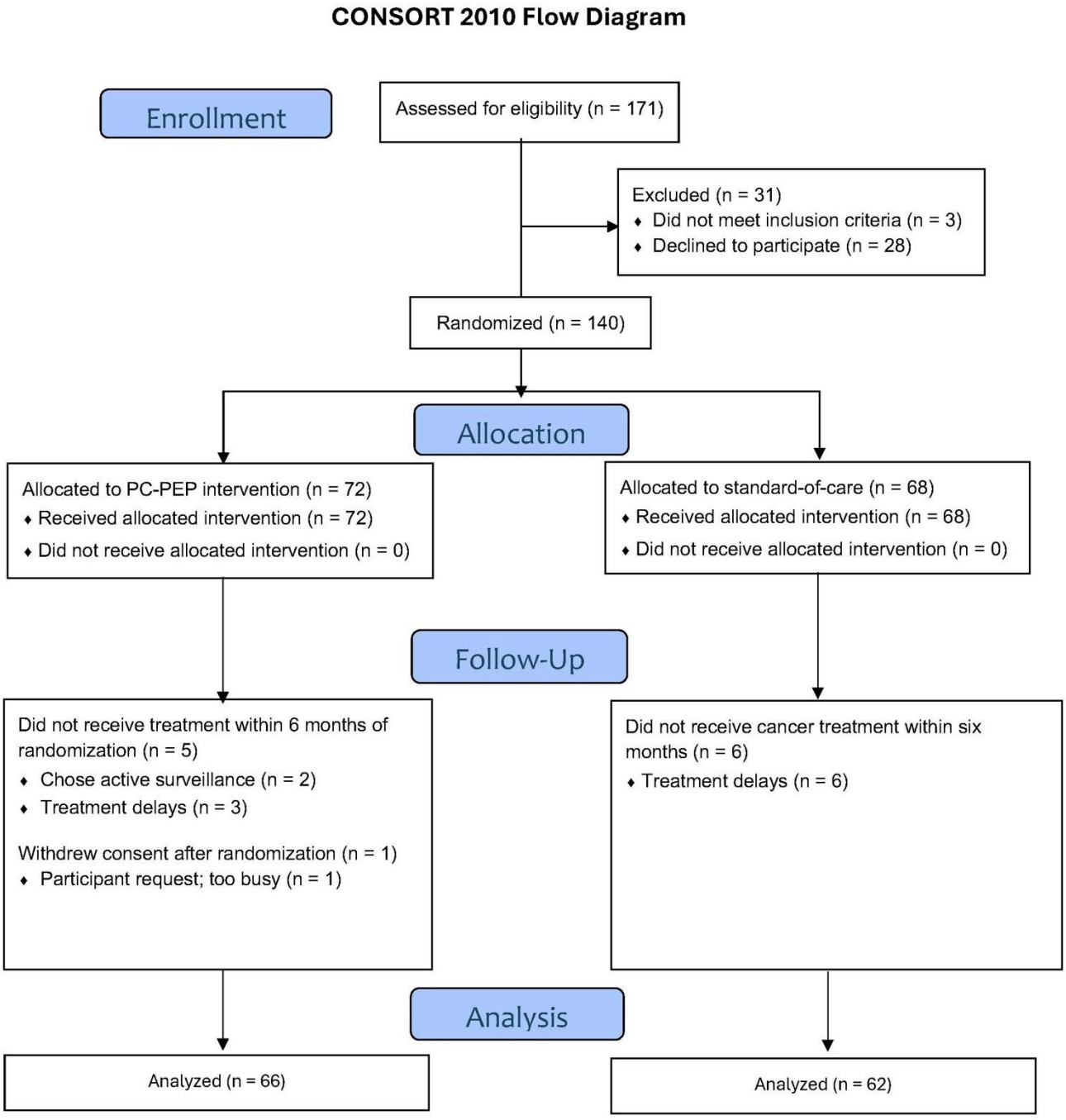


Figure 2. Mediation analysis of the effect of PC-PEP on psychological distress by (A) EPIC urinary incontinence; (B) EPIC urinary irritative/obstructive; and (C) EPIC sexual function scores. Mediation analyses were adjusted for age, Charlson comorbidity index, treatment modality, time between randomization and treatment, relationship status, prescribed medication for depression or anxiety, and baseline K10 and the corresponding EPIC domain score. N=125 for all analyses. b=regression coefficient; CI: confidence interval; EPIC: expanded prostate cancer index composite; K10: Kessler psychological distress scale; PC-PEP: Prostate Cancer-Patient Empowerment Program; SE: standard error.

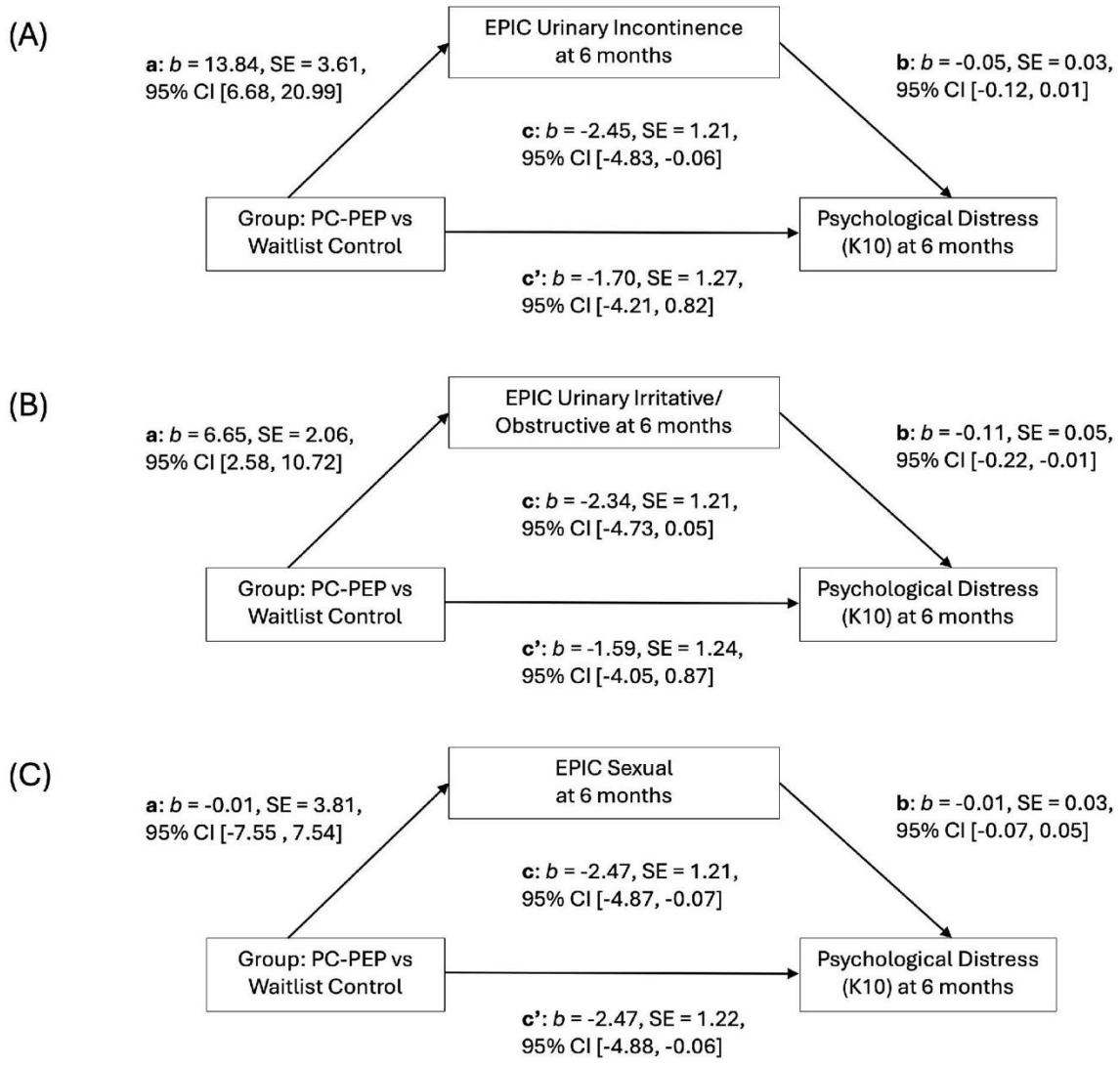
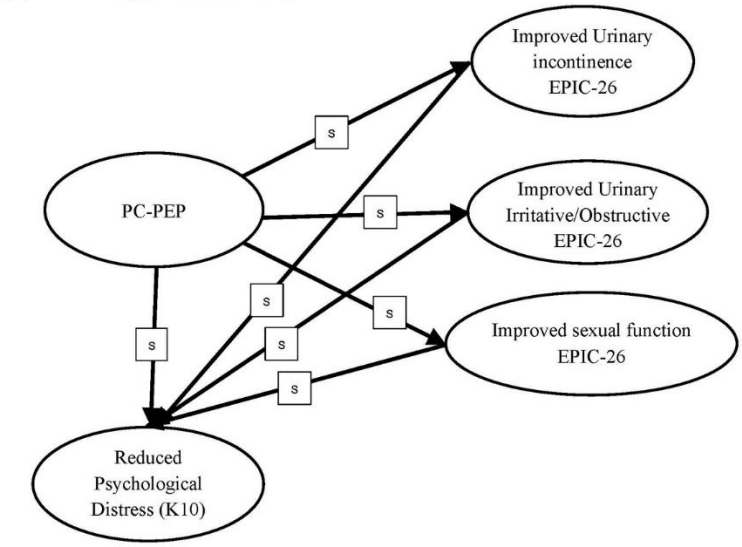


Figure 3. Hypothesized versus observed mediation pathways for the effect of PC-PEP on psychological distress. Panel A depicts the a priori hypothesized pathway in which assignment to PC-PEP improves urinary and/or sexual function (EPIC domains), which in turn reduces psychological distress (K10) at six months. Panel B summarizes the observed results: PC-PEP significantly improved urinary incontinence and urinary irritative/obstructive symptoms in the full cohort and improved sexual function primarily among postoperative participants; however, urinary and sexual function did not significantly predict K10 after adjustment for PC-PEP assignment and covariates, and all bootstrapped indirect effects had confidence intervals that included zero (no mediation). Solid arrows indicate statistically significant associations ($p<0.05$). Dashed arrows indicate non-significant associations ($p>0.05$). Indirect effects were considered non-significant when bootstrapped 95% confidence intervals included zero. EPIC: expanded prostate cancer index composite; PC-PEP: Prostate Cancer-Patient Empowerment Program.



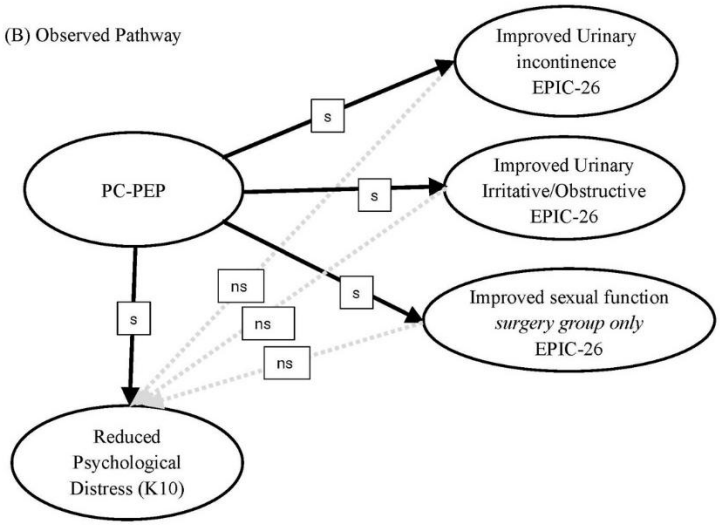


Table 1. Sample baseline characteristics comparison between the PC-PEP intervention and waitlist control groups among 128 prostate cancer patients undergoing curative-intent treatment in Nova Scotia, Canada

	PC-PEP, median (quartile) n, % (n=66)	**Waitlist control, median (quartile) n, % (n=62)**	**p**
Age (years)	66, 66 (60, 70)	62, 68 (61, 72)	0.2
Body mass index	66, 29 (24, 34)	62, 27 (23, 31)	0.5
Household income at baseline, >$30 000 CAD/past year	54, 82%	52, 84%	0.5
Race, white	60, 91%	61, 98%	0.068
Education, university or above	31, 47%	37, 60%	0.16
Employed (part- of full-time)	22, 33%	23, 37%	0.7
Charlson comorbidity index	66, 2 (2, 3)	62, 3 (2, 3)	0.5
Treatment modality			0.6
RP	29 (44%)	33 (53%)	
RT	27 (41%)	27 (44%)	
Salvage RT[a]	10, (15%)	2, 3%	
Prescribed ADT	27, 41%	21, 34%	
Time between randomization and RP or RT (including salvage) treatment (days)	66, 61 (34, 99)	62, 73 (29, 101)	0.3
Relationship status (currently in a relationship)	59 (89%)	61 (98%)	0.063
Prescribed medication for anxiety, depression, or both	12 (18%)	7 (11%)	0.3
Mediator and outcome scores			
Psychological distress sum score (K10)	66, 14 (12, 16)	62, 15 (12, 18)	0.7
EPIC urinary incontinence	66, 100 (92, 100)	62, 100 (90, 100)	0.7
EPIC irritative/obstructive	66, 94 (81, 100)	62, 94 (81,100)	0.4
EPIC sexual	66, 62 (30, 80)	62, 61 (36, 83)	0.9

Summary statistics are reported as n, median (interquartile percentages) for continuous variables, and n (%) for categorical variables. [a]The radiation therapy and salvage radiation groups were pooled together to allow for meaningful comparisons. ADT: androgen deprivation therapy; EPIC: expanded prostate cancer index composite. K10: Kessler psychological distress scale RP: radical prostatectomy; RT: radiation therapy.

Table 2. Mediation analysis of the association between PC-PEP and psychological distress at six months								
	Total			**Direct**			**Indirect**	
Mediator	**Effect size (95% CI)**	**SE**	**p**	**Effect size (95% CI)**	**SE**	**p**	**Effect size (95% CI)**	**SE**
EPIC urinary incontinence	-2.45 (-4.83, 0.06)	1.21	0.045	-1.70 (-4.21, 0.82)	1.27	0.18	-0.75 (-1.94, 0.09)	0.52
EPIC urinary obstructive	-2.34 (-4.73, 0.05)	1.21	0.055	-1.59 (-4.05, 0.87)	1.24	0.2	-0.75 (-2.22, 0.30)	0.65
EPIC sexual	-2.47 (-4.87, -0.07)	1.21	0.044	-2.47 (-4.88, -0.06)	1.22	0.045	0.0001 (-0.23, 0.31)	0.13

Psychological distressed sum scores measured with Kessler psychological distress scale (K10) at 6 months post-intervention. Mediation analyses were adjusted for prognostic covariates (age, Charleson comorbidity index, treatment modality, time between randomization and treatment, relationship status, prescribed medication for depression, anxiety, or both), and baseline sum K10 and EPIC scores (for the respective analysis). N=125 for all analyses. CI: confidence interval; EPIC: expanded prostate cancer index composite; SE: standard error.