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Examining the impact of androgen deprivation therapy, masculine self-esteem, and psychological flexibility on distress and quality of life in men with prostate cancer

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Abstract

Objective: Studies suggest that androgen deprivation therapy (ADT) exacerbates psychological and quality of life (QoL) issues associated with prostate cancer (PCa). However, quantitative research examining underlying psychosocial mechanisms for this is limited. We examined the association of PCa symptoms with distress and QoL in ADT-treated and ADT-naïve patients, and the influence of masculine self-esteem and psychological flexibility (PF) on these relationships.

Methods: Secondary analysis of a quantitative, cross-sectional survey of 286 PCa patients. Independent samples *t*-tests, moderation, and conditional process analysis were used to assess relationships between predictor, mediator, moderator, and outcome variables.

Results: ADT was associated with greater PCa symptomology, lower masculine self-esteem, and lower QoL. Moderation analysis showed that ADT potentiated adverse impacts of PCa symptomology on distress and QoL. High PF attenuated these relationships, though less so for ADT-treated participants. Conditional process analysis showed that masculine self-esteem mediated the predictive effect of symptoms on distress across treatments. However, ADT did not moderate this indirect effect, nor was moderation conditional on PF.

Conclusion: PF appears to: (1) attenuate psychological distress in ADT patients; and (2) improve distress, QoL, and masculine self-esteem in ADT-naïve patients. Interventions targeting PF may thus be a viable adjunct to established approaches. However, their effects may be comparatively limited in ADT patients, who may benefit from more intensive and tailored treatment.

KEYWORDS

acceptance and commitment therapy, androgen deprivation therapy, cancer, masculine self-esteem, oncology, prostate cancer, psychological flexibility

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1 | BACKGROUND

Androgen deprivation therapy (ADT), involving surgical or pharmaceutical suppression of testosterone, is the most common treatment for advanced prostate cancer (PCa).¹ Despite survival benefits, ADT is associated with adverse side effects, including cardiometabolic, neurocognitive, and sexual dysfunction.² Moreover, large-scale and longitudinal studies link it to long-term reductions in quality of life (QoL),³ particularly physical functioning,⁴ and to increased risk of depression relative to other PCa treatments.^{5,6}

Increasingly, research suggests that PCa and ADT affect mental health and QoL through masculinity-related psychosocial mechanisms.^{7,8} The well-documented impact of ADT on self-appraisal of masculinity, or masculine self-esteem, relates to changes in attributes traditionally associated with masculinity (e.g. gynecomastia, reduced libido),⁹ with patients reporting compromised body image and perceived loss of masculinity secondary to such changes.^{9,10} Importantly, masculine self-esteem impacts distress and QoL in PCa patients.^{11,12} While this phenomenon is observed across PCa treatments,⁸ it has been suggested that the constellation of symptoms associated with ADT may be especially disruptive.¹³

Difficulties adjusting to ADT-related changes appear to be linked to avoidant coping behaviours (e.g. social withdrawal, concealment of physical features) and attempts to maintain pretreatment social identity.¹⁴ Conversely, a growing body of qualitative research suggests that flexibility in masculine identity, values and coping improves psychosocial adjustment in this group.^{7,8} Accordingly, it has been suggested that psychosocial interventions for PCa could foster this, with psychological flexibility (PF) being a potential psychotherapeutic target.⁷ PF is the mechanism of action of Acceptance and Commitment Therapy (ACT),^{15,16} describing the ability to remain open and accepting to unpleasant internal and external experiences while adapting in accordance with personal values.¹⁷ Preliminary evidence suggests that PF not only improves mental well-being and QoL in mixed cancers,¹⁸ but also buffers masculinity-related distress in PCa patients.¹⁹ Given hallmarks of inflexibility observed in ADT, PF could putatively confer resilience to ADT-related distress and reduced masculine self-esteem.

The present study examined the effect of PCa symptomology—overall and as mediated by masculine self-esteem—on psychological distress and QoL in ADT-treated and ADT-naïve patients. Specifically, it assessed whether negative effects of PCa symptoms on masculine self-esteem, distress, and QoL are exacerbated for ADT patients, and whether high PF buffers these negative effects. We hypothesised that:

Hypothesis 1 (H1). Higher levels of PCa symptoms predict increased distress and reduced QoL.

Hypothesis 2 (H2). The relationships in H1 will be strengthened in men undergoing ADT.

Hypothesis 3 (H3). The relations hypothesised in H2 will be attenuated by higher PF.

Hypothesis 4 (H4). The adverse effect of PCa symptoms on distress will be mediated by reduced masculine self-esteem.

Hypothesis 5 (H5). The relationships in H4 will be strengthened in men undergoing ADT.

Hypothesis 6 (H6). The relationships in H5 will be attenuated by higher PF.

2 | METHODS

2.1 | Participants

Data for the present secondary analysis were obtained from a study examining the effects of psychological predictors on distress and QoL in PCa patients.¹⁹ Inclusion criteria was to have a diagnosis of PCa. There were no exclusion criteria. 311 participants completed an online questionnaire, all of whom were eligible.

2.2 | Procedures

The design of the parent study, described in-depth elsewhere,¹⁹ is briefly summarised. A quantitative, cross-sectional design was employed. Each participant completed an online survey at a single point in time. The survey contained clinical and demographic questions, and self-report measures of PCa symptoms, masculine self-esteem, distress, QoL, and PF. Surveys were distributed through UK-based PCa charities and support groups. Both the original study and the re-analysis was approved by University of Edinburgh's School of Health in Social Science Research Ethics Committee. Participants provided informed consent.

2.2.1 | Measures

Demographics

Participants self-reported demographic information, including age, employment, marital status, and disease stage.

Androgen deprivation therapy (ADT)

In response to the question “Please indicate which, if any, of the following treatments you have had for your prostate cancer”, participants could choose from 10 options. Those who self-reported either “Hormone Treatment” or “Novel Hormone Treatment (e.g. Abiraterone; Enzalutamide)” were categorised as ADT-treated, and as ADT-naïve otherwise.

*Depression anxiety and stress scale—Short version (DASS-21)*²⁰

The DASS-21 consists of 21 items and three scales measuring symptoms of depression, anxiety and stress, from which a total score for distress is calculated.²⁰ Items are scored using a 4-point Likert scale ranging from 0 (“Did not apply to me at all”) to 3 (“Applied to me very much”).²⁰ The DASS-21 has shown high internal consistency and validity in cancer populations.²⁰ In the current study, reliability was $\alpha = 0.95$.

*The functional assessment of cancer therapy—General (FACT-G)*²¹

The FACT-G, a 39-item questionnaire comprising four subscales—physical, functional, social and emotional well-being—, measures health-related QoL in cancer patients.²¹ Items are assessed on a 5-point Likert scale from 0 (“Not at all”) to 4 (“Very much”).²¹ It has demonstrated good content validity, internal consistency and reliability.²² In the current study, reliability was $\alpha = 0.92$.

*Prostate cancer symptoms (FACT-P)*²²

The FACT-P comprises 12 items measuring symptoms specific to PCa, scored on a 5-point Likert scale ranging from 0 (“Not at all”) to 4 (“Very much”).²² Example items include “I am losing weight” and “I have difficulty urinating”.²⁰ It has shown acceptable validity.²² In the current study, reliability was $\alpha = 0.79$.

*Comprehensive assessment of acceptance and commitment therapy processes measure (CompACT)*²³

The compACT is a 23-item self-report scale comprising three subscales—openness to experience, behavioural awareness, and valued action—and measures overall PF.²³ Items are scored on a 7-point Likert scale ranging from 0 (“Never true”) to 6 (“Always true”). It has demonstrated superior face and content validity compared to other measures of PF.²³ In the current study, reliability was $\alpha = 0.89$.

*Masculine self-esteem scale (MSE)*²⁴

The masculine self-esteem scale is an 8-item scale used to assess PCa patient’s appraisal of their masculinity.²⁴ Example items include “I feel as if I am no longer a whole man” and “I feel I have been too emotional”.²⁴ Each item is scored on a 5-point Likert scale from 1 (“Strongly disagree”) to 5 (“Strongly agree”). It has demonstrated good validity and internal consistency.²⁵ In the current study, reliability was $\alpha = 0.91$.

2.3 | Statistical analysis

Data analyses were performed using SPSS v25, and moderation and conditional process models tested using PROCESS Macro v3²⁶. Based on Bennett’s²⁷ guidelines for missing data, the parent study excluded cases where over 10% of data was missing, yielding a final sample of 286, with the proportion of remaining missing data being 0.14%; subsequent assessment of pattern of missingness using MCAR test

indicated that data were missing at random, and expectation-maximisation was used to impute missing data.^{19,28}

Hypotheses were tested in three stages. First, mean differences between ADT-treated and ADT-naïve participants for predictor and outcome variables were assessed using independent samples *t*-tests. Second, using two moderated-moderation models (Figure 1A–B) to test H1–H3, we assessed the effect of PCa symptoms on distress and QoL, whether this was moderated by ADT, and whether moderation by ADT was moderated by PF. Finally, using moderated-mediation (Figure 1C) and moderated-moderated-mediation (Figure 1D) models to test H4–H5 and H6, respectively, we assessed whether the effect of PCa symptoms on distress was mediated by changes to masculine self-esteem, whether this indirect effect was moderated by ADT, and whether moderation of the indirect effect by ADT was moderated by PF. Conditional effects and two-way interactions were probed using the pick-a-point approach,²⁶ with moderation by ADT conditioned at the 16th (“low” PF = 72), 50th (“moderate” PF = 94), and 84th (“high” PF = 109) percentiles of PF. Bootstrap resampling (10,000 samples) was used to estimate 95% confidence intervals.

3 | RESULTS

3.1 | Sample characteristics

In the current sample, mean age was 67 (*S.D.* = 7.81), and mean time since diagnosis 4.9 years (*S.D.* = 4.73). Participants were diagnosed with early stage (58.2%), locally advanced (29.6%) or advanced PCa (10.8%). 41.5% of participants had undergone ADT. Comprehensive demographic profiles and descriptive statistics for study measures are outlined elsewhere.¹⁹

3.2 | Demographic and covariate analysis

Analysis of variance (ANOVA) was conducted to inspect mean differences between demographic groups for outcome variables. Significant differences were observed for age, with men under 60 demonstrating higher distress than ages 70–75, and lower QoL than men over 60. Thus, age was entered as a covariate.

3.3 | Comparison of means

Independent samples *t*-tests were conducted to examine whether ADT-treated and ADT-naïve participants differed with respect to predictor and outcome variables. ADT-treated patients had significantly higher PCa symptoms (mean, 16.3; *S.D.*, 7.7 vs. mean, 14.3, *S.D.*, 7.8) ($t = 2.11, p < 0.05$), lower masculine self-esteem (mean, 26.9; *S.D.*, 7.5 vs. mean, 29.0, *S.D.*, 7.3) ($t = -2.43, p < 0.05$), and lower QoL

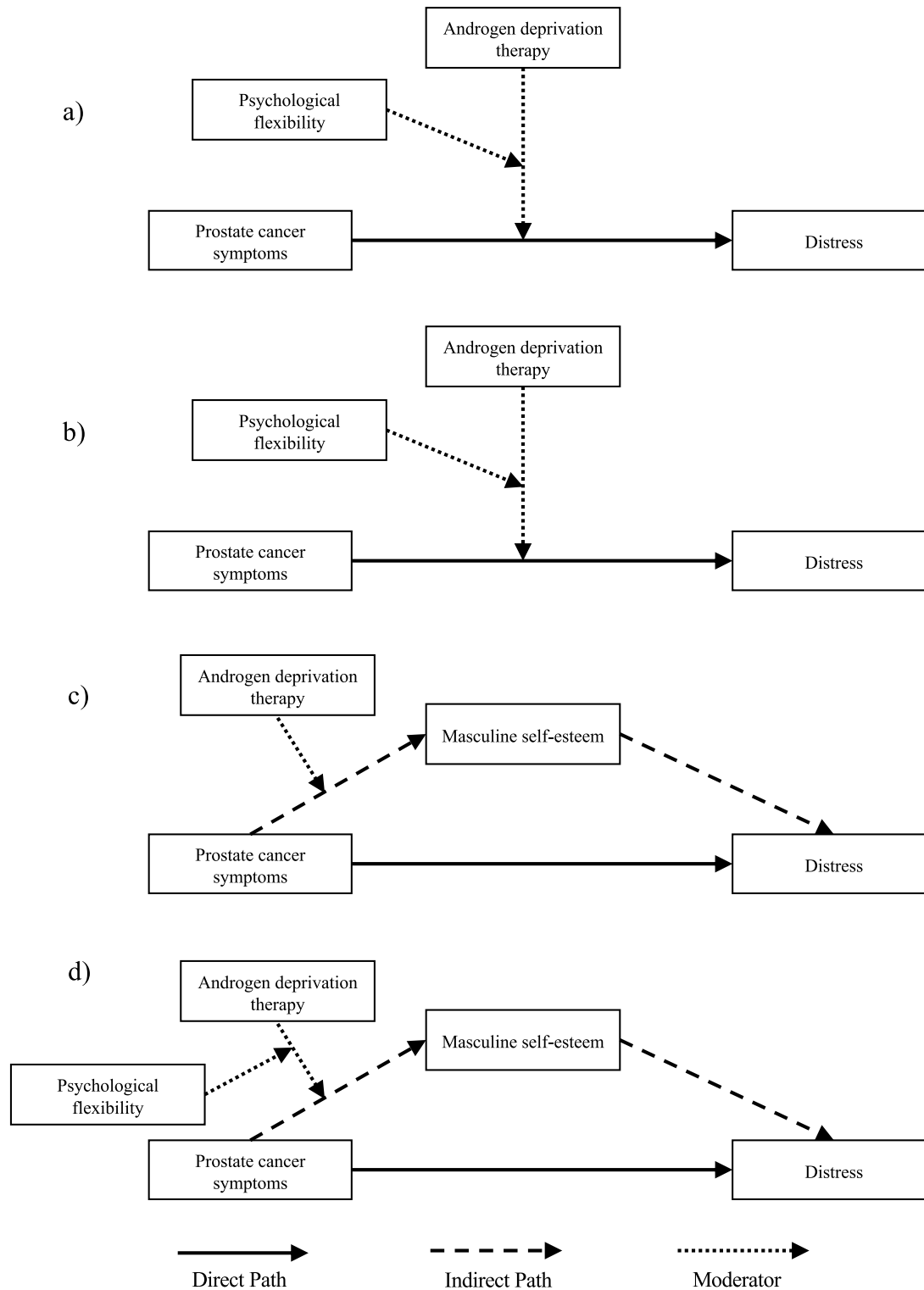


FIGURE 1 Conceptual diagrams of moderated-moderation models for distress (A) and QoL (B), moderated-mediation model for distress (C), and moderated-moderated-mediation model for distress (D).

(mean, 78.6; *S.D.* 17.3 vs. mean, 82.9; *S.D.*, 17.2) ($t = -2.08, p < 0.05$). ADT-treated patients (mean, 23.5; *S.D.*, 25.5) did not differ significantly from ADT-naïve patients (mean, 22.0; *S.D.*, 24.1) in distress

($t = 0.49, p = 0.62$), nor did ADT-treated patients (mean, 92.9; *S.D.*, 19.0) differ from ADT-naïve patients (mean, 90.6; *S.D.*, 18.8) in PF ($t = 0.99, p = 0.33$).

3.4 | Moderation analysis

The moderated-moderation model predicting distress accounted for 66% of the variance in distress ($R^2 = 0.66$, $F_{(8, 277)} = 66.89$, $p < 0.001$). Supporting H1, there was a significant positive association between PCa symptoms and distress. Moderation of this association by ADT was additionally conditional on PF. However, ADT did not moderate the predictive effect of PCa symptoms on distress for men low in PF, and moderation of this relationship by ADT was strengthened rather than attenuated at high PF. As such, H2 and H3 were not supported. Probing of conditional effects revealed that the association between PCa symptoms and distress was non-significant at high PF for ADT-naïve participants, but remained significant at high PF for ADT-treated participants.

The moderated-moderation model predicting QoL accounted for 66% of the variance in QoL ($R^2 = 0.66$, $F_{(9, 276)} = 58.89$, $p < 0.001$). Supporting H1, there was a significant negative association between PCa symptoms and QoL. Moderation of this association by ADT was also conditional on PF. However, ADT did not moderate the predictive effect of PCa symptoms on QoL for men low in PF, and moderation of this relationship by ADT was strengthened rather than attenuated at high PF. As such, H2 and H3 were not supported. Probing of conditional effects revealed that with increasing PF there was a greater reduction in the association of symptoms with QoL for ADT-naïve compared to ADT-treated participants, though the association remained significant at high PF for both groups.

Coefficients and 95% confidence intervals for main, interaction, and conditional effects for both models are presented in Table 1. Simple slopes depicting interaction effects for both models are presented in Figure 2.

3.5 | Conditional process analysis

The moderated-mediation model predicting distress accounted for 54.13% of the variance in distress ($R^2 = 0.54$, $F_{(3, 282)} = 110.94$, $p < 0.001$). The impact of PCa symptoms on distress was mediated by reduced masculine self-esteem for both ADT-treated and ADT-naïve participants, supporting H4. While increased symptoms were associated with a greater reduction in masculine self-esteem for ADT patients, the two-way interaction between symptoms and ADT was non-significant. Additionally, the index of moderated-mediation ($b = 0.12$, 95% $CI = -0.17, 0.38$) did not support potentiation by ADT of the indirect effect of symptoms on distress through masculine self-esteem. As such, H5 was not confirmed.

The moderated-moderated-mediation model predicting distress accounted for 46.84% of the variance in distress ($R^2 = 0.47$, $F_{(8, 277)} = 30.50$, $p < 0.001$). Significant indirect effects through masculine self-esteem on distress were observed in both ADT-treated and ADT-naïve participants across all levels of PF. Moreover, with increasing PF, a greater reduction in both the negative effect of PCa symptoms on masculine self-esteem and overall indirect effect on distress was observed for ADT-naïve compared to ADT-treated

participants. However, the three-way interaction between symptoms, ADT, and PF was non-significant, and the index of moderated-moderated-mediation ($b = 0.01$, 95% $CI = -0.003, 0.02$) did not support moderation of the indirect effect by ADT being conditional on PF. As such, H6 was not confirmed. Path diagrams for both models are depicted in Figure 3.

4 | DISCUSSION

To date, research examining the impact of masculine identity and flexible coping on psychosocial adjustment in ADT patients has largely been qualitative. Extending these findings, the current study quantitatively assessed the influence of ADT, masculine self-esteem, and PF on distress and QoL in PCa patients.

ADT patients exhibited higher PCa symptoms, lower masculine self-esteem, and lower QoL compared to ADT-naïve counterparts. As hypothesised, increased PCa symptoms predicted greater psychological distress and lower QoL, and ADT magnified these associations in a manner contingent on PF. Contrary to predictions however, potentiation by ADT occurred at high rather than low PF, as high PF buffered the negative impact of symptoms on distress and QoL less in patients undergoing ADT.

Our findings align with prior evidence highlighting the negative impact of PCa symptoms on distress and QoL,^{29,30} and the benefits of PF¹⁷ and its sub-components³¹ in PCa patients. A novel finding of our study was that PF attenuated PCa-related distress and QoL issues less in ADT-treated participants. This could reflect the overall severity of ADT-related symptoms and a reduction in global QoL.³² Alternatively, ADT could be causally associated with depression, either directly through putative mechanisms related to testosterone deficiency,⁵ or through downstream effects of symptoms, for example, depression secondary to hot flash-induced insomnia.⁹ As ADT strongly affects physical QoL,^{3,4} results could also reflect an inability of PF to buffer objective indices of physical impairment, as physical comorbidities have been shown to predict QoL independent of PF-related constructs in PCa patients.³¹ This could also explain why the impact of symptoms on QoL remained significant at high PF for both groups. Further research is needed to elucidate the mechanisms underlying ADT-related distress and depression, and to examine the impact of ADT on subdomains of QoL.

Another potential explanation for increased distress in ADT is that its side effects cause greater masculinity-related distress in men struggling to flexibly appraise their identity. Conditional process analysis confirmed that symptoms impacted distress via reduced masculine self-esteem across treatments, consistent with extensive evidence highlighting distress experienced by PCa patients secondary to masculinity concerns.⁸ However, despite being associated with lower mean levels of masculine self-esteem, ADT did not magnify the association between symptoms and reduced masculine self-esteem or the downstream effects of this on psychological distress. Moreover, moderation of these relationships by ADT was not contingent on PF, and non-significant amongst men low in PF. However, probing

TABLE 1 Coefficients and 95% confidence intervals for moderated-moderation models predicting distress and QoL.

Model predicting distress		coeff	se	t	p	LLCI	UCLI
PCS		5.46	0.71	7.72	<0.001	4.07	6.85
PCS × ADT		−2.02	1.06	−1.90	0.06	−4.11	0.08
PCS × ADT × PF		0.03	0.01	2.14	0.03	0.002	0.05
Age (banded)		−1.52	0.57	−2.67	0.01	−2.64	−0.40
Test of conditional “PCS × ADT” interaction at the 16 th and 84 th percentile of psychological flexibility							
PF	Effect	F	df1	df2	p		
Low	−0.21	0.43	1.00	277.00	0.51		
High	0.72	3.89	1.00	277.00	0.05		
Conditional effects of prostate cancer symptoms on distress at values of the moderators							
ADT	PF	Effect	se	t	p	LLCI	ULCI
No	Low	1.90	0.21	9.19	<0.001	1.49	2.30
No	Moderate	0.81	0.18	4.51	<0.001	0.45	1.16
No	High	0.06	0.24	0.26	<0.80	−0.42	0.54
Yes	Low	1.69	0.25	6.68	<0.001	1.19	2.18
Yes	Moderate	1.14	0.21	5.49	<0.001	0.73	1.55
Yes	High	0.78	0.27	2.90	0.004	0.25	1.30
Model predicting QoL		Coeff	se	t	p	LLCI	ULCI
PCS		−2.65	0.50	−5.30	<0.001	−3.63	−1.67
PCS × ADT		1.56	0.75	2.07	0.04	0.08	3.04
PCS × ADT × PF		−0.02	0.01	−2.35	0.02	−0.04	−0.003
Age (banded)		1.63	0.40	4.04	<0.001	0.84	2.43
Test of conditional “PCS × ADT” interaction at the 16 th , 50 th , and 84 th percentile of psychological flexibility							
PF	Effect	F	df1	df2	p		
Low	0.16	0.47	1.00	276.00	0.50		
High	−0.56	4.76	1.00	276.00	0.03		
Conditional effects of prostate cancer symptoms on QoL at values of the moderators							
ADT	PF	Effect	se	t	p	LLCI	ULCI
No	Low	−1.30	0.15	−8.95	<0.001	−1.59	−1.02
No	Moderate	−0.89	0.13	−7.06	<0.001	−1.14	−0.64
No	High	−0.61	0.17	−3.56	<0.001	−0.96	−0.27
Yes	Low	−1.15	0.18	−6.36	<0.001	−1.50	−0.79
Yes	Moderate	−1.16	0.15	−7.69	<0.001	−1.46	−0.86
Yes	High	−1.17	0.19	−6.08	<0.001	−1.55	−0.79

Note: Low PF = 72 (16th percentile), moderate PF = 94 (50th percentile), high PF = 109 (84th percentile).

Abbreviations: ADT, androgen deprivation therapy; LLCI, lower limit confidence interval; ULCI, upper limit confidence interval; PCS, prostate cancer symptoms; PF, psychological flexibility; QoL, quality of life.

of conditional effects and interactions revealed differences between ADT-treated and ADT-naïve participants in attenuation of the indirect effect by high PF.

The above findings indicate that undergoing ADT does not necessarily result in greater distress secondary to masculinity

concerns. However, given that undergoing ADT was associated with reduced masculine self-esteem, our results do not preclude the possibility that masculinity concerns are exacerbated in ADT, suggesting instead that this may not be a meaningful determinant of treatment-related differences in distress. Alternatively, differences in

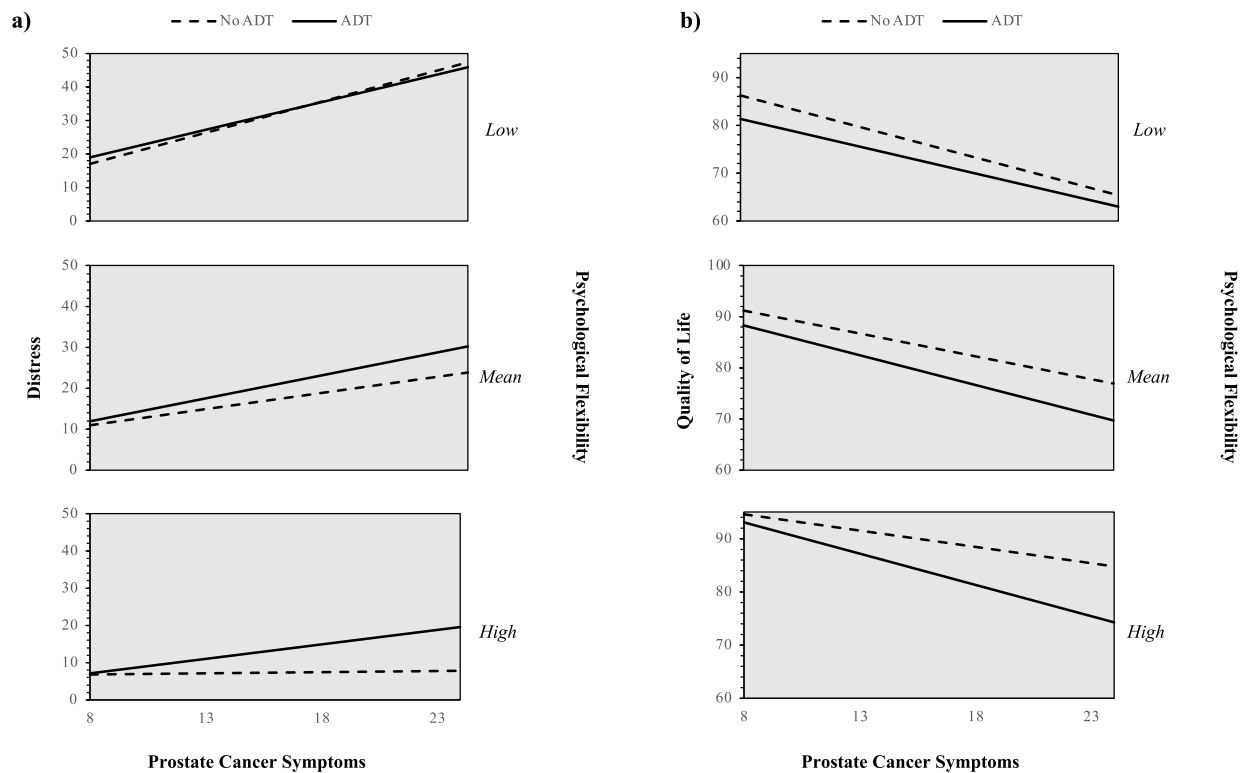


FIGURE 2 Three-way Interaction Effects for (A) Distress, and (B) Quality of Life. ADT, androgen deprivation therapy.

masculinity-related distress might have been more apparent in the presence of factors that interact with masculinity to influence psychosocial adjustment, for example, younger age,¹³ a consideration for future studies. Additionally, the Masculine Self-esteem scale²⁴ may not have adequately captured all aspects of masculinity, having previously been shown to result in a conflation of masculinity with sexual performance in PCa patients.³³ A measure with greater sensitivity to distinct facets of masculinity, such as the Masculinity in Chronic Disease Inventory (MCD-I),^{33,34} might better capture these relationships. While the extent of masculinity-related distress observed for low PF participants was similar across treatments, there was a discrepancy between treatments in attenuation of this by high PF, which appeared substantial for ADT-naïve yet negligible for ADT-treated participants. This finding should be interpreted cautiously given the non-significant three-way interaction and index of moderated-moderated-mediation,³⁵ but could tentatively suggest that PF does not buffer masculinity-related distress to the same extent in ADT patients. This could putatively reflect the severity of masculinity threatening symptoms associated with ADT.

4.1 | Clinical implications

Our results suggest that psychological interventions such as ACT that target PF may have therapeutic value for PCa, particularly in ADT-naïve patients. Given that ACT has shown efficacy in other clinical

populations in group-based and time-limited interventions,¹⁸ it could serve as an adjunct to existing treatments. However, our findings also indicate that ACT may improve psychological distress but have limited therapeutic benefit for QoL and masculine self-esteem in ADT patients, who may instead require other types of interventions for their psychosocial needs. This underscores the need for further research into underlying mechanisms and potential interventions, and reaffirms the importance of informed decision-making prior to treatment.³⁶

4.2 | Limitations

This study has several limitations. First, its cross-sectional nature precludes causal inference. As several of the variables assessed are likely subject to change over time, longitudinal research is needed to provide further insights. Second, study procedures such as self-report measures and convenience sampling have potential to introduce bias. Third, PF was assumed to accurately capture the kind of flexible coping that has been described in qualitative studies of PCa.⁸ Though support for this idea exists,⁷ it remains to be established. Fourth, we did not gather information on time since commencement, duration, or modality of ADT, and did not assess the impact of disease stage or primary treatment (e.g. active surveillance, prostatectomy, radiotherapy). These treatment-related factors may influence psychological and QoL-related outcomes in PCa patients,^{30,37,38} and

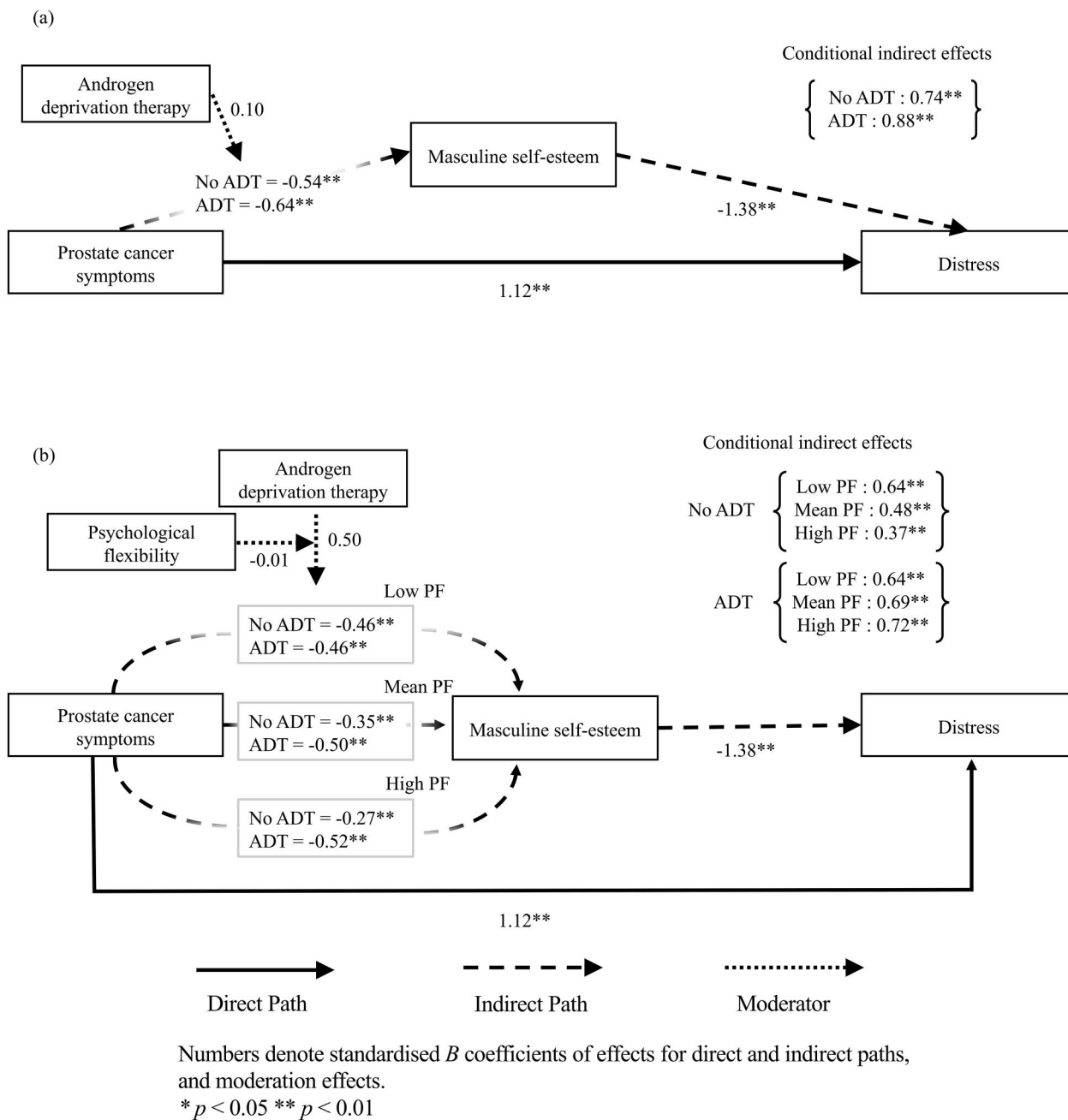


FIGURE 3 Path Diagram of (A) Moderated-Mediation, and (B) Moderated-Moderated-Mediation. ADT, androgen deprivation therapy; PF, psychological flexibility.

thereby alter the kinds of relationships tested in this study. Fifth, as previously noted, the Masculine Self-Esteem scale²⁴ might not adequately capture broad facets of masculinity. Future studies should consider alternative measures such as the MCD-I,³⁴ which has undergone extensive psychometric evaluation in men with PCa.³³ Finally, several antiandrogens that are employed in combination with ADT for PCa have been approved in the years following the collection of our dataset,³⁸ and our analysis does not reflect these developments. Given these limitations, our findings may be considered preliminary and suggestive of directions for future research in this area.

5 | CONCLUSION

The current study contributes to the extant literature with several important insights regarding the effects of ADT, masculine self-esteem, and PF on psychosocial adjustment in PCa patients. PF appears to attenuate the impact of symptoms on distress in patients undergoing ADT and otherwise, and to improve QoL and masculine self-esteem in ADT-naïve patients. Our findings also highlight challenges related to QoL and masculinity in ADT, reaffirming the importance of adequate psychosocial support. ACT may thus have therapeutic utility in PCa patients, but may potentially be more

effective for ADT-naïve patients. Further studies are needed to elucidate the mechanisms underlying ADT-related distress, masculinity, and QoL issues, in order to adequately address the psychosocial needs of this group.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are not publicly shared due to ethical restrictions.

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