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# Exercise intervention and sexual function in advanced prostate cancer: a randomised controlled trial

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## ABSTRACT

**Objectives** Treatments for prostate cancer such as androgen deprivation therapy (ADT), surgery and radiation therapy can adversely affect sexual, urinary and bowel function. Preliminary research has demonstrated the efficacy of exercise to preserve sexual function in men with localised prostate cancer receiving ADT, though this has yet to be investigated in a metastatic setting. We examined the effects of a 12-week exercise programme comprising resistance, aerobic and flexibility training on sexual health and function in men with advanced prostate cancer.

**Methods** Patients with prostate cancer (70.0±8.4 year; body mass index 28.7±4.0 kg/m<sup>2</sup>) with bone metastases (rib/thoracic spine, 66.7%; lumbar spine, 43.9%; pelvis, 75.4%; femur, 40.4%; humerus, 24.6%; other sites, 70.2%) were randomly assigned to supervised exercise 3 days/week (n=28) or usual care (n=29). Sexual health and function were assessed using the International Index of Erectile Function, the Expanded Prostate Cancer Index Composite and the EORTC-PR25 at baseline and 12 weeks.

**Results** Patients attended 89% of planned sessions and there were no adverse events. After adjusting for baseline values, there was no significant difference between groups for any measure of sexual function and activity (p>0.05). Additionally, there was no significant difference between groups for urinary and bowel function assessed by the EORTC-PR25 (p>0.05).

**Conclusions** A short-term programme of supervised exercise does not appear to enhance indices of sexual health and function in men with advanced prostate cancer. Limitations of the intervention included the conservative modular exercise programme, which deliberately avoided loading bone metastatic sites.

**Trial registration number** ACTRN12611001158954.

## BACKGROUND

Treatments for prostate cancer (PCa) such as androgen deprivation therapy (ADT), surgery and radiation therapy can adversely affect sexual, urinary and bowel function that may persist for years following cessation of treatment. The psychosexual burden on individuals with PCa is complex, impacted by the physical result of erectile dysfunction, in addition to the psychosocial impact of reduced sexual function, including shame, depression, loss of intimacy and so on.<sup>1</sup> Prior research supports the use of exercise as an effective countermeasure to many of the treatment-related toxicities experienced in men with PCa, though research in regards to exercise and sexual function in this area remains sparse. Nevertheless, higher levels of physical activity have been demonstrated to be significantly associated with better sexual functioning in men with PCa following radiotherapy.<sup>2</sup> Moreover, our group has previously demonstrated the ability of exercise to preserve sexual function in men with localised and locally advanced PCa receiving ADT.<sup>3</sup> However, the effects of exercise on sexual function in men with PCa in a metastatic setting have yet to be investigated.

We recently reported the findings from an exercise trial undertaken in patients with PCa with bone metastases in which self-reported improvements in physical function and objectively measured lower body strength resulted.<sup>4</sup> Here we report the effects of the 3-month multimodal exercise programme on sexual activity in this same patient cohort.

## METHODS

### Participants and recruitment

As previously reported,<sup>4</sup> 103 patients with PCa with established bone metastases were referred by their oncologist

or urologist to participate, with 57 patients enrolled in the trial. Individuals were excluded if they had any conditions that precluded safe exercise, or if patients were currently participating in structured exercise. The main reasons for exclusion were patients declined to participate (n=16), travel constraints/proximity to exercise site (n=9), other commitments (n=6), physician declined approval (n=5) and bone pain (n=5). Informed consent was obtained from all participants and the study was approved by the University Human Research Ethics Committee.

#### Study design and random assignment

This was a two-armed prospective randomised controlled trial.<sup>4</sup> Assessments of body composition (dual-energy X-ray absorptiometry), physical function, psychosocial measures and blood biomarkers were obtained at baseline and after the 12-week intervention. Following baseline assessments, patients were randomised in a ratio of 1:1 to either exercise or usual care using a computer-generated random assignment programme.

#### Exercise training programme

Details of the exercise programme have been described in detail elsewhere.<sup>4</sup> Briefly, the programme was undertaken three times per week in an exercise clinic for ~60 min, supervised and comprised resistance, aerobic and flexibility exercise, using a modular approach with extent/location of bone metastases taken into account to avoid loading of the affected sites. Resistance exercise targeted major upper and lower body muscle groups involved three sets at 10–12 repetition maximum intensity, using exercises (such as chest press, seated row, triceps extension, biceps curl, leg extension and leg curl) tailored to the individual in relation to metastases sites. Aerobic exercise involved 20–30 min at 60%–85% estimated maximal heart rate using modes such as walking and cycling, while flexibility training involved static stretching of the major muscle groups.

#### Outcomes

Outcome measures were erectile function using the International Index of Erectile Function (IIEF),<sup>5</sup> urinary, sexual, bowel and hormonal health-related quality of life domains using the Expanded Prostate Cancer Index Composite (EPIC)<sup>6</sup> and disease-specific health-related quality of life using the EORTC-PR25.<sup>7</sup> Higher scores on the IIEF and EPIC questionnaires indicate higher levels of sexual, urinary and bowel function and sexual activity. For the EORTC-PR25, higher scores on the urinary, bowel and treatment symptom scales indicate higher symptomology/problems while a higher score for sexual activity indicates a higher level of functioning.

#### Statistical analyses

Data were analysed using IBM SPSS (IBM, Armonk, New York, USA). Normality of the distribution was

determined using the Shapiro-Wilk test. Between-group differences in baseline characteristics were analysed using independent t-tests or the Mann-Whitney U test for continuous data, as appropriate, and  $\chi^2$  test for categorical data. Analysis of covariance adjusted for baseline values was used to assess intervention effects on study outcomes. Data for the three outcome questionnaires (IIEF, EPIC and EORTC-PR25) were not normally distributed, consequently all outcome data were log transformed for analysis. Due to incomplete responses to some of the questionnaires, analysis was conducted using complete cases. Tests were two-tailed with significance set at an alpha level of  $p \leq 0.05$ .

#### RESULTS

The men were aged 50–89 years with extensive bone metastatic lesions. There were no significant differences between groups at baseline for patient characteristics (online supplemental table S1 in online supplemental file) and sexual activity and function (table 1), except for the EPIC, which was significantly higher ( $p=0.004$ ) in the exercise group (table 1). No exercise-related adverse events or skeletal fractures were reported during the study and patients attended 89% of planned sessions. After adjusting for baseline values, there were no significant differences for any measure of sexual function and activity following exercise (table 1). Additionally, there were no significant differences for any measures of urinary and bowel function. When examining individual responsiveness to exercise, no patterns emerged for the outcome measures.

#### DISCUSSION

This is the first study reporting the effects of exercise on sexual activity and function in men with advanced PCa. The findings from our trial indicate that although patients with advanced PCa and bone metastases were able to undertake the exercise programme with no adverse events reported, it had no effect on indices of sexual function. A lack of effect of exercise in the current study may be due to the short-term nature of the exercise programme being only 3 months and the conservative modular exercise programme avoiding bone metastatic sites, providing an insufficient stimulus to induce change in sexual function or activity. For many patients, this conservative exercise prescription precluded compound resistance training exercises involving the large muscle groups. This likely limited neural, muscular, hormonal and systemic training adaptations potentially mechanistic in improving sexual function and activity. It is also possible that exercise alone may be insufficient to produce favourable changes in sexual function and activity in men with advanced disease compared with those with localised disease.<sup>3</sup>

Currently, there is insufficient evidence regarding which interventions are effective in helping to manage

**Table 1** Effects of exercise on sexual activity and function

Measure	Baseline		3 months		Adjusted change Mean (95% CI)	p value*
	Exercise	Control	Exercise	Control		
<b>IIEF</b>						
Erectile functioning (n=17 to 20)	3.4 (7.2)	2.7 (5.1)	3.7 (7.2)	3.8 (6.2)	-1.0 (-3.7 to 1.8)	0.484
Orgasmic functioning (n=17 to 20)	2.0 (1.8)	2.1 (1.6)	0.5 (1.2)	1.3 (2.8)	-0.6 (-1.9 to 0.7)	0.349
Sexual desire (n=16 to 20)	3.4 (2.1)	3.5 (1.9)	3.2 (2.4)	3.2 (1.7)	0.2 (-0.7 to 1.1)	0.644
Intercourse satisfaction (n=17 to 20)	0.9 (2.9)	1.0 (2.6)	1.6 (3.5)	1.5 (2.6)	0.1 (-1.4 to 1.6)	0.893
Overall satisfaction (n=15 to 20)	4.4 (2.8)	4.3 (3.2)	4.8 (2.8)	3.8 (2.4)	1.3 (-0.4 to 2.9)	0.122
<b>EPIC</b>						
Sexual summary (n=18 to 23)	28.8 (16.6)	15.9 (14.9) <sup>†</sup>	24.2 (15.0)	18.3 (19.3)	-4.1 (-12.2 to 3.9)	0.304
<b>EORTC QLQ-PR25</b>						
Sexual activity (n=19 to 26)	22.2 (27.3)	20.1 (19.6)	23.7 (23.7)	15.4 (19.9)	4.3 (-7.2 to 15.9)	0.455
Urinary symptoms (n=20 to 25)	16.2 (16.1)	20.1 (17.5)	13.9 (11.9)	22.0 (14.3)	-3.7 (-8.7 to 1.2)	0.079
Bowel symptoms (n=18 to 25)	4.4 (7.1)	6.3 (9.8)	6.9 (8.6)	6.0 (9.4)	1.4 (-3.7 to 6.5)	0.585
Treatment symptoms (n=19 to 26)	13.5 (14.8)	17.7 (15.3)	16.9 (13.0)	21.7 (14.2)	-3.2 (-10.4 to 4.1)	0.384

Values are the mean (SD), and adjusted change and 95% CI are from untransformed data. Numbers in parentheses represent the number of exercise and control patients.

\*Baseline differences were assessed using the Mann-Whitney U test and intervention effects using ANCOVA with p values derived from log-transformed data.

<sup>†</sup>Statistically significant difference at baseline.

ANCOVA, Analysis of Covariance; EORTC QLQ-PR25, The European Organisation for Research and Treatment of Cancer prostate cancer-specific module; EPIC, Expanded Prostate Cancer Index Composite; IIEF, International Index of Erectile Function.

sexual dysfunction in PCa. Sexual function and sexual satisfaction though interrelated are distinct entities that are likely impacted by the complex interplay between natural ageing, treatment-related factors and psychosocial or interpersonal variables such as coping and intimacy. Emerging evidence suggests that psychological therapies may be effective in improving sexual health in PCa.<sup>8</sup> It is likely that exercise may play a role in a larger, multimodal framework (including psychosexual therapy, couples support, pharmacology etc.), rather than as a stand-alone intervention. Further, given the extensive benefits experienced by men with PCa undertaking exercise, including enhanced muscle mass, strength, physical function and quality of life, future research empirically testing an integrative model of PCa care may look to include exercise as a core component. In addition, the inclusion of targeted pelvic floor exercise as part of the overall programme might also be beneficial for this patient group, especially for those with extensive bone disease and unable to perform multiple resistance exercises and could be considered in future studies. In summary, although exercise was well tolerated and improved physical function, the results of our trial suggest that a short-term stand-alone exercise programme has no effect on indices of sexual health in men with advanced PCa with bone metastases.

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**Contributors** DAG, DRT, SKC, NS, DJ and RUN collaboratively developed the concept and protocol, including intervention, outcomes of interests, data analysis procedures

and final reporting. DAG, DRT, SKC, CMF, NS, DJ and RUN contributed to writing, reviewing, editing and final approval of the manuscript.

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