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Immediate Versus Delayed Exercise on Health-related Quality of Life in Patients Initiating Androgen Deprivation Therapy: Results from a Year-long Randomised Trial

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Abstract

Background and objective: An array of treatment-related toxicities result from androgen deprivation therapy (ADT) in patients with prostate cancer (PCa), compromising function and health-related quality of life (HRQoL). Exercise has been demonstrated to counter a number of these adverse effects including decreased HRQoL; however, when exercise should be initiated is less clear. This study aims to examine whether commencing exercise when ADT is initiated rather than later during treatment is more effective in countering adverse effects on HRQoL.

Methods: Men with PCa (48–84 yr) initiating ADT were randomised to immediate exercise (IMEX; $n = 54$) or delayed exercise (DEL; $n = 48$) for 12 mo. IMEX consisted of 6 mo of supervised resistance/aerobic/impact exercise commenced at the initiation of ADT with 6 mo of follow-up. DEL consisted of 6 mo of usual care followed by 6 mo of the same exercise programme. HRQoL was assessed using the Short Form-36 at baseline and 6 and 12 mo. Intention to treat was utilised for the analyses that included group × time repeated-measures analysis of variance using log transformed data.

Key findings and limitations: There were a significant group × time interaction for the physical functioning domain ($p = 0.045$) and physical component summary score ($p = 0.005$), and a significant time effect for bodily pain ($p < 0.001$) and vitality domains ($p < 0.001$), with HRQoL maintained in IMEX and declining in DEL at 6 mo. Exercise in DEL reversed declines in vitality and in the physical component summary score, with no differences at 12 mo compared with baseline. Limitations include treatment alterations during the intervention.

Conclusions and clinical implications: Concurrently initiating exercise and ADT in patients with PCa preserves HRQoL, whereas exercise initiated while on established ADT regimens reverses declines in some HRQoL domains.

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Patient summary: To avoid initial treatment-related adverse effects on health-related quality of life, exercise medicine should be initiated at the start of treatment.

1. Introduction

Androgen deprivation therapy (ADT) is routinely used as a neoadjuvant, adjuvant, or stand-alone treatment across the disease trajectory for patients with prostate cancer (PCa). However, while effective in disease management [1], ADT is accompanied by an array of adverse effects, including reduced muscle and bone mass [2], reduced muscle strength and physical function [3], sexual dysfunction [4], increased fat mass [2], fatigue [5], cardiometabolic disease risk [6], and reduced health-related quality of life (HRQoL) [7,8]. The declines in HRQoL can be quite rapid, with changes noted 3 mo following the onset of treatment [7].

Ours [9] and other [10] studies have shown that exercise can improve HRQoL in patients who are on established ADT regimens. Moreover, in patients commencing ADT, we reported [11] that 3 mo of twice-weekly aerobic and resistance exercise resulted in improvements in social functioning and mental health. As with the other adverse effects of androgen ablation, for HRQoL outcomes, the question arises as to when is the most appropriate time to commence exercise, that is, from the outset when ADT is initiated to prevent adverse effects from occurring or after treatment has commenced, where exercise is undertaken with rehabilitative intent. As a result, we initiated a 12-mo trial [12] to address this question. In the trial, patients initiating ADT concurrently underwent 6 mo of exercise or 6 mo of usual care followed by the same exercise programme for 6 mo. We have previously reported that exercise initiated with the onset of ADT preserved lumbar spine bone density, muscle mass, and muscle density [13], and enhanced muscle strength and physical function [14]. Here, we report the findings from the trial on HRQoL. We hypothesised that exercise concurrently initiated with ADT would mitigate or prevent declines in HRQoL, and declines that occur with androgen suppression would be reversed when exercise was subsequently undertaken.

2. Patients and methods

Of the 219 patients referred by their radiation oncologist/urologist for screening from August 2013 to April 2015, 104 entered the 12-mo trial, as reported previously [13,14]; the progress through the study is shown in Figure 1. This was a single-blinded (investigators blinded to group allocation) randomised controlled trial with partial crossover (delayed exercise [DEL] group crossed over following 6 mo to receive the same intervention). Following referral, patients were screened and entered into the trial by the study coordinator. The inclusion criteria were commencing ADT and intending to remain on it for at least 6 mo, no regular and structured exercise in the previous 3 mo, and ability to walk 400 m. The exclusion criteria were prior ADT, established metastatic disease, established osteoporosis, medications affecting bone metabolism, acute illness, and any musculoskeletal, cardiovascular, or neurological disorder that could inhibit or put patients at risk from exercising. The study was approved by the Edith Cowan University Human Research Ethics Committee and registered with the Australian New Zealand Clinical Trials Registry (ACTRN12612000097842). All participants provided written informed consent and had consent from their physician to participate in the study.

Following familiarisation and baseline assessments (including stature and body mass, body composition and bone density by dual x-ray absorptiometry, questionnaires including the Leisure Score Index (LSI) of the Godin Leisure-Time Exercise Questionnaire to assess physical activity [15], muscle strength, physical function, and blood draw), patients were randomised to immediate exercise (IMEX; n = 54) or DEL (n = 50), stratified by age ($\leq$70 and >70 yr) and smoking status (yes/no), using a computer random assignment program by a research consultant. IMEX included a 6-mo supervised resistance/aerobic/impact exercise programme initiated at the onset of ADT with 6 mo of follow-up where no formal intervention took place, while DEL consisted of 6 mo of usual care followed by 6 mo of the identical exercise programme. Exercise was undertaken in university-affiliated exercise clinics in Perth and testing at the Exercise Medicine Research Institute, Edith Cowan University, in Perth, Western Australia. Among the participants assigned to DEL, one did not complete the HRQoL questionnaire at any of the three time points, and one withdrew after baseline testing and did not complete the questionnaire. Consequently, these patients were excluded from the current analysis, resulting in n = 48 participants for DEL.

2.1. Exercise programme

The multicomponent exercise programme was undertaken thrice weekly and has been described previously [12–14]. Briefly, the resistance exercise component targeting the muscular system consisted of upper and lower body exercises for the major muscle groups, for two to four sets per exercise at a maximum intensity of six to 12 repetitions (the maximal weight able to be lifted six to 12 times). The resistance was increased by 5–10% for the next set or training session when the patients could perform more than the target number of repetitions in the set. Aerobic exercise targeting the cardiorespiratory system consisted of walking or jogging on a treadmill, and cycling or rowing on an ergometer for 25–40 min at 60–85% estimated maximal heart rate (220 – age) [16]. Patients were fitted with a heart rate watch, and workload was adjusted to maintain target

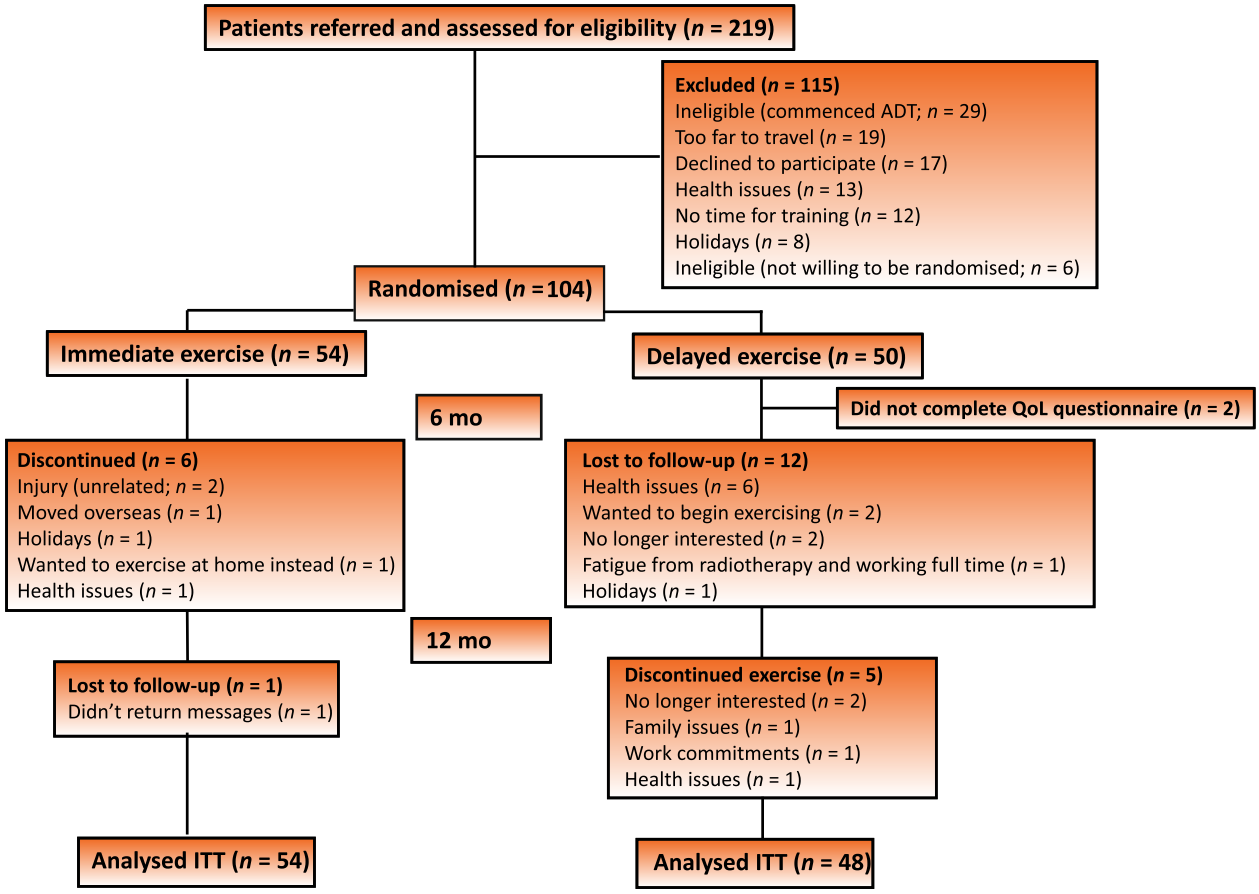

Fig. 1 – CONSORT diagram. ADT = androgen deprivation therapy; ITT = intention to treat; QoL = quality of life.

intensity. Impact loading exercises targeting the skeletal system consisted of two to four rotations of hopping, skipping, leaping, drop jumping, and bounding activities that progressed in volume and intensity over the 6-mo training period. The volume, intensity, and progression were as follows: weeks 1–8, two rotations of skipping (30 s), bounding (15 cm hurdles), and jumping (ten times), with jumping replaced in weeks 5–8 by drop jumping (15 cm, ten times); weeks 9–16, three rotations of bounding (15–30 cm hurdles), drop jumping (15–20 cm, ten times), and skipping (30 s), with skipping replaced in weeks 13–16 by hopping/leaping (ten times); and thereafter four rotations of hopping/leaping (ten times), bounding (30 cm hurdles), and drop jumping (20 cm, ten times) [13]. Exercise frequency was alternated weekly, with two resistance/impact sessions and one aerobic/impact session performed for 1 wk, with two aerobic/impact sessions and one resistance/impact session the alternate week. Sessions were 60 min in duration, undertaken in small groups, and supervised by an accredited exercise physiologist.

2.2. Health-related quality of life

The Short Form-36 (SF-36; version 2) was used to assess HRQoL [17,18] at baseline, and 6 and 12 mo. The SF-36 consists of eight domains: physical functioning, role physical (role limitations due to physical health problems), bodily pain, general health, vitality, social functioning, role emotional (role limitations due to emotional problems), and mental health, as well as two summary measures: the physical component summary (PCS) and the mental component summary. Norm-based scoring was used with a mean of 50 and a standard deviation of 10, where higher scores indicate higher HRQoL.

2.3. Statistical analyses

Sample size for the overall trial was based on the primary outcome of hip and lumbar spine bone mineral density, and to achieve 80% power at an alpha level of 0.05 (two tailed), a total of 124 patients were required to be randomised in a ratio of 1:1 to IMEX and DEL, as reported previously [12]. Data were analysed using IBM SPSS version 29 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to assess the normality of the distribution. Differences in baseline characteristics between IMEX and DEL were assessed using independent *t* tests or the Mann-Whitney U test, as appropriate, for continuous data; chi-square test for categorical data; and a two-way (group × time) repeated-measure analysis of variance for change over time (baseline, and 6 and 12 mo). The HRQoL data were not normally distributed and log transformed (ln) for the analysis. Follow-up tests were performed if the interaction or main effect for time was significant. Where appropriate,

the Bonferroni post hoc procedure for multiple comparisons was used to locate the source of significant differences. Intention to treat (ITT) was utilised for analyses using maximum likelihood imputation of missing values (expectation maximisation), with estimates based on the baseline value and change over time according to group allocation. Estimates of effect size were calculated using Cohen's d, where a small effect is between ≥0.2 and <0.5, medium effect is between ≥0.5 and <0.8, and large effect is ≥0.8 [19], with a trivial effect considered to be <0.2. A sensitivity analysis to ensure data robustness was undertaken using a complete case approach [20]. Tests were two tailed, with statistical significance set at $p < 0.05$.

3. Results

There were no differences between groups at baseline (Table 1). Men were aged 48–84 yr, had a mean of 29.7 ± 5.2% body fat, and 6 ± 2 d since their first treatment of a GnRH agonist. As reported previously [13,14], in the initial 6-mo period, six patients withdrew from IMEX and 12 from DEL, and in the second 6-mo period, five patients withdrew from DEL and one patient from IMEX was lost to follow-up. The main reasons for withdrawal were health issues, wanting to begin exercise (DEL patients), and no longer interested. Treatment alterations occurred for ADT, with ten men in the IMEX and five in the DEL group ceasing treatment in the initial 6 mo, and 40 men in the IMEX and 30 in the DEL group commencing radiotherapy. During the second 6-mo period, 19 men in the IMEX and 16 in the DEL group ceased ADT, with one patient in the IMEX group recommencing ADT, while four men in the IMEX and two in the DEL group commenced radiotherapy, and eight patients in the IMEX and four in the DEL group who previously underwent external beam radiotherapy had brachytherapy.

Physical activity levels based on the Godin LSI increased in the IMEX group ($p = 0.001$) at 6 and 12 mo compared with baseline, and there was a change in the DEL group ($p = 0.033$) over the course of the trial, with an apparent increase between 6 and 12 mo, although it was not significant in follow-up testing ($p = 0.058$). Exercise session attendance was 79% for IMEX and 69% for DEL ($p = 0.093$). There were no major adverse events as a result of the exercise intervention. Regarding nonserious adverse events related to the intervention, 15 patients in the IMEX (27.8%) and 12 in the DEL (25.0%) group reported at least one adverse event, with the most common adverse events being knee pain, lower back pain, muscle strain/soreness, and ankle/foot pain. Of these, knee and ankle/foot pain appeared to be related to the impact exercise component.

3.1. Health-related quality of life

There was no difference in any HRQoL domain or summary measure between groups at baseline ($p = 0.071$–0.822). In ITT analyses, there was a significant group × time interaction for the physical functioning domain ($p = 0.045$) and physical component summary score ($p = 0.005$), and a significant time effect for bodily pain ($p < 0.001$) and vitality domains ($p < 0.001$), with HRQoL being maintained in the IMEX and declining in the DEL group at 6 mo (Table 2). Change in the role physical domain approached significance for a time effect ($p = 0.090$), and in an explorative follow-up analysis, the value in the DEL group was significantly lower at 6 mo ($p = 0.005$) than at baseline and 12 mo. For DEL, the mean changes at 6 mo were −3.4 points for physical functioning, −4.0 points for PCS, −3.5 points for bodily pain, and −2.3 points for vitality. Exercise in the DEL group reversed the decline in vitality and the PCS such that there were no significant differences between baseline and

Table 1 – Participant baseline characteristics

	IMEX ($n = 54$)	DEL ($n = 48$)	p value
Age (yr)	69.0 ± 6.3	67.9 ± 7.6	0.417
Stature (cm)	173.4 ± 7.1	172.5 ± 6.0	0.487
Body mass (kg)	82.9 ± 16.4	84.2 ± 13.0	0.649
BMI (kg/m^2)	27.5 ± 4.4	28.3 ± 4.0	0.322
Body fat (%)	29.0 ± 5.1	30.3 ± 5.2	0.192
Married, *N* (%)	42 (77.8)	39 (81.3)	0.929
Currently employed, *N* (%)	13 (24.1)	15 (31.3)	0.418
Tertiary education, *N* (%)	13 (24.1)	10 (20.8)	0.696
Current smoker, *N* (%)	5 (9.3)	3 (6.3)	0.573
Drinks per week, median (IQR)	4.3 (0.0–10.5)	4.0 (1.0–15.0)	0.341
Number of medications	3.0 (2.0–5.0)	3.0 (2.0–5.8)	0.834
Godin LSI, median (IQR)	10.0 (0.0–24.5)	10.0 (0.0–27.0)	0.872
Gleason score	7.6 ± 1.0	7.6 ± 0.8	0.829
PSA (ng/ml), median (IQR)	3.4 (0.7–6.4)	4.1 (0.5–10.3)	0.405
Testosterone (nmol/l), median (IQR)	8.0 (2.0–16.0)	4.6 (1.8–15.5)	0.447
Time since ADT injection (d)	6.4 ± 2.1	5.7 ± 1.9	0.122
Prostatectomy, *N* (%)	15 (27.7)	15 (31.3)	0.746
Radiation, *N* (%)	4 (7.4)	3 (6.3)	0.817
Number of comorbidities [a]	1.0 (1.0–2.0)	2.0 (1.0–2.0)	0.517

ADT = androgen deprivation therapy; BMI = body mass index; DEL = delayed exercise; IMEX = immediate exercise; IQR = interquartile range; LSI = Leisure Score Index, with a moderate to strenuous LSI of ≥24 classed as active and ≤23 classed as insufficiently active; PSA = prostate-specific antigen; SD = standard deviation.
Values are the mean ± SD unless stated otherwise.
[a] Cardiovascular disease, hypertension, diabetes, and dyslipidaemia.

Table 2 – Health-related quality of life (SF-36) at baseline, and 6 and 12 mo

	Baseline (0)	6 mo	12 mo	ES (95% CI) 0–6 mo	ES (95% CI) 6–12 mo	*p* value [a] Time	Group × time	Comparison [b]
Physical functioning								
IMEX	51.6 ± 6.1	51.6 ± 7.2	50.6 ± 6.8	−0.01 (−0.27, 0.20)	−0.30 (−0.57, −0.02)	0.015	0.045	
DEL	49.5 ± 7.6	46.1 ± 8.8	47.7 ± 8.9	−0.57 (−0.87, −0.26)	0.30 (0.01, 0.58)			0>6
Role physical								
IMEX	49.9 ± 8.0	49.4 ± 7.4	49.4 ± 8.0	−0.05 (−0.31, 0.22)	0.00 (−0.27, 0.27)	0.090	0.119	
DEL	47.6 ± 10.1	44.7 ± 9.1	47.9 ± 9.7	−0.49 (−0.78, −0.18)	0.53 (0.23, 0.83)			
Bodily pain								
IMEX	54.6 ± 7.2	52.0 ± 9.2	51.9 ± 7.9	−0.32 (−0.59, −0.04)	−0.00 (−0.27, 0.27)	<0.001	0.955	0 > 12
DEL	53.1 ± 7.9	49.6 ± 8.1	50.1 ± 7.8	−0.54 (−0.84, −0.23)	0.08 (−0.21, 0.36)			0 > 6, 12
General health								
IMEX	50.4 ± 8.7	51.1 ± 8.5	51.3 ± 8.5	0.13 (−0.14, 0.40)	0.03 (−0.24, 0.30)	0.123	0.113	
DEL	47.6 ± 9.7	45.8 ± 9.2	48.3 ± 9.6	−0.22 (−0.50, 0.07)	0.51 (0.21, 0.81)			
Vitality								
IMEX	52.3 ± 9.8	51.3 ± 8.9	54.1 ± 8.7	−0.11 (−0.38, 0.16)	0.49 (0.20, 0.77)	<0.001	0.378	
DEL	49.0 ± 11.0	46.7 ± 10.5	51.1 ± 10.4	−0.39 (−0.68, −0.09)	1.02 (0.66, 1.36)			0, 12 > 6
Social functioning								
IMEX	50.1 ± 8.7	50.2 ± 8.4	51.8 ± 7.3	0.02 (−0.25, 0.29)	0.24 (−0.03, 0.51)	0.095	0.382	
DEL	48.9 ± 10.5	46.9 ± 11.2	49.0 ± 10.2	−0.31 (−0.59, −0.01)	0.29 (−0.01, 0.57)			
Role emotional								
IMEX	49.5 ± 9.1	50.4 ± 7.0	50.6 ± 7.2	0.09 (−0.18, 0.35)	0.03 (−0.23, 0.30)	0.932	0.376	
DEL	50.9 ± 9.4	50.0 ± 9.0	49.7 ± 8.5	−0.12 (−0.40, 0.17)	−0.04 (−0.33, 0.24)			
Mental health								
IMEX	54.1 ± 7.1	53.7 ± 8.2	54.5 ± 7.9	−0.07 (−0.33, 0.20)	0.17 (−0.10, 0.44)	0.972	0.436	
DEL	51.5 ± 10.2	51.8 ± 9.6	50.9 ± 9.5	0.03 (−0.25, 0.31)	−0.20 (−0.48, 0.09)			
Physical component summary								
IMEX	51.4 ± 7.0	50.4 ± 7.4	50.0 ± 7.5	−0.16 (−0.42, 0.11)	−0.08 (−0.34, 0.19)	<0.001	0.005	
DEL	48.8 ± 7.0	44.8 ± 7.7	48.1 ± 7.0	−0.65 (−0.96, −0.33)	0.71 (0.39, 1.02)			0, 12>6
Mental component summary								
IMEX	51.4 ± 9.0	51.5 ± 8.0	53.6 ± 8.2	0.02 (−0.25, 0.28)	0.49 (0.20, 0.77)	0.213	0.560	
DEL	50.7 ± 11.1	50.9 ± 10.8	50.9 ± 9.7	0.02 (−0.26, 0.30)	0.01 (−0.27, 0.29)			

ANOVA = analysis of variance; DEL = delayed exercise (n = 48); ES = effect size; IMEX = immediate exercise (n = 54); SD = standard deviation.
Values are norm-based score and mean ± SD. Higher values indicate higher health-related quality of life.
[a] Statistical analysis based on intention to treat using log transformed data (group × time repeated-measure ANOVA).
[b] Within-group Bonferroni-corrected multiple comparisons for baseline (0), and 6 and 12 mo (p < 0.05).

12 mo. Between 6 and 12 mo, there was no change in any HRQoL domain or summary score for IMEX.

In sensitivity analyses, results were similar, with a significant time effect for physical functioning (p = 0.029), bodily pain (p = 0.009), vitality (p = 0.004), and the physical component summary score (p = 0.020). The magnitude of declines in the DEL group at 6 mo were similar to the ITT analysis, at −3.5 points for physical functioning, −4.1 points for bodily pain, −3.1 points for vitality, and −3.4 for PCS. In post hoc analyses, vitality and the PCS at 6 mo were lower than those at 12 mo, but not significantly different from baseline, whereas bodily pain at 6 mo was significantly different from that at baseline. There was no significant change in any HRQoL domain or summary score for IMEX at 6 or 12 mo.

4. Discussion

There were two important findings from this year-long trial in relation to quality of life: (1) initiating exercise concurrently with the commencement of hormone therapy preserved HRQoL, and (2) exercise implemented in the DEL group after 6 mo of ADT reversed some of the declines in HRQoL, as assessed using the SF-36 questionnaire. Consequently, to avoid initial adverse effects on HRQoL, exercise should be implemented when ADT is commenced.

The changes observed in the DEL group with declines in the physical functioning, bodily pain, and vitality domains, and in the PCS are comparable with those reported by Alibhai et al [7] in men with nonmetastatic PCa commencing ADT, where they also observed declines in these domains of the SF-36 as well as the PCS, and that these changes occurred within 3 mo of commencing treatment. As in our study, there were no changes in the mental health domain. Of note, these declines in HRQoL observed early on in treatment persisted over 36 mo, which is important given that patients may be on ADT for prolonged periods of time [21]. In a prospective study of patients with nonmetastatic PCa within 6 wk of commencing ADT compared with PCa controls not receiving ADT, Cheung et al [8] also reported decreased HRQoL, as reflected by the SF-12 physical component score following 12 mo of treatment, with no change in the mental component score.

Regarding the significance or meaningfulness of the changes observed, the reported minimal clinically important difference (MCID) for the SF-36 domains and summary scores vary based on the population studied. For various

oncology patient groups, the MCID for the PCS has been reported to be between 3.6 and 5 points [22,23]. The change that we observed in the DEL group at 6 mo for the PCS of −4.0 points is within the range reported for being clinically meaningful, while the domains where there was a decline in the DEL group at 6 mo are similar to those reported in other patient groups [24] and may be potentially clinically meaningful.

However, concurrent initiation of exercise with ADT was effective in preventing declines from occurring in HRQoL. Exercise may preserve HRQoL in patients commencing ADT as well as aid in reversing declines that occur from treatment via increased physical fitness, functional capacity, and social interaction (with the exercise physiologist/specialist and peers/other exercisers), providing a sense of control over their health, attenuating treatment-related symptoms, and enhancing masculinity. Segal and colleagues [10] in their early work on resistance exercise in men on ADT proposed that improvement in HRQoL may be attributed to the undertaking of exercise itself as well as the environment in which it is undertaken, and improvements resulting from exercise. We examined mediators of the benefits in HRQoL in our study of resistance and aerobic exercise in men on established ADT [9], and found that PCS improvements were mediated by upper body muscle strength and walking speed, while improvements in the general health domain were mediated by walking speed and fatigue [25]. Indeed, improvements in physiological variables resulting from exercise participation as well as improved functional status are part of the causal pathway in the HRQoL conceptual model of Wilson and Cleary [26], which links clinical variables with HRQoL in patients. Moreover, the lack of change or reversal in HRQoL between 6 and 12 mo in the IMEX group may be due to physical activity, as determined by the Godin LSI remaining elevated during this time period compared with baseline.

Exercise can also enhance masculinity [27,28] at a time when it is being threatened as a result of treatment-related adverse effects, such as sexual dysfunction (loss of libido and erectile dysfunction) and change in body habitus (reduced muscle mass/increased fat mass, penile shrinkage, and gynaecomastia), leading to a sense of feminisation and poorer body image [29]. Moreover, undertaking exercise can also counter the loss of control over their body and health experienced by men following the impact of PCa diagnosis and treatment undertaken, as well as provide a sense of achievement [27,29]. The overall result is that undertaking exercise may increase the patient's physical self-efficacy [29], positively impacting HRQoL. To this end, apart from clinic- or gym-based exercise programmes, recreational football, which promotes health and embodies masculine ideals, has been proposed as a physical activity that may be appealing to PCa patients and their masculine identity [30].

There are several strengths and limitations of the study worthy of comment. First, we compared exercise as a preventative measure compared with exercise with rehabilitative intent to address ADT-related effects on HRQoL. Second, we used the SF-36, which is a validated generic self-report instrument [17,18] that has extensively been used in both well-functioning and patient populations [31] including those with cancer [7], and often considered the gold standard for assessing HRQoL [32]. Third, the exercise programme undertaken by patients was supervised and included differing exercise modes to counter a range of common ADT-induced toxicities. The multicomponent exercise programme was based on the principle of specificity of training, in that certain exercise modes target specific physiological systems and hence several adverse effects of ADT. However, there are several limitations that need to be recognised. First, there were treatment alterations during the trial as well as a number of patients in both groups were undergoing radiotherapy, although this reflects the nature of clinical practice based on patient responses to treatment and disease progression, in addition to patients being referred by radiation oncologists. These treatment alterations could potentially confound the results during the exercise and nonexercise periods. Second, established metastatic disease was part of the exclusion criteria, and therefore our results do not apply to men with metastatic disease. Third, the somewhat lower exercise session attendance in the DEL group may have had a modest effect on the magnitude of change in the outcomes of interest compared with IMEX. Lastly, as this was an exercise trial and patients agreed to participate, the results may not apply to all men with PCa undergoing ADT.

5. Conclusions

Commencing a multimodal exercise programme when hormone therapy is initiated in patients with PCa preserves HRQoL. Commencement of exercise after the patient is on an established ADT regimen is also beneficial in that declines in some HRQoL domains can be reversed. Consequently, where possible, as a countermeasure to prevent declines in HRQoL as well as other ADT-related toxicities [13,14], it would be recommended for clinicians to coprescribe (with referral to an exercise physiologist/specialist health professional) exercise medicine with the onset of hormone treatment.

***Author contributions*:** Dennis R. Taaffe 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: Taaffe, Newton, Chambers, Spry, Joseph, Gardiner, Hayne, Galvão.
Acquisition of data: Galvão, Newton, Taaffe, Chambers, Spry, Joseph, Gardiner, Hayne.
Analysis and interpretation of data: Taaffe, Newton, Chambers, Nelson, Spry, Luo, Schumacher, Joseph, Gardiner, Hayne, Galvão.
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