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ABSTRACT

Purpose: Resistance training (RT) improves an array of treatment-related adverse effects in men with prostate cancer, however, the minimal dosage required is unknown. We systematically reviewed the RT effects in prostate cancer patients to determine the minimal dosage regarding the exercise components (type, duration, volume, and intensity) on body composition, physical function, muscle strength, cardiorespiratory fitness, body mass index (BMI), and prostate-specific antigen (PSA). **Methods:** Using PRISMA guidelines, MEDLINE, CINAHL, EMBASE, SPORTDiscus, and Web of Science databases were searched. Eligible randomised controlled trials examined prostate cancer patients undertaking resistance-based exercise programs during or following treatment. Meta-analysis was undertaken when more than 3 studies were included. Associations between mean differences and the exercise components were tested by univariate and multivariate meta-regression analysis. **Results:** Twenty-four papers describing 22 trials and involving 1,888 prostate cancer patients were included. Exercise improved fat mass (-1% in body fat and -0.5 kg in fat mass), lean mass (+0.5 kg in lean and appendicular lean mass), functional capacity (i.e., chair rise, 400-m test, 6-m fast walk and stair climb tests) and fitness outcomes (i.e., VO_2 peak and muscle strength) (P=0.040 - <0.001) with no change in BMI or PSA (P= .440 - .735). Meta-regression indicated no association between exercise type, RT duration, weekly volume and intensity and primary outcomes (P= .075 - .965). There was a significant association between RT intensity and chest press muscle strength (favouring moderate-intensity, P= .012), but not in other secondary outcomes. **Conclusion:** In untrained older men with prostate cancer initiating an exercise program, lower volume at moderate-to-high intensity is as effective as

higher volume RT for enhancing body composition, functional capacity and muscle strength in the short-term.

Keywords: Prostate cancer; resistance training; dose-response effects; minimal dosage; health-related outcomes.

1. INTRODUCTION

The benefits of exercise medicine have been widely attested in different cancer populations (1, 2). In prostate cancer patients, for example, resistance exercise alone, or combined with aerobic training has been shown to reduce post-surgical impairments from prostatectomy (3), reverse the array of adverse effects from androgen deprivation therapy (ADT) (4-11), and preserve physical function in those with bone metastases (12), in addition to improvements in quality of life (5, 8, 12). However, although the role of exercise medicine is being expanded to include low-grade cancer patients undergoing active surveillance (13-15), or high-grade patients in order to enhance tumour growth suppression (16) and survival (17), information regarding the actual exercise dose-response still needs to be determined (18).

Considering the overall exercise benefits in prostate cancer patients, the assumption that a given exercise dosage will promote benefits in all outcomes is premature. In the most recent exercise guideline for cancer patients (19), a specific resistance exercise dosage (e.g., 2 sets of 8-15 reps at 60-85% of one-repetition maximum (1RM)) was recommended to address or counter anxiety, fatigue, and depressive symptoms based on high-quality publications. However, the disproportionately large number of breast cancer trials compared to other cancer trials from which the recommendations were derived precludes more accurate recommendations for prostate cancer patients (19). Further, the paucity of comparative trials regarding resistance training components (i.e., frequency, intensity, and volume) makes it difficult to establish the dose-response effect on commonly reported outcomes. In this report, we examined the resistance exercise dosage in body composition and functional capacity given their strong association with risk of progression and mortality in prostate cancer patients (20-23).

Thus, the aim of the present study is to: 1) systematically review and analyse the resistance training effects on body composition measures, functional capacity tests, cardiorespiratory fitness, muscle strength, body mass index (BMI), and prostate-specific antigen (PSA) levels; and 2) verify the minimal dose regarding the prescribed exercise components (i.e., type, duration, volume, and intensity) and effects on these outcomes.

2. METHODS

2.1. Study selection procedure

The study was undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (24, 25), and the method used was based on the minimum criteria established by the Cochrane Back Review Group (CBRG) (26). This systematic review was not registered in any prospectively systematic review database (e.g., PROSPERO).

This review included published data from randomised controlled trials that evaluated the effects of resistance-based exercise programs in prostate cancer patients at any treatment stage (e.g., presurgical, during treatment, and with bone metastases). The primary outcomes of this review were body composition (i.e., body fat percentage, fat mass, trunk fat mass, lean mass, and appendicular lean mass), and functional capacity tests (i.e., 30s sit-to-stand-test, 6-minute walk, 400-m walk, 6-m usual and fast walk, timed up-and-go, stair climb, and repeated sit-to-stand where patients repeated the task 5 times). The secondary outcomes were cardiorespiratory fitness (i.e., VO_2peak or VO_2max), muscle strength (i.e., chest press, leg press, leg extension, and seated

row), PSA and BMI. Trials were excluded when: 1) home-based exercise was used in the whole intervention period; 2) involved mixed cancer patients without specific information on prostate cancer patient results; 3) did not include or report the specific outcomes included in this review, or did not include sufficient information for analysis; and 4) written in a language other than English. Eligibility was assessed independently evaluated in duplicate, with differences resolved by consensus.

The search was conducted up to November 2019 using the following electronic databases: MEDLINE, CINAHL, EMBASE, SPORTDiscus, and Web of Science. The terms used were: 'prostate cancer' and 'resistance training' in association with a list of sensitive terms to search for experimental studies. In addition, we performed a manual search of the reference lists provided in the selected papers as well as previous systematic reviews and meta-analytic studies (27-33) to detect studies potentially eligible for inclusion. The search strategy used is shown in the Supplemental Digital Content Table S1 (see in Supplemental Digital Content 1, literature search strategy, http://links.lww.com/MSS/C125).

2.2. Data extraction

Titles and abstracts of all articles identified by the search strategy were independently evaluated in duplicate. Abstracts that did not provide sufficient information regarding the inclusion and exclusion criteria were selected for full-text evaluation. In the second phase, the same reviewers independently evaluated these full-text articles and selected them in accordance with the eligibility criteria. Disagreements between reviewers were resolved by consensus. The data extraction was performed via a standardised form. Information on the interventions,

outcomes, and patients were collected. Study characteristics, intervention duration, components of the resistance training prescription (i.e. frequency, intensity, volume, and modality), adherence (i.e., number of patients that completed the program), attendance (i.e., number of sessions attended), compliance (i.e., number of patients that successfully completed the exercise prescription), and adverse events were extracted, along with the main outcomes. The prescribed resistance training was summarised as follows: frequency (number of sessions per week), intensity (prescribed intensity of resistance training), type (resistance training, combined resistance and aerobic training, or multimodal exercise program), and volume (sets and repetitions). When studies incorporated supervised and unsupervised periods of training, information was extracted on the longest period of the supervised exercise intervention. Outcomes were extracted in their absolute units (e.g., kg for lean and fat mass assessments). When graphs were used instead of numerical data, the graphs were measured through their plots using a specific tool for data extraction (WebPlotDigitizer, San Francisco, California, USA) (34).

2.3. Assessment of Risk of Bias

Risk of bias of individual studies was evaluated according to the 2nd version of the Cochrane risk-of-bias tool for randomised trials (RoB 2) (35), focusing on different aspects of the trial design, conduct and reporting. Each assessment using the RoB 2 tool is focused at the outcome level. The six-item instrument evaluates: 1) the randomisation process; 2) deviation from intended interventions; 3) missing outcome data; 4) measurement of the outcome; 5) selection of the reported result; and 6) overall bias, and was used to evaluate each included randomised controlled trial for each outcome of interest. Risk of bias for each of the six domains was expressed as “low risk”, “some concern” and “high risk” (35).

2.4. Data analysis

The pooled-effect estimates were obtained from the mean difference of baseline to the final assessment of the intervention for each group. These values were expressed as the mean difference between-groups. In studies with multiple exercise interventions, the groups were divided with each respective sample size, within-group mean difference, and SD or 95% CI for further analysis. Meta-analyses were conducted for overall studies and a subgroup analysis was provided based on RoB 2.0 *low risk* classification when more the 3 studies were included. Calculations were performed using a random-effects model (36). The level of significance was set at $P \leq 0.05$. Statistical heterogeneity was assessed using the Cochran Q test. A threshold P-value of 0.1 as well as values greater than 50% in the statistical test of heterogeneity (I^2) were considered indicative of high heterogeneity (37). Heterogeneity between studies was explored by omitting one study at a time and comparing the pooled with the original estimates, while the presence of publication bias was explored by contour-enhanced funnel plots along with Egger's test, considering a P-value <0.1 as indicative of publication bias (38, 39). When necessary, the trim-and-fill computation was used to estimate the effect of publication bias on the interpretation of results (40, 41). Analyses were conducted using the package *metan*, *confunnel*, *metabias*, and *metatrim* from Stata 14.0 software (Stata, College Station, USA). Forest plots presented for the outcome measures are after sensitivity analysis and/or trim-and-fill procedure adjustments.

In addition, we tested the association between the mean difference effect and the exercise components to identify a dose-response relationship using univariate and multivariate meta-regression. Using one variable at a time or multivariable models we assessed whether

components such as type, intervention duration, prescribed weekly volume and peak intensity influence the association of resistance-based exercise with the main effects. Analyses were undertaken in outcomes significantly affected by exercise provided the models had more than 5 studies. For intervention duration, prescribed weekly volume and peak intensity, analyses were considered when the values presented a range higher than 5%, while exercise type was coded as 0= resistance training alone, and 1= resistance training combined with other components (e.g., aerobic, flexibility, impact-loading, or balance). Analyses were conducted using the package *metareg* from Stata 14.0 software (Stata, College Station, USA).

3. RESULTS

3.1. Studies included

All studies selected reported the aim to investigate the effect of resistance training (i.e. resistance training alone, combined with aerobic exercise, or included in a multimodal exercise program) in prostate cancer patients at any treatment stage. We retrieved 1,030 studies, 794 of which were retained for screening after duplicate removals. Of these, 694 were excluded and 100 full-text articles were assessed for eligibility (Figure 1). The eligibility assessment resulted in 23 papers (describing 21 trials) (5-12, 42-56) which were included in the present review and meta-analyses (see in Table S2, Supplemental Digital Content 2, characteristics of included studies, http://links.lww.com/MSS/C126), with 6 to 13 studies being included in the dose-response relationship analysis involving exercise type, intervention duration, prescribed weekly volume and peak intensity.

INSERT FIGURE 1 HERE

3.2. Prostate cancer patients and exercise intervention characteristics

A total of 1,748 prostate cancer patients with an average age of 69.5±2.1 yrs participated in the included studies. Exercise interventions were predominantly undertaken in patients on ADT (17 of 23 studies) (5, 7-9, 11, 42, 44-49, 52-56). Exercise modality included predominantly combined resistance and aerobic training (12 of 23 studies) (5-7, 9, 10, 42, 44, 46, 51-53, 56) followed by multimodal exercise program (4 of 23 studies) (11, 12, 49, 55), resistance training plus impact-loading (5 of 23 studies) (7, 9, 45, 47, 50), and resistance training only (4 of 23 studies) (8, 43, 48, 54), in a cohort of 901 patients allocated to the intervention group compared to 847 patients in the control group. In addition, 3 studies (42, 44, 49) also provided nutrition advice during the intervention. Studies were designed to compare the exercise intervention vs. usual care control (15 of 23 studies) (5, 8, 11, 12, 42-44, 46, 48-50, 51-53, 56), a home-based program involving aerobic or flexibility training and physical activity (6 of 23 studies) (6, 10, 45, 47, 54, 55), or to a delayed exercise group (2 of 23 studies) (7, 9). Two studies compared multiple exercise interventions (7, 9).

The mean exercise intervention duration was 19.5±10.7 wks with an average of 2.4±0.7 sessions per week. The average total prescribed resistance training volume was 9,136±4,534 repetitions with a weekly training volume of 468±177 repetitions. In addition, the mean peak intensity reached throughout the resistance training program was 79±8% of 1-RM ranging from 60 to 85%. Information about resistance training frequency was not reported by one study (54), while 4 studies did not report volume (42, 44, 49, 55), or intensity (42, 51, 55, 56), respectively. Exercise program adherence ranged from 74 to 100% (reported in 22 of 23 studies) (5-9, 11, 12,

42-56), while the attendance and compliance ranged from 65 to 100% (reported in 21 of 23 studies) (5-12, 42, 43, 45-47, 49-56), and from 85 to 94% (reported in 5 of 23 studies) (42, 43, 48, 50, 54), respectively. Adverse events related to the exercise interventions were identified in 8 studies (6, 8, 9, 46, 48, 51, 52, 55), while 14 studies (5, 7, 11, 12, 42-45, 47, 49, 50, 53, 54, 56) reported no adverse events throughout the intervention period. The adverse events were mostly related to musculoskeletal pain (e.g., back, shoulder, and knee), and only 1 study (54) presented a moderate adverse event with no detail provided.

3.3. Risk of bias assessment

For the primary outcomes of this review, 13.3% of the studies presented some concern for risk of bias in body composition assessment (2 of 15 studies) (49, 56), and 76.9% in the functional capacity tests (10 of 13 studies) (5, 6, 9, 12, 43, 46, 48, 51, 52, 54). The concerns in body composition were mainly due to the *measurement of the outcome* as 2 studies (49, 56) evaluated body composition outcomes through the use of bioelectrical impedance. For functional capacity, the concerns were mainly due to the *measurement of the outcome as* studies performed non-blinded assessments on *measurement of the outcome* (76.9%, 10 of 13 studies) (5, 6, 9, 12, 43, 46, 48, 51, 52, 54) and one study (7.7%, 1 of 13 studies) (51) did not report the concealment of allocation in the *randomisation process*. For the secondary outcomes, concerns were observed in cardiorespiratory fitness (*some concerns*: 60.0%, 3 of 5 studies) (44, 54, 55), muscle strength (*some concerns*: 84.6%, 11 of 13 studies) (5, 6, 7, 8, 10, 12, 43, 46, 48, 51, 54), and BMI (16.7%, 1 of 6 studies) (48). Concerns were not observed in the PSA assessment. The overall risk of bias assessment is shown in Table S3 (see in Supplemental Digital Content 3, overall risk of bias of included studies, http://links.lww.com/MSS/C127), while the individual assessment is presented

in Figure S1 (see in Supplemental Digital Content 4, individual risk of bias assessment, http://links.lww.com/MSS/C128).

3.4. Exercise effects on body composition

Exercise resulted in significant positive overall effects in percent body fat (-1.0%, 95% CI: -1.3 to -0.6%), fat mass (-0.6 kg, 95% CI: -0.8 to -0.3 kg), trunk fat mass (-0.3 kg, 95% CI: -0.6 to -0.0 kg), lean mass (0.5 kg, 95% CI: 0.3 to 0.7 kg) and appendicular lean mass (0.4 kg, 95% CI: 0.3 to 0.7 kg) with heterogeneity ranging from I^2= 0 to 47% after sensitivity analysis and/or trim-and-fill procedure adjustments (Figure 2 and 3). The samples ranged from 490 to 917 participants (see in Table S4, Supplemental Digital Content 5, overall and subgroup analyses, http://links.lww.com/MSS/C129). In subgroup analysis, the main effects were significantly maintained in the outcomes (I^2= 0 to 47%; P= <.001 to .025). Outliers were identified in the overall analysis for body fat percentage (6) and trunk fat mass (53), and subgroup analysis of appendicular lean mass (7), while publication bias and trim and fill procedure suggested that data from 3 studies were missing for appendicular lean mass (P= .050). These studies were omitted from the abovementioned overall and subgroup effects (Figure 2 and 3). The meta-analysis power to detect changes in body composition was 1-β= 1.0.

INSERT FIGURE 2 HERE

In the dose-response analysis, the univariate (P= .075 to .965; see in Table S5, Supplemental Digital Content 6, univariate meta-regression results, http://links.lww.com/MSS/C130) and multivariate meta-regression models (P= .203 to .785; see

in Table S6, Supplemental Digital Content 7, multivariate meta-regression results, http://links.lww.com/MSS/C131) did not explain the variation in body composition outcomes.

INSERT FIGURE 3 HERE

3.5. Exercise effects on functional capacity

There was a significant positive overall exercise effect for the time to perform the 30s sit-to-stand repetitions (2.8 reps, 95% CI: 1.7 to 4.0 reps), repeated sit-to-stand test (-1.0 sec, 95% CI: -1.4 to -0.6 sec), 400-m walk (-8.3 sec, 95% CI: -12.4 to -4.2 sec), 6-m fast walk (-0.1 sec, 95% CI: -0.2 to -0.0) and stair climb (-0.2 sec, 95% CI: -0.3 to -0.1 sec) with an heterogeneity ranging from I^2=0 to 45.2% after sensitivity analysis and/or trim-and-fill procedure adjustments (Figure 4). The samples ranged from 213 to 519 participants (see in Table S4, Supplemental Digital Content 5, overall and subgroup analyses, http://links.lww.com/MSS/C129). Subgroup analyses were not undertaken on these outcomes as well as the overall analyses in the 6-min walk test and 6-m backwards walk test given the small number of studies included (<3). The study of Galvão et al. (12) was considered an outlier in the 6-m fast walk time analysis and omitted from the abovementioned results, while publication bias was only found for the 400-m walk (P=.063) with no trimming needed to be performed (data unchanged). The meta-analysis power to detect change in the 6-m usual walk and timed-up and go test was 1-β= 0.57 and 0.64, respectively, while a 1-β= 1.0 was found for the remaining functional capacity outcomes.

INSERT FIGURE 4 HERE

In the dose-response analysis, the univariate (P= .182 to .341; see in Table S5, Supplemental Digital Content 6, univariate meta-regression results, http://links.lww.com/MSS/C130) and multivariate meta-regression models (P=.358; see in Table S6, Supplemental Digital Content 7, multivariate meta-regression results, http://links.lww.com/MSS/C131) were not statistically significant in explaining the variation in 400-m test performance. Analyses of 30s sit-to-stand, 6-min walk test, 6-m usual and fast walk, stair climb, and repeated sit-to-stand tests were not undertaken due to the small number of studies (≤5) reporting on these components. Performing univariate meta-regression resulted in non-significant associations between exercise type, resistance training duration, weekly volume and peak intensity with 30s sit-to-stand (P= .311 for exercise type and resistance training duration), 6-minute fast walk (P= .165 - .793), stair climbs (P= .523 – .930) and repeated sit-to-stand tests (P= .681 - .868).

3.6. Exercise effects on secondary outcomes

There was a significant increase in chest press (3.9 kg, 95% CI: 2.9 to 4.9 kg), leg press (23.5 kg, 95% CI: 15.2 to 31.7 kg), leg extension (8.8 kg, 95% CI: 6.9 to 10.7 kg) and seated row strength (5.2 kg, 95% CI: 3.9 to 6.5 kg) with heterogeneity ranging from I^2= 0 to 77.4% after sensitivity analysis and/or trim-and-fill procedure adjustments (Figure 5). The samples ranged from 321 to 728 participants (see in Table S4, Supplemental Digital Content 5, overall and subgroup analyses, http://links.lww.com/MSS/C129). Subgroup analyses were not undertaken for these outcomes due to the small number of studies that were considered of *low risk* (<3). Outliers were identified in the overall analysis for chest press (8), leg extension (12) and seated row test (54). Meta-analysis power to detect change in muscle strength was 1-β= 1.0.

INSERT FIGURE 5 HERE

Regarding VO_{2peak}, there was a positive overall effect of 1.3 ml.kg.min^{-1} (95% CI: 0.8 to 1.7 ml.kg.min^{-1}) after the publication bias and trim and fill procedure suggesting that data were missing from 2 studies (P= .078; see in Table S4, Supplemental Digital Content 5, overall and subgroup analyses, http://links.lww.com/MSS/C129, and Figure 6). Finally, exercise did not result in a significant change in BMI or PSA levels (P= .440 - .735; see in Table S4, Supplemental Digital Content 5, overall and subgroup analyses, http://links.lww.com/MSS/C129, and Figure 6). Meta-analysis power to detect change in VO_{2peak} was 1-β= 1.0, while power for BMI and PSA was 0.25 and 0.57, respectively.

INSERT FIGURE 6 HERE

In the univariate dose-response analysis, resistance training type and intensity (r^2= 64.0%, P= .010; and r^2= 100%, P< .001, respectively; see in Table S5, Supplemental Digital Content 6, univariate meta-regression results, http://links.lww.com/MSS/C130) explained the variation in chest press muscle strength. In the multivariate model, gain in chest press muscle strength (r^2= 100%, P= .012, see in Table S6, Supplemental Digital Content 7, multivariate meta-regression results, http://links.lww.com/MSS/C131) was greater in studies prescribing resistance training with moderate intensity (P= .022). Although the resistance training volume was significant in the univariate model to explain leg extension and leg press muscle strength (P= .043 and .050, respectively; see in Table S5, Supplemental Digital Content 6, univariate meta-regression results,

http://links.lww.com/MSS/C130), the results were not maintained in the multivariate meta-regression model (P= .147 - .204). Dose-response analyses of VO_{2peak} and the seated row test were not undertaken due to the small number of studies (≤5) reporting on these components. Performing univariate meta-regression resulted in non-significant associations between exercise type, resistance training duration, weekly volume and peak intensity with VO_{2peak} (P= .598 - .651, see in Table S5, Supplemental Digital Content 6, univariate meta-regression results, http://links.lww.com/MSS/C130), while seated row test variation was explained by exercise type (coefficient ± SE: -14.9±2.9, P= .014; favouring resistance training alone), resistance training weekly volume (coefficient ± SE: 0.0±0.1, P= .032; favouring higher weekly volume), but not resistance training duration (P= .624; see in Table S5, Supplemental Digital Content 6, univariate meta-regression results, http://links.lww.com/MSS/C130).

4. DISCUSSION

The present review produced four important findings in prostate cancer patients. First, body composition is enhanced by resistance exercise (i.e., increase in whole body and regional lean mass and decrease in fat mass) regardless of type, duration, weekly volume and peak intensity. Second, exercise promotes significant improvements in multiple components of physical function, in a non-linear dose-response fashion. Third, muscle strength and cardiorespiratory fitness are improved with exercise, with greater effects in chest press strength resulting from resistance training performed at a moderate intensity. Finally, resistance-based exercise does not modify BMI or affect PSA levels. Therefore, the resistance training prescription combined with different exercise components is a potent therapy against an array of

treatment-related adverse effects in prostate cancer patients regardless of the weekly volume prescribed when moderate-to-high intensity is achieved.

Obesity has been associated with an increased risk of biochemical recurrence and mortality in prostate cancer patients in a dose-response fashion (20). In the meta-analysis by Cao & Ma (20), a 5 $kg.m^{-2}$ increase in BMI was associated with a 21% increased risk for biochemical recurrence and a 20% increased risk for prostate cancer specific-mortality. In our study, PSA levels did not change in response to exercise involving resistance training indicating no impact of this exercise mode on disease progression (e.g., albeit not expected to change as most studies were short in duration with the majority of patients having local disease). In addition, few studies reported adverse events, and these were generally minor in nature. Moreover, the similar magnitude of change observed in lean mass and fat mass (i.e., increase in lean mass and decrease in fat mass) accounts for the maintenance in BMI and may result in metabolic health benefits and enhanced survival (57, 58). Furthermore, the lack of relationship between resistance training weekly volume, intensity and duration indicates the potential benefit of low dosage resistance training to improve overall body composition. Likewise, in a previous report by Stamatakis et al. (59), a low weekly dosage of resistance training was associated with a ~25% reduced risk of mortality. Thus, undertaking exercise programs that include resistance training results not only in benefits for body composition in men with prostate cancer, but may also provide a protective effect against cancer recurrence and cancer-specific mortality even when performed at a low weekly dosage. These results are of importance for prostate cancer patients and the prescription of exercise for this patient group as it suggests that even modest amounts of exercise may result

in the accrual of significant body composition benefits and this may also contribute to increased attendance and compliance to an exercise program.

Considering the *World Health Organization* (WHO) report (60), the concept of healthy ageing should be seen as the process of developing and maintaining functional capacity. Several studies report the association between muscle strength, cardiorespiratory fitness and functional tests with independence, hospitalization rate, and mortality (61-66). Thus, the observed gains in muscle strength and cardiorespiratory fitness, and functional capacity support translation of exercise medicine effects into functional independence and autonomy in older prostate cancer patients. For example, the reduction in time to walk 400-m represents an increase in the safety margin before the threshold for disability and may help to reduce the risk for complications such as risk for falls and fractures (67, 68), and mortality (21). Reduced risk of mortality is also associated with enhanced repeated sit-to-stand and stair climb test performance (22, 23). In this way, the progression of moderate-to-high intensity in resistance training combined with other exercise components appears to be sufficient to achieve significant improvements in functional capacity of patients with prostate cancer regardless of the number of weekly repetitions. Thus, the present findings provide an appropriate approach for prostate cancer patients as it allows a conservative exercise prescription commencement (e.g., less repetitions per exercise at moderate-to-high loads) and gradual progression according to comorbidities and the patient's treatment-related side effects (69). Furthermore, following the non-significant relationship between intervention duration and study outcomes, it is also possible to maintain a low dosage resistance training program for longer periods which may help patients to keep active during and following treatment.

One of the critical considerations in the design of exercise trials and of its potential and feasibility in cancer patients is related to the exercise dose-response (18, 19, 69). However, to date the assessment and quantification of exercise dosage, as well as the lack of reporting preclude a minimal dosage prescription for prostate cancer patients. The present review and analysis provide information that less repetitions per exercise at moderate-to-high intensity (i.e., 60-85% of 1-RM) could be sufficient to achieve significant benefits for prostate cancer patients, at least in the short-term. We hypothesize that due to the large window for adaptation in these undeveloped qualities, these men adapt at a similar rate within the volumes and intensities of the studies analysed, at least over the relatively short duration of these interventions. Our results partially agree with previous studies comparing different resistance training dosages in older adults (70-72), with similar results for various dosages following 12 weeks training (70, 72) but not for longer training periods such as 20 weeks (71, 72). This could be due to the lower threshold for muscular adaptations in untrained older participants in the initial stages of training, and the need for a greater stimulus following this initial period. However, the lack of influence of intervention duration suggests the potential use of low-volume resistance training during longer periods in prostate cancer patients, different than that observed in healthy older adults (71, 72). Future studies will be necessary to elucidate if higher dosage and longer duration accrues greater benefits in prostate cancer patients. Furthermore, considering the meta-analytic adjustments and heterogeneity, the positive exercise results observed in body composition and multiple components of physical function are likely to be observed across different treatment phases (e.g., during ADT or after primary treatment). Given the lower between-studies heterogeneity in the meta-analysis ($I^2 < 30\%$), the observed results in body fat, muscle mass, 6-minute walk, 400-m

walk, stair climb, repeated sit-to-stand and cardiorespiratory fitness indicate that prostate cancer patients may experience similar benefits in these outcomes regardless of the treatment phase. Thus, the low resistance training dosage could be a useful strategy to improve body composition and muscle function in patients at different treatment stages.

The strengths of this review and analysis is that it included a large number of exercise trials encompassing prostate cancer patients at different disease stages (21 trials reported in 23 papers with 1,748 patients included) in a conservative approach employing univariate and multivariate meta-regression models, as well as sensitivity analysis to explore the common objectively assessed physical health-related outcomes. However, there are also some limitations that are worthy of comment. First, although our findings indicate a minimal dosage for health-related outcomes based on studies undertaken to date, it should not be seen as an "optimal" dosage for each of the outcomes investigated. Second, the use of prescribed dosage (not the actual dosage undertaken) may be considered a limitation in the present study. Although the compliance ranges from 65 to 94% in the included studies (42, 43, 48, 50, 54), most did not report this metric, precluding a determination of how much exercise was actually undertaken in the attended sessions. We recently reported on compliance in an exercise trial on men with prostate cancer who had bone metastases (73) and outlined the methodology and metrics that can be employed in future studies. Finally, the exercise program duration was considered short in most of the included studies. Only two papers from the same trial (45, 47) lasted longer than 6 months and, as a result, it is difficult to infer our results regarding exercise dosage beyond a period of 24 weeks in duration. Future trials involving longer exercise durations will be necessary to confirm these results.

In conclusion, the results indicate that there is no difference in effect when prescribing low and high volume or moderate and high intensity resistance exercise in untrained older men with prostate cancer on body composition, functional capacity and muscle strength outcomes, at least in the short-term. Considering the array of benefits observed in the present study, a low resistance training weekly volume could represent a time-efficient approach during and after active treatment, resulting in higher adherence, attendance and compliance while accruing similar health and function benefits to that of higher volume exercise. We suggest the examination of resistance training dose-response in future trials to determine if a minimal dose-approach could culminate in substantial cancer-related benefits.

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Figure Legends/Captions:

Figure 1. Flow chart of study selection process. *, Primary outcome.

Figure 2. Mean difference effects of resistance-based exercise compared with control on percentage body fat (A), fat mass (B) and trunk fat mass (C). Overall and subgroup analyses conducted with a random effects model. Grey and white circles represent study specific estimates based on risk of bias assessment (*Low risk*, and *some concern* or *high risk* of bias, respectively); I^2 represents the heterogeneity test; diamonds represent pooled estimates of random-effect meta-analysis. *, Combined resistance and aerobic group; #, Resistance training plus impact-loading group.

Figure 3. Mean difference effects of resistance-based exercise compared with control on lean mass (A) and appendicular lean mass (B). Overall and subgroup analyses conducted with a random effects model. Grey and white circles represent study specific estimates based on risk of bias assessment (*Low risk*, and *some concern* or *high risk* of bias, respectively); I^2 represents the heterogeneity test; diamonds represent pooled estimates of random-effect meta-analysis. *, Combined resistance and aerobic group; #, Resistance training plus impact-loading group.

Figure 4. Mean difference effects of resistance-based exercise compared with control on 30s sit-to-stand repetitions (A), 5 sit-to-stand test (B), 400-m walk test (C), 6-m usual walk test (D), 6-m fast walk test (E), timed-up and go test (F) and stair climb test (G). Overall and subgroup analyses conducted with a random effects model. Grey and white circles represent study specific

estimates based on risk of bias assessment (*Low risk*, and *some concern* or *high risk* of bias, respectively); I^2 represents the heterogeneity test; diamonds represent pooled estimates of random-effect meta-analysis. *, combined resistance and aerobic group; #, resistance training plus impact-loading group; 30SS, 30s sit-to-stand test; TUG, timed-up and go test.

Figure 5. Mean difference effects of resistance-based exercise compared with control on chest press (A), leg press (B), leg extension (C) and seated row (D). Overall and subgroup analyses conducted with a random effects model. Grey and white circles represent study specific estimates based on risk of bias assessment (*Low risk*, and *some concern* or *high risk* of bias, respectively); I^2 represents the heterogeneity test; diamonds represent pooled estimates of random-effect meta-analysis. *, combined resistance and aerobic group; #, resistance training plus impact-loading group.

Figure 6. Mean difference effects of resistance-based exercise compared with control on VO_2peak (A), body mass index (B) and prostate-specific antigen levels (C). Overall and subgroup analyses conducted with a random effects model. Grey and white circles represent study specific estimates based on risk of bias assessment (*Low risk*, and *some concern* or *high risk* of bias, respectively); I^2 represents the heterogeneity test; diamonds represent pooled estimates of random-effect meta-analysis. BMI, body mass index; PSA, prostate-specific antigen.

Supplemental Digital Content (SDC)

SDC1.docx - **(SDC 1) Table S1.** Literature search strategy used for the PubMed database.

SDC2.docx - **(SDC 2) Table S2.** Study characteristics: treatment stage, sample size, exercise prescription, adherence, attendance, compliance and outcomes assessed.

SDC3.docx - **(SDC 3) Table S3.** Risk of bias of included studies.

SDC4.docx - **(SDC 4) Figure S1.** Individual risk of bias assessment at outcome level for A) body composition, B) functional capacity, C) cardiorespiratory fitness, D) muscle strength, E) prostate-specific antigen and F) body mass index. Green circles, low risk; yellow circles, some concerns; red circles, high risk of bias.

SDC5.docx - **(SDC 5) Table S4.** Overall and subgroup analysis effects on body composition, functional capacity, and the secondary outcomes in prostate cancer patients.

SDC6.docx - **(SDC 6) Table S5.** Univariate meta-regression on main outcomes mean difference and exercise type, resistance training duration, weekly volume and peak intensity.

SDC7.docx - **(SDC 7) Table S6.** Multivariate meta-regression on main outcomes mean difference and exercise type, resistance training duration, weekly volume and peak intensity.

Figure 1

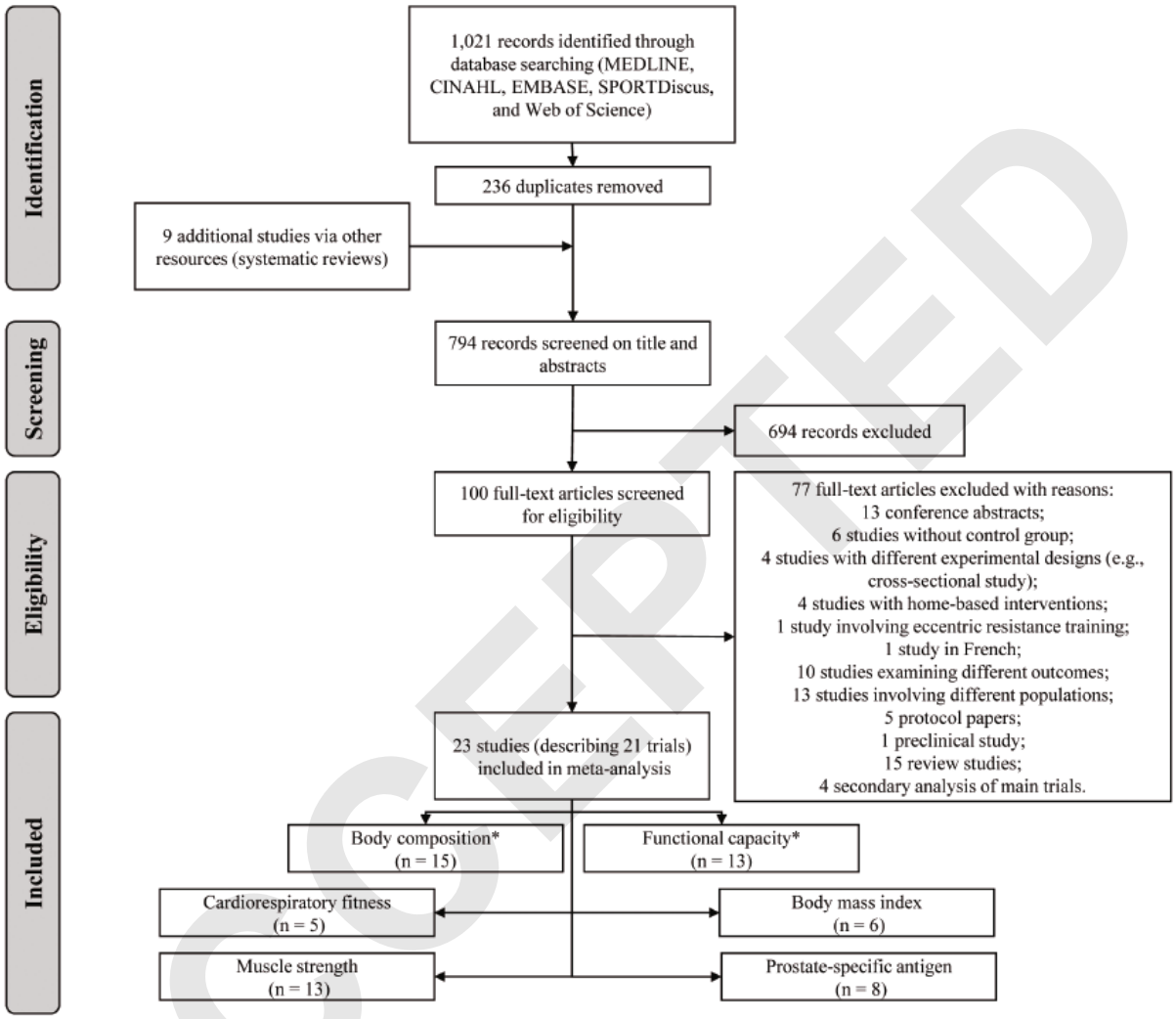


Figure 2

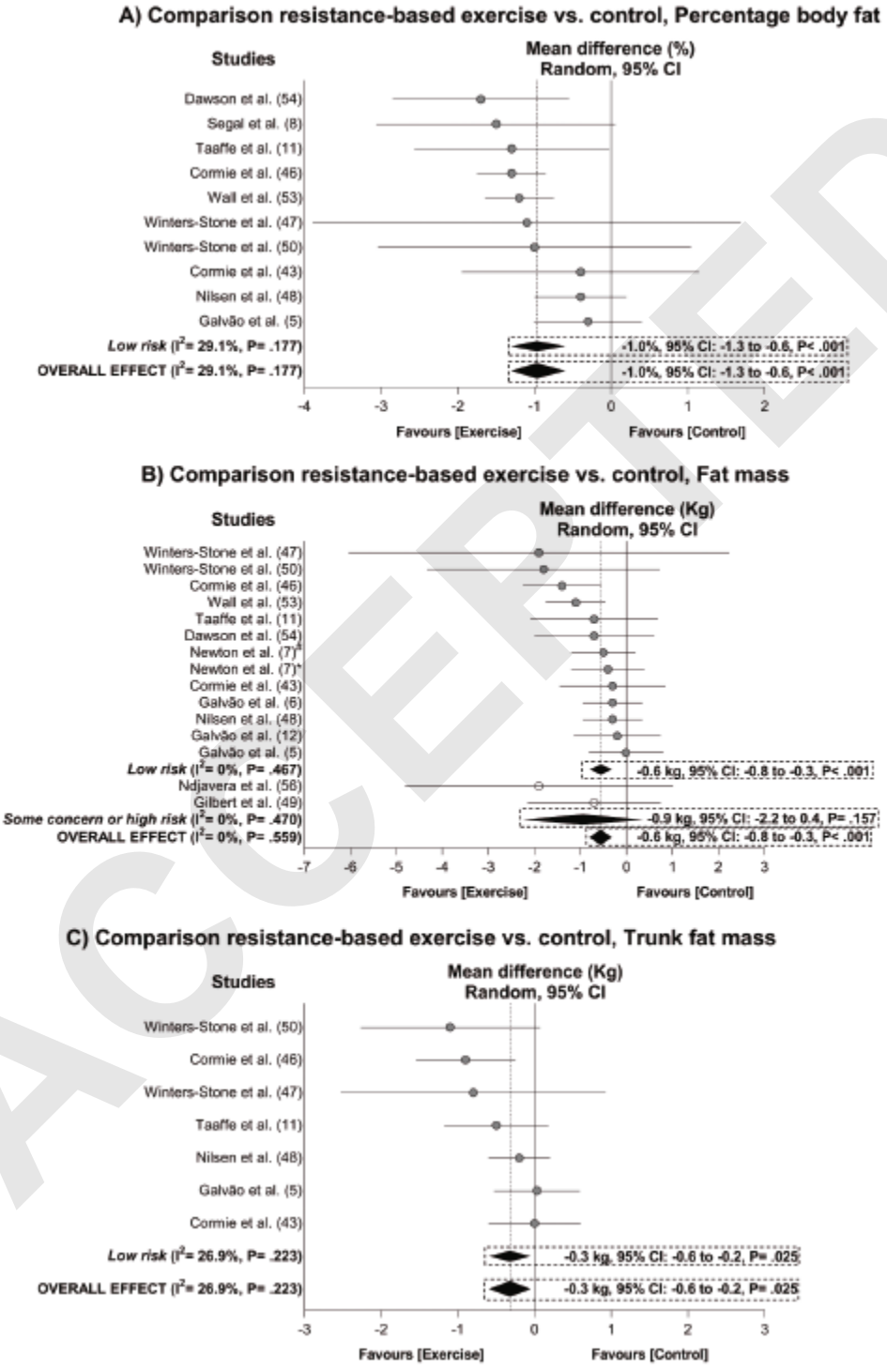


Figure 3

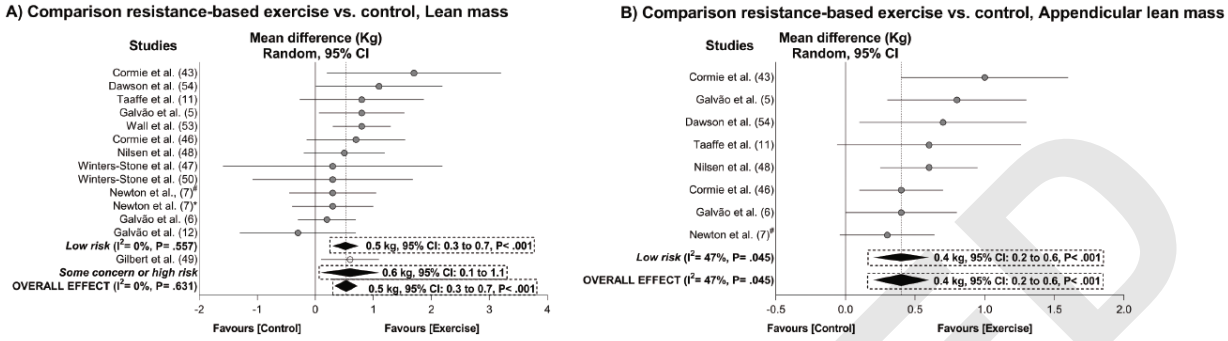


Figure 4

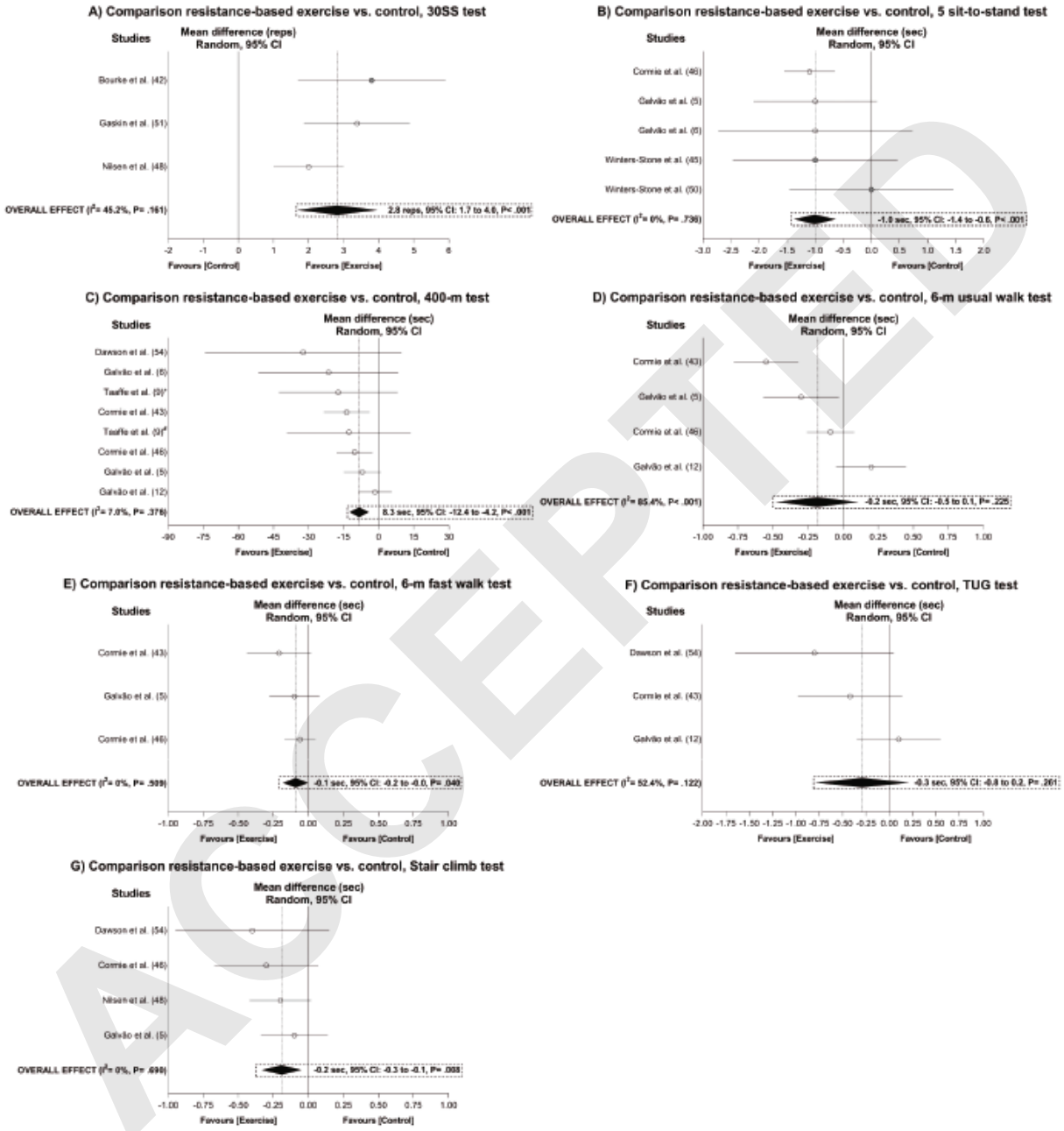


Figure 5

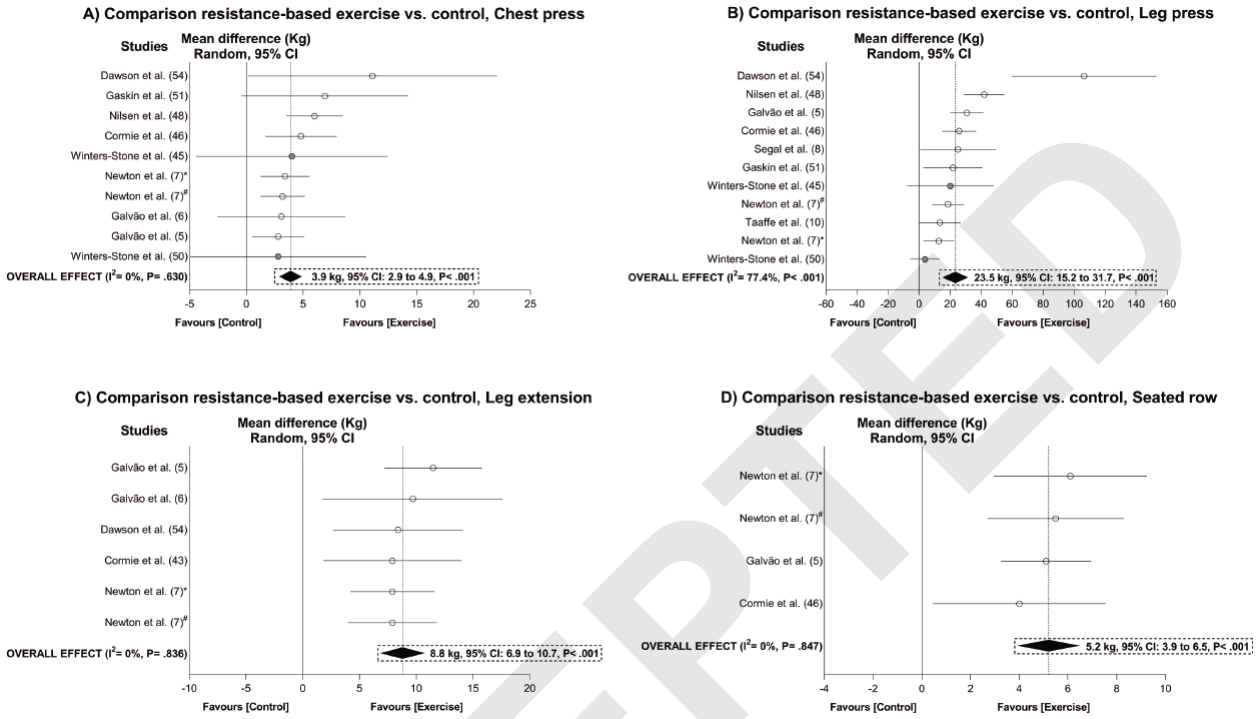
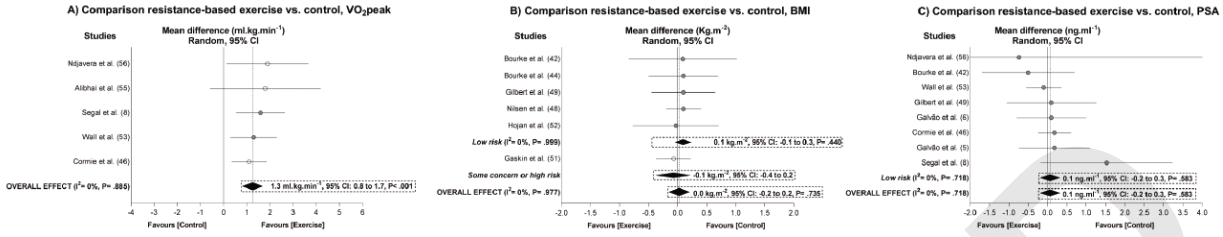


Figure 6



(SDC 1) Table S1. Literature search strategy used for the PubMed database

#1" Search "prostate cancer"(Mesh) OR Prostate Neoplasms (title/abstract) OR Neoplasms, Prostate (title/abstract) OR Neoplasm, Prostate (title/abstract) OR Prostate Neoplasm (title/abstract) OR Neoplasms, Prostatic (title/abstract) OR Neoplasm, Prostatic (title/abstract) OR Prostatic Neoplasm (title/abstract) OR Prostate Cancer (title/abstract) OR Cancer, Prostate (title/abstract) OR Cancers, Prostate (title/abstract) OR Prostate Cancers (title/abstract) OR Cancer of the Prostate (title/abstract) OR Prostatic Cancer (title/abstract) OR Cancer, Prostatic (title/abstract) OR Cancers, Prostatic (title/abstract) OR Prostatic Cancers (title/abstract) OR Cancer of Prostate (title/abstract)
#2" Search "resistance training"(Mesh) OR Training, Resistance (title/abstract) OR Strength Training (title/abstract) OR Training, Strength (title/abstract) OR Weight-Lifting Strengthening Program (title/abstract) OR Strengthening Program, Weight-Lifting (title/abstract) OR Strengthening Programs, Weight-Lifting (title/abstract) OR Weight Lifting Strengthening Program (title/abstract) OR Weight-Lifting Strengthening Programs (title/abstract) OR Weight-Lifting Exercise Program (title/abstract) OR Exercise Program, Weight-Lifting (title/abstract) OR Exercise Programs, Weight-Lifting (title/abstract) OR Weight Lifting Exercise Program (title/abstract) OR Weight-Lifting Exercise Programs (title/abstract) OR Weight-Bearing Strengthening Program (title/abstract) OR Strengthening Program, Weight-Bearing (title/abstract) OR Strengthening Programs, Weight-Bearing (title/abstract) OR Weight Bearing Strengthening Program (title/abstract) OR Weight-Bearing Strengthening Programs (title/abstract) OR Weight-Bearing Exercise Program (title/abstract) OR Exercise Program, Weight-Bearing (title/abstract) OR Exercise Programs, Weight-Bearing (title/abstract) OR Weight Bearing Exercise Program (title/abstract) OR Weight-Bearing Exercise Programs (title/abstract).
#1 AND #2

(SDC 2) Table S2. Study characteristics: treatment stage, sample size, exercise prescription, adherence, attendance, compliance and outcomes assessed.

Author, year	Disease stage	Treatment stage	Experimental design	Exercise prescription and sample	Adherence Attendance Compliance	Adverse events	Outcomes
Segal et al., 2009(8)	I-IV; Gleason Score: 6.7±0.9	Radiotherapy; Radiotherapy plus ADT	121 randomised RT vs. AT vs. UC	**Resistance training** n=40, 3 sessions per week for 24 weeks performing 2 sets of 8-12 reps at 60-70% of 1-RM	Adh: 82.5% Att: 88.0% Comp: NR	In the resistance training group, one man experienced chest pain during exercise.	Body fat; Cardiorespiratory fitness; Chest press and leg press 1-RM; PSA
Galvão et al., 2010(5)	Localised and nodal metastases; Gleason Score: 7.3	ADT	57 randomised Combined resistance and aerobic training vs. UC	**Combined resistance and aerobic training** n=29, 2 sessions per week for 12 weeks; RT: 2-4 sets of 6-12RM AT: 15-20min at 65-80% HR	Adh: 96.6% Att: 94.0% Comp: NR	No adverse events.	Body fat, Fat mass, Trunk fat mass, Lean mass, Appendicular lean mass; 400-m walk, 6-m usual, fast and backwards walk, stair climb, repeated sit-to-stand; Chest press, leg press and seated row 1-RM; PSA
Bourke et al., 2011(42)	Gleason Score: 7±1.1	ADT	50 randomised Lifestyle intervention (combined resistance and aerobic training,	**Combined resistance and aerobic training** n=25, 2 sessions per week for 12 weeks;	Adh: 84.0% Att: 95.2% Comp: 87.0%	No adverse events.	30s sit-to-stand repetitions; BMI

			nutrition advice, and home-based AT) vs. UC	AT: 30min at 55-85% HR; RT: 2-4 sets			
Cormie et al., 2013(43)	Gleason Score: 8.2	Bone metastasis	20 randomised RT plus home-based AT vs. UC	**Resistance training** n=10, 2 sessions per week for 12 weeks performing 2-4 sets of 8-12RM	Adh: 80.0% Att: 83.0% Comp: 93.2%	No adverse events.	Body fat, Fat mass, Trunk fat mass, Lean mass, Appendicular lean mass; 400-m walk, 6-m usual and fast walk, Timed up-and-go; leg extension 1-RM
Galvão et al., 2014(6) (RADAR trial)	II-IV	Previous ADT and radiotherapy	100 randomised Combined resistance and aerobic training plus home-based AT vs. physical activity material	**Combined resistance and aerobic training** n=50, 2 sessions per week for 24 weeks RT: 2-4 sets of 6-12RM AT: 20-30min at 70-85% HR	Adh: 84.0% Att: 77.0% Comp: NR	One participant with pre-existing back pain elected to cease the exercise program, as did one patient with a pre-existing knee injury.	Body fat, Fat mass, Lean mass, Appendicular lean mass; 400-m walk, repeated sit-to-stand; Chest press and leg extension 1-RM; PSA
Bourke et al., 2014(44)	NR	ADT	100 randomised Lifestyle intervention (combined resistance and aerobic training, nutrition advice, and home-based AT) vs. UC	**Combined resistance and aerobic training** n=50, 2 sessions per week during 12 weeks; AT: 30min at 55-75% of HR; RT: 2-4 sets of 8-12 reps	Adh: 94.0% Att: 94.0% Comp: NR	No adverse events.	BMI; PSA

				at 60% of 1-RM			
Winters-Stone et al., 2015(45)	NR	ADT; Chemotherapy; Radiotherapy; Bone metastasis	51 randomised Impact + RT plus home-based AT vs. home-based AT and FLX	**Impact + Resistance training** n=29, 2 sessions per week for 48 weeks; Impact: 50 two-footed jumps from the ground with weighted vests RT: 1-3 sets of 8-12RM	Adh: 82.8% Att: 83.0% Comp: NR	No adverse events.	Repeated sit-to-stand; Chest press and leg press 1-RM
Cormie et al., 2015(46)	Gleason Score: 7.5	ADT; Chemotherapy; Radiotherapy	63 randomised Combined resistance and aerobic training plus home-based AT vs. UC	**Combined resistance and aerobic training** n=32, 2 sessions per week for 12 weeks; AT: 20-30min at 70-85% HR; RT: 1-4 sets of 6-12RM	Adh: 93.8% Att: 96.2% Comp: NR	One participant from the exercise group withdrew from the intervention due to feeling too nauseous, dizzy and fatigued to attend the exercise sessions.	Body fat, Fat mass, Trunk fat mass, Lean mass, Appendicular lean mass; 400-m walk, 6-m usual, fast and backwards walk, stair climb, repeated sit-to-stand; Cardiorespiratory fitness; chest press, leg press and seated row 1-RM; PSA
Winters-Stone et al., 2015(47)	Including bone metastases	ADT; Chemotherapy; Radiotherapy	51 randomised Impact + RT plus home-based AT vs. home-based AT and FLX	**Impact + Resistance training** n=29, 2 sessions per week for 48 weeks; Impact: 50 two-footed	Adh: 82.8% Att: 84.0% Comp: NR	No adverse events.	Body fat, Fat mass, Trunk fat mass, Lean mass

				jumps from the ground with weighted vests RT: 1-3 sets of 8-12RM			
Nilsen et al., 2015(48)	Intermediate and high-risk based on PSA and primary tumour	Radiotherapy plus ADT; following ADT	58 randomised RT vs. UC	**Resistance training** n=28, 3 sessions per week for 16 weeks performing 1-3 sets of 10RM on Mondays, 2-3 sets of 10 reps at 80-90% of 10RM on Wednesdays, and 2-3 sets of 6RM on Fridays.	Adh: 78.6% Att: NR Comp: 85.0%	Three patients in the resistance training group discontinued the intervention due to pain, two due to pain in the knee and one patient due to back pain.	Body fat, Fat mass, Trunk fat mass, Lean mass, Appendicular lean mass; 30s sit-to-stand-test, stair climb; Chest press and leg press 1-RM; BMI
Gilbert et al., 2016(49)	NR	ADT	50 randomised Multimodal exercise program plus home-based AT and RT vs. UC	**Multimodal exercise program** n=25, 2 sessions per week for 12 weeks; AT: 30min at 55-75% HR RT: 2-4 sets of 8-12 reps at 60% of 1-RM BAL: NR	Adh: 80.0% Att: 93.0% Comp: NR	No adverse events.	Fat mass, Lean mass BMI; PSA
Winters-Stone et al., 2016(50)	NR	Patients following primary treatment other than hormone therapy and not currently undergoing radiation or	64 randomised Impact + RT vs. UC Sessions with patients and spouses training together	**Impact + Resistance training** n=32, 2 sessions per week for 24 weeks; Impact: 1 set of 8–15 repetitions with weighted vests RT: 1 set of 8-15RM	Adh: 100% Att: 78.0% Comp: 94.0%	No adverse events.	Body fat, Fat mass, Trunk fat mass, Lean mass; repeated sit-to-stand; Chest press and leg press 1-RM

		chemotherapy					
Gaskin et al., 2016(51)	I-III	Surgery; Radiotherapy; Surgery plus radiotherapy; ADT plus radiotherapy; Surgery plus radiotherapy and ADT.	119 randomised Combined resistance and aerobic training plus home-based AT and RT vs. UC	**Combined resistance and aerobic training** n=53, 2 sessions per week for 12 weeks; AT: 20-30min at 40-70% HR RT: 2 sets of 8-12 reps	Adh: 98.1% Att: 75.0% Comp: NR	One man in the intervention condition aggravated a previous rotator cuff injury during exercise training. One man in the control condition aggravated a previous meniscus injury during baseline testing.	30s sit-to-stand-test, 6-minute walk; BMI; Chest press and leg press 1-RM
Hojan et al., 2017(52)	Gleason Score: 8.8±1.9	ADT	72 randomised Combined resistance and aerobic training vs. UC	**Combined resistance and aerobic training** n=36, 3 sessions per week for 12 weeks; AT: 30min at 70-80% HR RT: 2 sets of 8 reps at 70-75% of 1-RM	Adh: 97.2% Att: 86.0% Comp: NR	Three overuse injuries to the lower extremities were reported in the exercise group.	6-minute walk; BMI
Taaffe et al., 2017(9) (NHMRC trial)	Localised and nodal metastases; Gleason Score: 7.8	ADT; ADT plus radiotherapy; ADT plus antiandrogen; ADT plus surgery	159 randomised Impact + RT vs. Combined resistance and aerobic training plus home-based AT vs. Delayed AT	**Impact + Resistance training** n=57, 2 sessions per week for 24 weeks; Impact: bounding, skipping, drop jumping, hopping, and leaping activities RT: 2-4 sets of 6-12RM	Adh: 74.1% & 87.0% Att: 65.0 and 69.0% Comp: NR	Two men in Impact + RT group withdrew due to compressed spinal discs and shoulder issues. Two men in Combined RT and AT had	400-m walk

				Combined resistance and aerobic training n=54, 2 sessions per week for 24 weeks; AT: 20-30min at 60-85% HR RT: 2-4 sets of 6-12RM		cardiovascular problems, with one requiring heart bypass surgery while another participant developed back pain.	
Wall et al., 2017(53)	Gleason Score: 8.0	ADT; ADT plus radiotherapy; ADT plus antiandrogen	97 randomised Combined resistance and aerobic training plus home-based AT vs. UC	**Combined resistance and aerobic training** n=50, 2 sessions per week for 24 weeks; RT: 2-4 sets of 6-12RM AT: 20-30min at 70-90% HR	Adh: 86.0% Att: 69.0% Comp: NR	No adverse events.	Body fat, Fat mass, Trunk fat mass, Lean mass; Cardiorespiratory fitness; PSA
Taaffe et al., 2018(10) (RADAR trial)	II-IV	Previous ADT and radiotherapy	57 randomised Combined resistance and aerobic training plus home-based AT vs. physical activity material	**Combined resistance and aerobic training** n=28, 2 sessions per week during 24 weeks; RT: 2-4 sets of 6-12RM AT: 20-30min at 70-85% HR	Adh: NR Att: 77.0% Comp: NR	NR	Leg press 1-RM
Galvão et al., 2018(12)	Patients with established bone metastatic disease	ADT; Prostatectomy; Radiotherapy; Brachytherapy; Chemotherapy	57 randomised Multimodal exercise program vs. UC	**Multimodal exercise program** n=28, 3 sessions per week for 12 weeks; RT: 2 sets of 10-12 reps at 10-12RM AT: 20-30min at 60-85% HR	Adh: 82.1% Att: 89.0% Comp: NR	No adverse events.	Fat mass and Lean mass; 400-m walk, 6-m usual, fast and backward walk, Timed up-and-go, repeated sit-to-stand;

				FLX: 2-4 reps for 30-60 seconds			Leg extension 1-RM
Dawson et al., 2018(54)	Including bone and nodal metastases Gleason Score: 7.5	ADT; Antiandrogen; Radiotherapy; Surgery; Chemotherapy	37 randomised RT vs. home-based FLX Part of the sample received whey protein isolate (~50%)	**Resistance training** n=16, 3 sessions per week for 12 weeks performing 3 sets of 8-15 reps at 60-83% of 1-RM	Adh: 87.5% Att: 93.8% Comp: 88.3%	No adverse events.	Body fat, Fat mass, Lean mass, Appendicular lean mass; 400-m walk, timed up-and-go, stair climb; Chest press, leg extension, leg press and seated row 1-RM
Alibhai et al., 2019(55)	Gleason score range from 6 to 10	ADT	53 randomised Personal supervised vs. group supervised vs. home-based exercise program	**Multimodal exercise program** n=19, 3 sessions per week for 24 weeks	Adh: 85.0% Att: 75.0% Comp: NR	Three adverse events (two grade 2 events in home-based exercise program participants and one grade 1 event in a personal supervised participant; primarily musculoskeletal)	Cardiorespiratory fitness
Ndjavera et al., 2019(56)	Locally advanced and metastatic patients; Gleason score range from 6 to	ADT; ADT plus radiotherapy	50 randomised Combined resistance and aerobic training plus home-based AT and RT vs. UC	**Combined resistance and aerobic training** n=24, 2 sessions per week during 12 weeks; AT: 6 bouts of 5 min at 55-85% HR	Adh: 91.7% Att: 70.0% Comp: NR	No adverse events.	Fat mass; Cardiorespiratory fitness; PSA

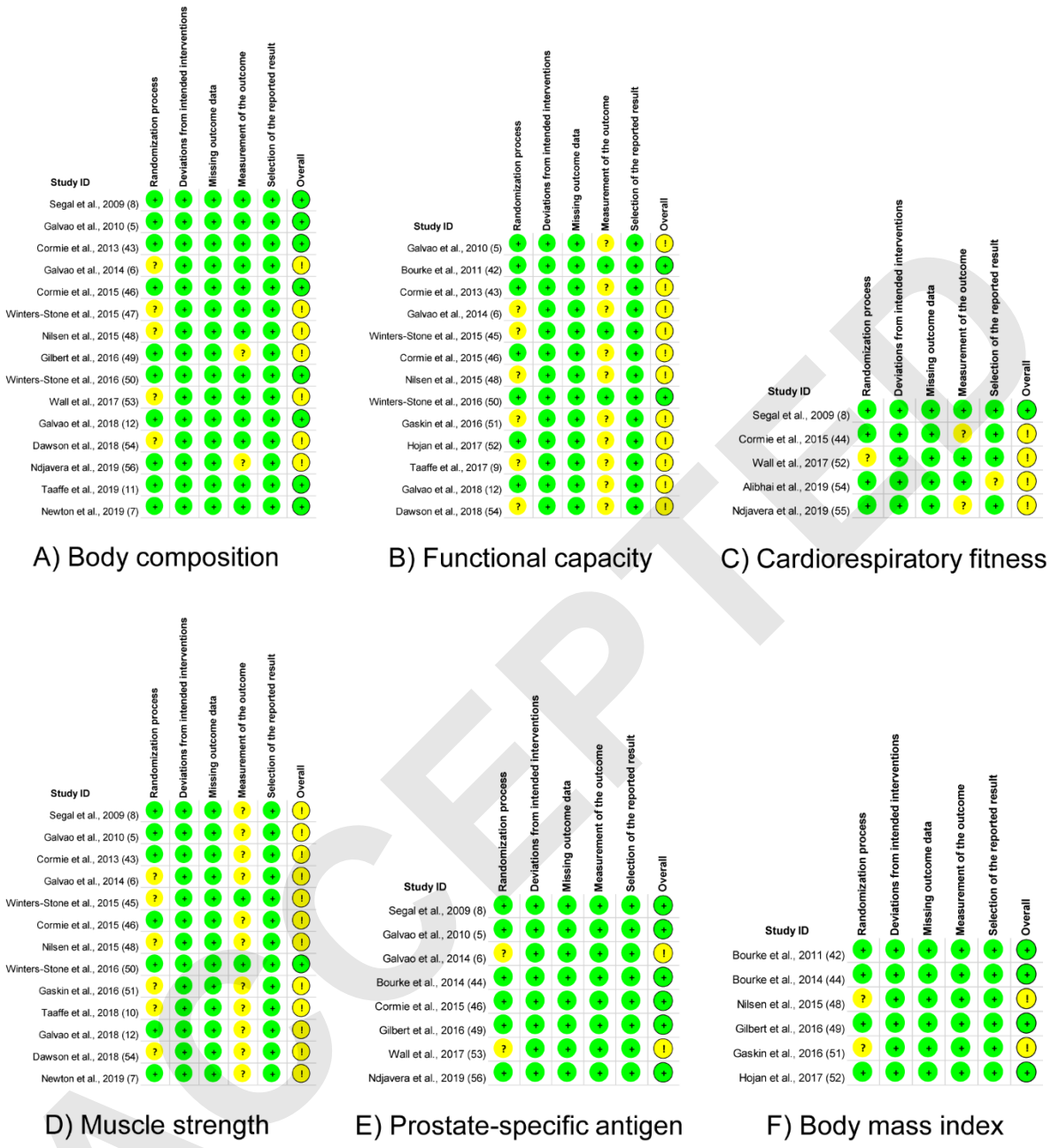
	10			RT: 2-4 sets of 10 reps at 11-15 RPE			
Taaffe et al., 2019(11)	Gleason score: 7.6	ADT; ADT plus surgery; ADT plus radiotherapy	104 randomised Combined resistance and aerobic training + Impact loading plus home-based AT vs. UC All patients received standard daily supplementation with calcium and vitamin D3	**Multimodal exercise program** n=54, 3 sessions per week for 24 weeks; Impact: bounding, skipping, drop jumping, hopping, and leaping activities RT: 2-4 sets of 6-12RM AT: 25-40min at 60-85% HR	Adh: 88.9% Att: 79.0% Comp: NR	No adverse events.	Body fat, Fat mass, Trunk fat mass, Lean mass, Appendicular lean mass
Newton et al., 2019(7) (NHMRC trial)	Localised and nodal metastases; Gleason Score: 7.8	ADT; ADT plus radiotherapy; ADT plus antiandrogen.	154 randomised Impact + Resistance training vs. Combined resistance and aerobic training plus home-based AT vs. Delayed AT	**Impact + Resistance training** n=57, 2 sessions per week for 24 weeks; Impact: bounding, skipping, drop jumping, hopping, and leaping activities RT: 2-4 sets of 6-12RM **Combined resistance and aerobic training** n=50, 2 sessions per week for 24 weeks; AT: 20-30min at 60-85% HR RT: 2-4 sets of 6-12RM	Adh: 73.7% & 86.0% Att: 65.0 and 70.0% Comp: NR	No adverse events.	Fat mass, Lean mass, Appendicular lean mass; Chest press, leg press, leg extension and seated row 1-RM

Legend: 1-RM, 1-repetition maximum; Add, Adherece, ADT, Androgen deprivation therapy; AT, Aerobic training; Att, Attendance; BAL, balance exercises; BMI, Body mass index; Comp, Compliance; FLX, Flexibility training; GnRH, Gonadotrophin-releasing hormone; NHMRC, National Health and Medical Research Council; NR, Not reported; PSA, Prostate-specific antigen; RT, Resistance training; UC, Usual care control group; VO_{2peak}, Peak Oxygen Uptake

(SDC 3) Table S3. Risk of bias of included studies.

Outcome	Randomisation process	Deviation from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall bias
Body composition, n= 15						
Low risk	15 (100%)	15 (100%)	15 (100%)	13 (86.7%)	15 (100%)	13 (86.7%)
Some concerns	0	0	0	2 (13.3%)	0	2 (13.3%)
High risk	0	0	0	0	0	0
Functional capacity, n= 13						
Low risk	12 (92.3%)	13 (100%)	13 (100%)	3 (23.1%)	13 (100%)	3 (23.1%)
Some concerns	1 (7.7%)	0	0	10 (76.9%)	0	10 (76.9%)
High risk	0	0	0	0	0	0
Cardiorespiratory fitness, n= 5						
Low risk	5 (100%)	5 (100%)	5 (100%)	3 (60.0%)	4 (80.0%)	2 (40.0%)
Some concerns	0	0	0	2 (40.0%)	1 (20.0%)	3 (60.0%)
High risk	0	0	0	0	0	0
Muscle strength, n= 13						
Low risk	12 (92.3%)	13 (100%)	13 (100%)	2 (15.4%)	13 (100%)	2 (15.4%)
Some concerns	1 (7.7%)	0	0	11 (84.6%)	0	11 (84.6%)
High risk	0	0	0	0	0	0
PSA, n= 8						
Low risk	8 (100%)	8 (100%)	8 (100%)	8 (100%)	8 (100%)	8 (100%)
Some concerns	0	0	0	0	0	0
High risk	0	0	0	0	0	0
BMI, n= 6						
Low risk	5 (83.3%)	6 (100%)	6 (100%)	6 (100%)	6 (100%)	5 (83.3%)
Some concerns	1 (16.7%)	0	0	0	0	1 (16.7%)
High risk	0	0	0	0	0	0

Legend: BMI, Body mass index; n, number of studies; PSA, Prostate-specific antigen.



(SDC 4) Figure S1. Individual risk of bias assessment at outcome level for A) body composition, B) functional capacity, C) cardiorespiratory fitness, D) muscle strength, E) prostate-specific antigen and F) body mass index. Green circles, low risk; yellow circles, some concerns; red circles, high risk of bias.

(SDC 5) Table S4. Overall and subgroup analysis effects on body composition, functional capacity, and the secondary outcomes in prostate cancer patients.

Outcomes	Analysis	n	Sample	Mean difference	95% CI	I^2	P-value
Body composition							
Body fat, %	All[#]	10	603	-1.0	-1.3 to -0.6	29.1%	<.001
	Low risk[#]	10	603	-1.0	-1.3 to -0.6	29.1%	<.001
Fat mass, kg	All	15	917	-0.6	-0.8 to -0.3	0%	<.001
	Low risk	13	825	-0.6	-0.8 to -0.3	0%	<.001
Trunk fat mass, kg	All[#]	7	490	-0.3	-0.6 to -0.0	26.9%	.025
	Low risk[#]	7	490	-0.3	-0.6 to -0.0	26.9%	.025
Lean mass, kg	All	14	914	0.5	0.3 to 0.7	0%	<.001
	Low risk	13	825	0.5	0.3 to 0.7	0%	<.001
Appendicular lean mass, kg	All[†]	9	578	0.4	0.2 to 0.6	47.0%	<.001
	Low risk[†]	9	578	0.4	0.2 to 0.6	47.0%	<.001
Functional capacity							
30 seconds sit-to-stand-up, reps	All	3	220	2.8	1.7 to 4.0	45.2%	<.001
	Low risk[‡]	-	-	-	-	-	-
Repeated sit-to-stand, sec	All	5	325	-1.0	-1.4 to -0.6	0%	<.001
	Low risk[‡]	-	-	-	-	-	-
400-m walk, sec	All[†]	8	519	-8.3	-12.4 to -4.2	7.0%	<.001
	Low risk[‡]	-	-	-	-	-	-
6-m usual walk, sec	All	4	189	-0.2	-0.5 to 0.1	85.4%	.225
	Low risk[‡]	-	-	-	-	-	-
6-m fast walk, sec	All[#]	3	140	-0.1	-0.2 to -0.0	0%	.040
	Low risk[‡]	-	-	-	-	-	-
Timed-up and go, sec	All	3	102	-0.3	-0.8 to 0.2	52.4%	.261
	Low risk[‡]	-	-	-	-	-	-
Stair climb, sec	All	4	213	-0.2	-0.3 to -0.1	0%	.008
	Low risk[‡]	-	-	-	-	-	-
Secondary outcomes							
VO_{2peak}, $ml.kg.min^{-1}$	All[†]	5	331	1.3	0.8 to 1.7	0%	<.001
	Low risk[‡]	-	-	-	-	-	-
Chest press, kg	All[#]	10	728	3.9	2.9 to 4.9	0%	<.001
	Low risk[‡]	-	-	-	-	-	-
Leg extension, kg	All[#]	6	399	8.8	6.9 to 10.7	0%	<.001
	Low risk[‡]	-	-	-	-	-	-
Leg press, kg	All	11	769	23.5	15.2 to 31.7	77.4%	<.001
	Low risk[‡]	-	-	-	-	-	-
Seated row, kg	All[#]	4	321	5.2	3.9 to 6.5	0%	<.001
	Low risk[‡]	-	-	-	-	-	-
BMI, $kg.m^{-2}$	All	6	418	0	-0.2 to 0.2	0%	.735
	Low risk	5	299	0.1	-0.1 to 0.3	0%	.440
PSA, $ng.ml^{-1}$	All	8	576	0.1	-0.2 to 0.3	0%	.586
	Low risk	8	576	0.1	-0.2 to 0.3	0%	.586

#, Adjustment after sensitivity analysis omitting one study at a time. †, Trim-and-fill adjustment after significant effect of publication bias in egger's test. ǂ, Insufficient data for analysis. BMI, Body mass index; n, Number of comparisons; PSA, Prostate-specific antigen; VO2peak, Peak Oxygen Uptake.

(SDC 6) Table S5. Univariate meta-regression on main outcomes mean difference and exercise type, resistance training duration, weekly volume and peak intensity.

Outcomes	n	RT components	Range	Coeff ± SE	95% CI	P-value
Body composition						
Body fat, %	11	Type	RT alone/ RT combined	0.1±0.5	-1.0 to 1.1	.888
	11	Training duration, wk	12 to 48	-0.0±0.03	-0.07 to 0.07	.965
	11	RT weekly volume, reps	306 to 975	-0.0±0.001	-0.002 to 0.001	.650
	10	RT intensity, 1-RM	70 to 85%	0.05±0.06	-0.1 to 0.2	.456
Fat mass, kg	15	Type	RT alone/ RT combined	-0.3±0.3	-1.0 to 0.5	.458
	15	Training duration, wk	12 to 48	-0.01±0.02	-0.06 to 0.04	.628
	14	RT weekly volume, reps	306 to 975	0.001±0.001	-0.0 to 0.003	.139
	14	RT intensity, 1-RM	60 to 85%	-0.004±0.03	-0.06 to 0.06	.897
Trunk fat mass, kg	8	Type	RT alone/ RT combined	-0.5±0.3	-1.4 to 0.3	.149
	8	Training duration, wk	12 to 48	-0.03±0.02	-0.08 to 0.02	.158
	8	RT weekly volume, reps	306 to 682	0.002±0.001	-0.001 to 0.004	.129
	8	RT intensity, 1-RM‡	80 to 85%	-	-	-
Lean mass, kg	14	Type	RT alone/ RT combined	-0.3±0.3	-1.0 to 0.3	.303
	14	Training duration, wk	12 to 48	-0.01±0.02	-0.05 to 0.02	.385
	13	RT weekly volume, reps	306 to 975	-0.0±0.001	-0.002 to 0.001	.819
	14	RT intensity, 1-RM	60 to 85%	-0.0±0.01	-0.02 to 0.02	.965
Appendicular lean mass, kg	9	Type	RT alone/ RT combined	-0.3±0.2	-0.7 to 0.05	.076
	9	Training duration, wk	12 to 24	-0.03±0.01	-0.06 to 0.003	.075
	9	RT weekly volume, reps	320 to 975	0.0±0.001	-0.001 to 0.002	.589
	9	RT intensity, 1-RM‡	80 to 85%	-	-	-
Functional capacity						
400-m walk, sec	8	Type	RT alone/ RT combined	7.7±5.9	-6.7 to 22.2	.239
	8	Training duration, wk	12 to 24	-0.8±0.7	-2.5 to 1.0	.332
	8	RT weekly volume, reps	270 to 975	0.02±0.02	-0.02 to 0.05	.341
	8	RT intensity, 1-RM	75 to 87%	-0.7±0.5	-1.9 to 0.5	.182
Secondary outcomes						
VO_2peak, ml.kg.min-1	5	Type	RT alone/ RT combined	-0.3±0.6	-2.3 to 1.6	.630
	5	Training duration, wk	12 to 24	0.0±0.0	-0.1 to 0.2	.651

	4	RT weekly volume, reps	305 to 720	0.0±0.0	-0.1 to 0.1	.598
	3	RT intensity, 1-RM	70 to 85%	-0.0±0.0	-0.6 to 0.5	.614
Chest press, kg	11	Type	RT alone/ RT combined	-6.1±1.9	-10.4 to -1.9	.010
	11	Training duration, wk	12 to 48	-0.02±0.1	-0.3 to 0.3	.907
	10	RT weekly volume, reps	135 to 504	0.02±0.01	-0.01 to 0.04	.110
	10	RT intensity, 1-RM	70 to 85%	-0.6±0.1	-0.9 to -0.4	<.001
Leg extension, kg	7	Type	RT alone/ RT combined	-0.6±3.1	-8.7 to 7.4	.851
	7	Training duration, wk	12 to 24	0.1±0.2	-0.5 to 0.6	.738
	6	RT weekly volume, reps	135 to 324	-0.03±0.01	-0.06 to -0.002	.043
	6	RT intensity, 1-RM‡	80 to 85%	-	-	-
Leg press, kg	11	Type	RT alone/ RT combined	-21.2±10.2	-44.4 to 1.9	.068
	11	Training duration, wk	12 to 48	-0.8±0.6	-2.1 to 0.6	.220
	10	RT weekly volume, reps	149 to 379	0.1±0.1	-0.0001 to 0.3	.050
	10	RT intensity, 1-RM	70 to 85%	0.3±1.4	-2.9 to 3.5	.854
Seated row, kg	5	Type	RT alone/ RT combined	-14.9±2.9	-24.1 to -5.6	.014
	5	Training duration, wk	12 to 24	-0.3±0.5	-2.0 to 1.4	.624
	5	RT weekly volume, reps	160 to 683	0.03±0.01	0.01 to 0.05	.032
	5	RT intensity, 1-RM‡	83 to 85%	-	-	-

‡, insufficient data for analysis; 1-RM, 1-repetition maximum; 95% CI, 95% confidence intervals; BMI, Body mass index; Coeff, Meta-regression coefficient; n, Number of comparisons; PSA, Prostate-specific antigen; RT, Resistance training; SE, Standard error; VO_2peak, Peak Oxygen Uptake; wk, Weeks.

(SDC 7) Table S6. Multivariate meta-regression on main outcomes mean difference and exercise type, resistance training duration, weekly volume and peak intensity.

Outcomes	n	RT components	Range	Coeff ± SE	95% CI	P-value	Model
Body composition							
Body fat, %	10	Type	RT alone/ RT combined	-1.0±0.9	-3.4 to 1.4	.326	r^2=-73.0% I^2=44.3% P=.785
	10	Training duration, wk	12 to 48	-0.01±0.03	-0.1 to 0.1	.799	
	10	RT weekly volume, reps	306 to 975	-0.002±0.002	-.01 to 0.0	.359	
	10	RT intensity, 1-RM	70 to 85%	0.05±0.07	-0.1 to 0.2	.544	
Fat mass, kg	13	Type	RT alone/ RT combined	0.15±0.5	-1.0 to 1.3	.771	r^2=-77.9% I^2=13.2% P=.777
	13	Training duration, wk	12 to 48	-0.01±0.03	-0.08 to 0.06	.780	
	13	RT weekly volume, reps	306 to 975	0.001±0.001	-0.002 to 0.004	.334	
	13	RT intensity, 1-RM	60 to 85%	0.002±0.06	-0.14 to 0.14	.977	
Trunk fat mass, kg	8	Type	RT alone/ RT combined	-0.08±0.5	-1.6 to 1.4	.896	r^2=43.0% I^2=33.5% P=.334
	8	Training duration, wk	12 to 48	-0.02±0.02	-0.09 to 0.04	.344	
	8	RT weekly volume, reps	306 to 682	0.001±0.002	-0.004 to 0.01	.467	
	8	RT intensity, 1-RM‡	80 to 85%	-	-	-	
Lean mass, kg	13	Type	RT alone/ RT combined	-0.7±0.5	-1.8 to 0.4	.162	r^2=100% I^2=0% P=.386
	13	Training duration, wk	12 to 48	-0.01±0.02	-0.06 to 0.03	.449	
	13	RT weekly volume, reps	306 to 975	-0.002±0.001	-0.004 to 0.001	.207	
	13	RT intensity, 1-RM	60 to 85%	0.03±0.05	-0.1 to 0.2	.522	
Appendicular lean mass, kg	9	Type	RT alone/ RT combined	-0.3±0.3	-1.1 to 0.4	.299	r^2=100% I^2=0% P=.203
	9	Training duration, wk	12 to 24	-0.02±0.02	-0.06 to 0.03	.361	
	9	RT weekly volume, reps	320 to 975	-0.0±0.0	-0.002 to 0.001	.657	
	9	RT intensity, 1-RM‡	80 to 85%	-	-	-	
Functional capacity							
400-m walk, sec	8	Type	RT alone/ RT combined	9.5±5.4	-7.6 to 26.7	.175	r^2=100% I^2=0% P=.358
	8	Training duration, wk	12 to 24	-0.6±0.8	-3.0 to 1.9	.500	
	8	RT volume, weekly reps	270 to 975	-0.01±0.03	-0.1 to 0.1	.794	
	8	RT intensity, 1-RM	75 to 87%	-1.0±1.0	-4.1 to 2.1	.392	
Secondary outcomes							
Chest press, kg	10	Type	RT alone/ RT combined	-2.9±1.5	-6.6 to 0.8	.104	r^2=100% I^2=0%
	10	Training duration, wk	12 to 48	-0.03±0.1	-0.3 to 0.2	.746	

	10	RT volume, weekly reps	135 to 504	-0.0±0.01	-0.02 to 0.02	.959	P= .012
	10	RT intensity, 1-RM	70 to 85%	-0.5±0.2	-0.9 to -0.1	.022	
Leg extension, kg	6	Type	RT alone/ RT combined	-3.7±3.2	-17.4 to 10.0	.366	r^2=100% I^2=0% P=.204
	6	Training duration, wk	12 to 24	-0.3±0.2	-1.2 to 0.6	.313	
	6	RT volume, weekly reps	135 to 324	-0.04±0.02	-0.1 to 0.02	.087	
	6	RT intensity, 1-RM‡	80 to 85%	-	-	-	
Leg press, kg	10	Type	RT alone/ RT combined	-68.4±44.0	-181.5 to 44.6	.181	r^2=88.2% I^2=57.4% P=.147
	10	Training duration, wk	12 to 48	-0.4±0.6	-1.9 to 1.1	.498	
	10	RT volume, weekly reps	149 to 379	-0.2±0.2	-0.8 to 0.3	.375	
	10	RT intensity, 1-RM	70 to 85%	3.2±2.2	-2.4 to 8.8	.205	

‡, insufficient data for analysis; 1-RM, 1-repetition maximum; 95% CI, 95% confidence intervals; BMI, Body mass index; Coeff, Meta-regression coefficient; I^2= Statistical test of heterogeneity; n, Number of comparisons; PSA, Prostate-specific antigen; r^2, Adjusted coefficient of determination; RT, Resistance training; SE, Standard error; VO2peak, Peak Oxygen Uptake; wk, Weeks