applied sciences

MDPI

Systematic Review

From Evidence to Practice: A Systematic Review and Meta-Analysis on the Effects of Supervised Exercise on Fatigue in Breast and Prostate Cancer Survivors

Arturo Cano-Uceda [1,2], Pablo García-Fernández [1,*], Blanca Peuyadé-Rueda [3,4], Ana María Cañuelo-Marquez [2], Cristian Solís-Mencía [5], Carmen Lucio-Allende [6], Luis De Sousa-De Sousa [1,7] and José Luis Maté-Muñoz [1]

1 Faculty of Nursing, Physiotherapy and Podiatry, Complutense University of Madrid, 28040 Madrid, Spain; arcano01@ucm.es (A.C.-U.); luisdeso@ucm.es (L.D.S.-D.S.); jmate03@ucm.es (J.L.M.-M.)
2 Faculty of Health Sciences, Alfonso X El Sabio University, 28691 Madrid, Spain; acanumar@uax.es
3 HM Faculty of Health Sciences, Camilo José Cela University, Villanueva de la Cañada, 28692 Madrid, Spain; blanca.pedauye@ucjc.edu
4 Instituto de Investigación Sanitaria HM Hospitales, 28015 Madrid, Spain
5 Department of Medicine, Faculty of Health Sciences, University of Deusto, 48007 Bilbao, Spain; c.solis@deusto.es
6 Physiotherapy, Occupational Therapy and Speech Therapy Unit, Infanta Leonor University Hospital, Vallecas, 28031 Madrid, Spain; carmen.lucio@salud.madrid.org
7 School of Engineering and Built Environment, Griffith University, Brisbane, QLD 4111, Australia
* Correspondence: pablga25@ucm.es

Abstract

Background: Breast and prostate cancer represent a significant global public health burden. Among the adverse effects of oncological treatments, fatigue is one of the most prevalent, persistent, and disabling symptoms. Therapeutic exercise has been shown to be effective for its management, with supervision identified as a key factor that may enhance adherence, safety, and intensity control. This systematic review and meta-analysis aimed to compare the effects of supervised exercise programs versus usual care on cancer-related fatigue in patients with breast or prostate cancer. **Methods**: A systematic search (September–December 2024) was conducted in six databases (PubMed, Web of Science, Scopus, Cochrane, PEDro, Scielo), selecting RCTs from the past 10 years in English or Spanish. Studies compared supervised exercise with unsupervised exercise or usual care in stage I–III breast or prostate cancer patients within five years post-treatment. Methodological quality was assessed with the PEDro scale and risk of bias with Cochrane's RoB 2.0. A random-effects model was used to calculate pooled effect sizes (ES, 95% CI), with heterogeneity (I^2), sensitivity, subgroup, and publication bias analyses. **Results**: A total of 25 interventions from 19 randomized controlled trials involving over 2200 participants were included. Supervised exercise significantly reduced cancer-related fatigue compared to usual care (effect size = 0.34; 95% CI: 0.22–0.47; $p < 0.001$; $I^2 = 56\%$). Sensitivity analyses supported the robustness of the findings. Subgroup analyses revealed greater effects in combined exercise programs, in men, and in patients with prostate cancer. No evidence of publication bias was observed. While 73.7% of studies were rated as having good methodological quality, the risk of bias was often unclear or high. **Conclusions**: Supervised therapeutic exercise programs are effective and safe for reducing fatigue in breast and prostate cancer survivors. These interventions should be incorporated into comprehensive care plans, with individualization based on patients' clinical and demographic characteristics. Further research is needed to identify the most effective and sustainable strategies for different patient subgroups.

Academic Editors: Valerio Sansone and Fausto Famà

Received: 1 May 2025
Revised: 2 June 2025
Accepted: 20 June 2025
Published: 29 July 2025

Citation: Cano-Uceda, A.; García-Fernández, P.; Peuyadé-Rueda, B.; Cañuelo-Marquez, A.M.; Solís-Mencía, C.; Lucio-Allende, C.; De Sousa-De Sousa, L.; Maté-Muñoz, J.L. From Evidence to Practice: A Systematic Review and Meta-Analysis on the Effects of Supervised Exercise on Fatigue in Breast and Prostate Cancer Survivors. *Appl. Sci.* **2025**, *15*, 8399. https://doi.org/10.3390/app15158399

Keywords: therapeutic exercise; supervised; fatigue; breast cancer; prostate cancer

1. Introduction

Cancer is one of the leading causes of morbidity and mortality worldwide [1], representing a significant public health challenge on a global scale [2]. In 2020, it was responsible for approximately one in six deaths globally [3]. Breast and prostate cancer, in particular, represent a significant burden to global health: breast cancer is the most commonly diagnosed malignancy and the leading cause of cancer-related death in women across more than 100 countries, while prostate cancer is the most frequent among men. Together, they account for 11.7% and 7.3% of new cases, respectively [4,5]. In 2018, the World Cancer Research Fund estimated that approximately 18% of all cancer cases in the United States could be attributed to physical inactivity, poor diet, and/or excess adiposity [6]. In this context, adopting a healthy lifestyle is considered an important protective factor and an effective tool in cancer prevention and control [7].

Cancer treatment is typically multimodal. In the case of breast cancer, conservative surgery followed by radiotherapy is common and has been associated with a 21.7% reduction in local recurrence at 10 years, a 5.4% reduction in breast cancer mortality, and a 5.3% reduction in all-cause mortality at 15 years [8]. For prostate cancer, prostatectomy is a frequent intervention, often combined with radiotherapy [9]. Chemotherapy is also commonly used to prevent recurrence in patients with stage I–III cancer, alongside immunotherapy in certain cases [10,11]. However, these treatments can induce multiple adverse effects, including fatigue, pain, cognitive impairment, sarcopenia, osteoporosis, and cardiotoxicity, among others [12–15].

Fatigue is among the most prevalent and debilitating symptoms experienced by cancer patients [16], often persisting for years after treatment completion [17]. Cancer-related fatigue is defined by the National Comprehensive Cancer Network as "a distressing, persistent, and subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or its treatment, which is not proportional to recent activity and interferes with usual functioning" [18]. It affects physical, emotional, and cognitive domains; tends to be disproportionate to the level of exertion; and significantly interferes with patients' daily functioning [19]. Fatigue may even occur prior to treatment initiation and is frequently exacerbated during chemotherapy [20], radiotherapy [21], or hormone therapy [22]. This condition negatively impacts functional capacity, activities of daily living, and emotional well-being, and may predict lower overall survival and recurrence-free survival [19,23].

Given the high prevalence and impact of cancer-related fatigue, numerous non-pharmacological interventions have been studied to alleviate it [24]. Among these, therapeutic exercise has been shown to be an effective strategy with a strong benefit–risk profile [18,24,25]. Therapeutic exercise programs have demonstrated positive effects in reducing cancer-related fatigue [24,25], as well as additional benefits for quality of life, strength, and overall physical function [26].

Among the variables influencing exercise program outcomes, supervision stands out as a key factor [27]. Supervised programs provide continuous professional guidance, which can enhance adherence and improve intervention effectiveness [28–30]. They also ensure proper technique, reduce the risk of injury [31], and allow for tailored adjustments of intensity and exercise type based on the patient's physical condition [30]. The American Society of Clinical Oncology (ASCO) also supports supervised exercise, highlighting that both aerobic and combined aerobic–resistance training are effective in reducing fatigue among cancer patients [32]. In contrast, unsupervised programs, while offering greater

flexibility and accessibility, may compromise adherence, increase perceived exertion, and reduce safety [28–31], which can ultimately diminish the program's benefit–risk balance.

Various exercise modalities (aerobic, resistance, or combined) have been evaluated for fatigue management in patients with breast and prostate cancer [33–36], yielding variable results depending on the type of intervention applied. However, many systematic reviews have focused exclusively on one cancer type [37,38], potentially introducing sex-related biases. Furthermore, the umbrella review by Zhou et al. found no systematic reviews meeting high methodological quality standards [39]. Some reviews fail to distinguish between supervised and unsupervised programs [38,40], or evaluate unrelated outcomes such as sleep parameters [41]. Others include overly heterogeneous populations, limiting the generalizability of their findings [42–45]. A notable example is the meta-analysis by Van Vulpen et al. [40], which included multiple cancer types and both supervised and unsupervised interventions, finding significantly greater effects in the supervised ones. Similarly, in 2011, Cramp and Byron-Daniel reported benefits only from aerobic programs, not from resistance training [46].

Considering these discrepancies and the need for more detailed evaluation, the present systematic review and meta-analysis aims to analyze and compare the effects of supervised therapeutic exercise programs (based on aerobic, resistance, stretching, or combined training) versus usual care in reducing fatigue among patients treated for breast and prostate cancer.

2. Methods

2.1. Search Strategy

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [47] and followed the recommendations of the Cochrane Handbook for Systematic Reviews [48]. This systematic review and meta-analysis was registered in the Open Science Framework (OSF) under the digital object identifier https://doi.org/10.17605/OSF.IO/E23RT.

A systematic search was carried out from September to December 2024 to identify studies evaluating the effect of exercise interventions on fatigue in cancer patients. The search was conducted across the following databases: Web of Science (WOS), PubMed, PEDro, Scielo, Cochrane, and Scopus. A PICO-based strategy was employed, using both controlled vocabulary and natural language terms, which were reviewed by a health sciences librarian. The search included the following terms: "Breast cancer"; "Prostate cancer"; "supervised exercise"; "strength"; "aerobic"; "resistance"; "stretching"; and "Fatigue". The goal was to gather all available scientific evidence on the effects of supervised therapeutic exercise programs on cancer-related fatigue compared to usual care or unsupervised exercise. The complete search strategy is presented in Table 1.

Table 1. Search strategy.

Search Strategy	Natural Terms and Equations	Results Obtained
Pubmed		
#1	("Breast cancer" [Title/Abstract] OR "Prostate cancer" [Title/Abstract])	
#2	("supervised exercise" [Title/Abstract] OR "strength" [Title/Abstract] OR "aerobic" [Title/Abstract] OR "resistance" [Title/Abstract] OR "stretching" [Title/Abstract]))	
#3	("Fatigue" [Title/Abstract])	
#4	#1 AND #2 AND #3	848

Table 1. *Cont.*

Search Strategy	Natural Terms and Equations	Results Obtained
Scielo		
#1	(ab:(“Breast cancer” OR “Prostate cancer”))	
#2	(ab:(“ Supervised exercise” OR ab: “strength” OR ab:”aerobic” OR ab:”resistance” OR ab:”stretching”))	
#3	(ab:(“Fatigue”))	
#4	#1 AND #2 AND #3	5
Web of Science		
#1	(“Breast cancer” OR “Prostate cancer”)	
#2	(“supervised exercise” OR aerobic OR strength OR resistance OR strecthing)	
#3	(“Fatigue”)	
#4	Tittle/abstract: #1 AND #2 AND #3	1215
Cochrane		
#1	(“Breast cancer” OR “Prostate cancer”)	
#2	(“supervised exercise” OR aerobic OR strength OR resistance OR stretching)	
#3	(“Fatigue”)	
#4	Tittle/Abstract/Keywords #1 AND #2 AND #3	1945
Scopus		
#1	(TITLE-ABS-KEY (“breast cancer”) OR TITLE-ABS-KEY (“Prostate cancer”))	
#2	(TITLE-ABS-KEY (“supervised exercise”) OR TITLE-ABS-KEY (aerobic) OR TITLE-ABS-KEY(strength) OR TITLE-ABS-KEY(resistance) OR TITLE-ABS-KEY(stretching))	
#3	(TITLE-ABS-KEY(“Fatigue”)	
#4	#1 AND #2 AND #3	2407
PEDro		
Subdiscipline	Oncology	
Body Part	#1 Chest #2 Perineum or genito urinary system	
Therapy	#3 fitness training #4 strength training	
	#1 + #3; #1 + #4; #2 + #3; #2 + #4	72
TOTAL	Pubmed +Scielo + Web of Science + Cochrane + Scopus + PEDro	6492

2.2. Eligibility Criteria

Two independent reviewers (A.C.U. and P.G.F.) screened the titles and abstracts of the retrieved articles to identify studies meeting the inclusion criteria. Articles with titles and abstracts deemed relevant to the review’s objective were further evaluated by accessing or requesting the full text. Studies were included if they met the following criteria: (1) published within the past 10 years; (2) written in English or Spanish; (3) randomized controlled trials with a usual care control group, in which the intervention group received supervised therapeutic exercise (strength training, aerobic/cardiorespiratory training, stretching, or any combination thereof); (4) included patients with breast or prostate cancer who began the exercise program no more than 5 years after completing cancer treatment; (5) cancer stages I–III with no comorbid conditions; (6) exercise interventions not combined with

other treatments (e.g., pharmacological, dietary, psychological, or supplemental therapies), aside from standard oncological care; and (7) outcomes included cancer-related fatigue.

Exclusion criteria were as follows: (1) animal studies, (2) systematic reviews, and (3) non-RCTs (including pilot studies, single-arm trials, non-randomized or uncontrolled studies, retrospective or cross-sectional studies).

2.3. Data Extraction and Quality Assessment

Using a customized data extraction table based on the Cochrane "Data Collection Form for Intervention Reviews: RCTs and non-RCTs," two authors (A.C.U. and P.G.F.) independently extracted the following information from each included study: author, year, country, cancer type, sample size, age, sex, intervention characteristics, duration of intervention, fatigue assessment tool, and main results. Disagreements were resolved by a third reviewer (J.L.M.M.). Duplicate records were removed using Mendeley Reference Manager (version 2.100).

Risk of bias was assessed using the Cochrane risk of bias tool (RoB 2.0) [49], which evaluates five domains: (1) bias arising from the randomization process, (2) bias due to deviations from intended interventions (including blinding of participants and personnel), (3) bias due to missing outcome data, (4) bias in outcome measurements (including blinding of outcome assessors), and (5) bias in the selection of the reported results. As with study selection and data extraction, risk of bias assessments were performed independently by two reviewers (A.C.U. and P.G.F.), with any disagreements resolved by a third reviewer (J.L.M.M.).

The methodological quality of the included trials was assessed using the PEDro scale [50], which includes 11 items covering external validity (item 1), internal validity (items 2–9), and statistical reporting (items 10–11). Items are scored as "yes" or "no," and only clearly satisfied criteria receive a "yes." The total score is based on items 2 through 11, with a maximum possible score of 10. Studies scoring below 4 points were rated as "poor," scores of 4–5 were "fair," 6–8 as "good," and 9–10 were "excellent."

2.4. Data Analysis

From each included study, pre- and post-intervention data were extracted to calculate individual effect sizes (ESs) as standardized mean differences (SMDs), along with their corresponding 95% confidence intervals (95% CI) and standard errors (SEs) [51]. ESs were considered positive when favoring the intervention group and negative when favoring the control group. For the quantitative synthesis, we estimated pooled effect sizes and their 95% confidence intervals using a random-effects model based on the DerSimonian and Laird method [52].

The overall effect size for exercise interventions compared to control groups was calculated by assessing the direction and magnitude of the observed change. Between-study heterogeneity was assessed using the I^2 statistic, which quantifies the proportion of variability across studies due to true heterogeneity rather than chance. I^2 values were interpreted as follows: 0–30% (low), >30–50% (moderate), >50–80% (substantial), and >80–100% (considerable). Associated *p*-values and confidence intervals for I^2 were also reported for a more precise interpretation of heterogeneity [53]

In studies including multiple exercise intervention arms, effect sizes were calculated separately for each modality to avoid data duplication in the pooled synthesis. To assess the robustness of the overall findings, a sensitivity analysis was conducted by sequentially removing each study to detect potential outliers or influential studies.

Subgroup analyses were performed based on participant sex, exercise modality, cancer type, and intervention duration to explore potential sources of heterogeneity and variations in effect magnitude across clinical and methodological characteristics.

Finally, publication bias was assessed through visual inspection of funnel plots and Egger's regression test, which detects asymmetry related to study size [54]. All statistical analyses were conducted using SPSS software (version 30.0.0.0, IBM Corp.).

3. Results

3.1. Systematic Review

3.1.1. Study Selection

The search strategy identified 6492 potentially eligible studies. Of these, 19 were included in the final systematic review. The selection process is illustrated in Figure 1, following the PRISMA 2020 guidelines.

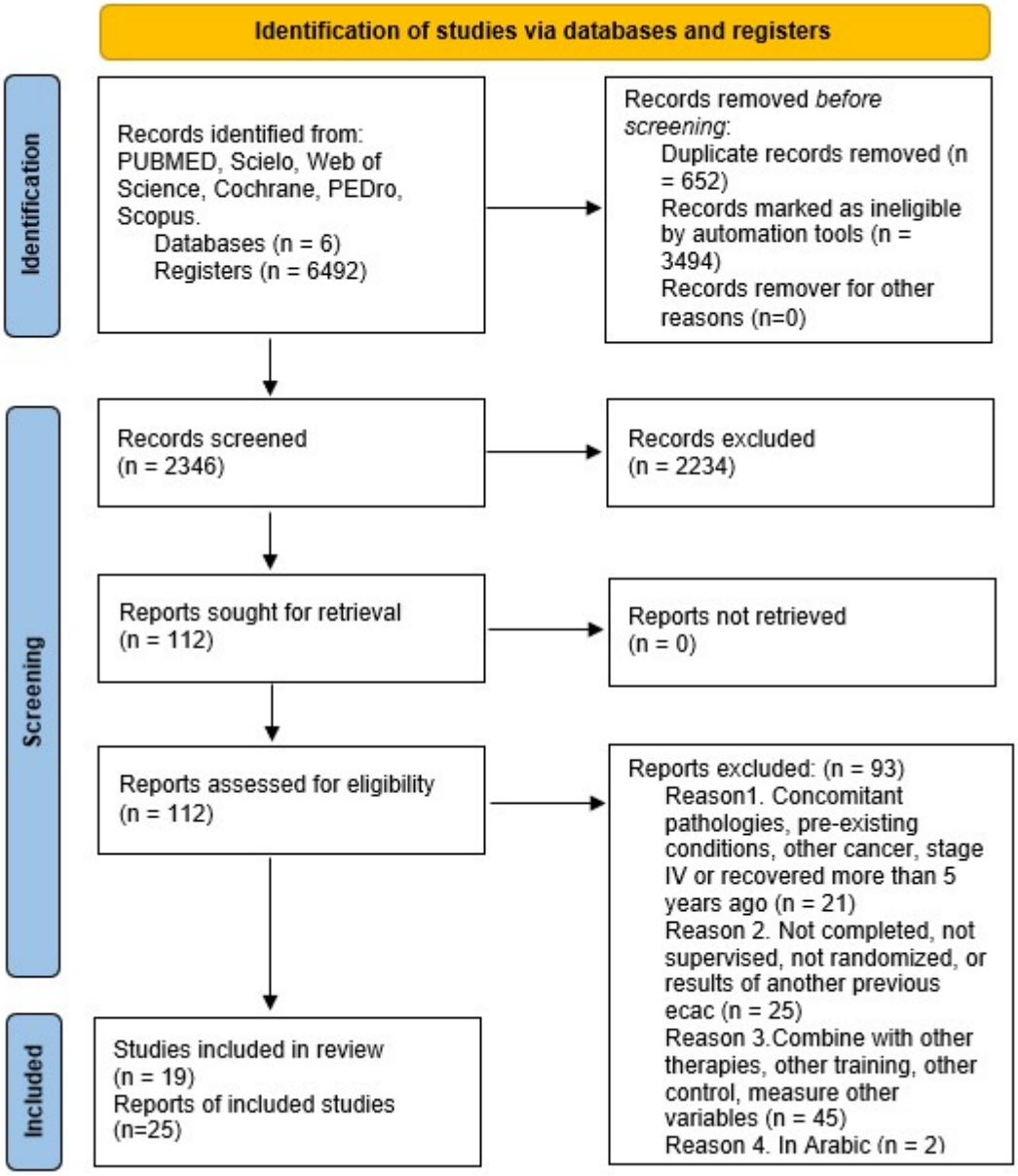

Figure 1. Flowchart of article selection.

3.1.2. Study and Intervention Characteristics

Table 2 provides a summary of the results from the studies included in the final review, detailing information on participants, experimental conditions, and the measurement tools used.

Table 2. Included studies.

Author/Year	Country	Cancer Type	Sample Size	Age (SD)	Sex	Intervention Characteristics	Duration of Intervention	Measurement Tool	Results
Al-Majid et al., 2015 [55]	USA	Breast	IG: 7 CG: 7	IG: 47.9 (10.4) CG: 52.7 (10.7)	W	IG: AT CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	12 weeks 2 days/week	PFS	IG Pre: 3.0 ± 0.7 Post: 3.0 ± 0.8 CG Pre: 0.8 ± 0.5 Post: 4.6 ± 0.9
Schmidt et al., 2015 [56]	Germany	Breast	IG: 49 CG: 46 ITT	IG: 52.2 (9.9) CG: 53.3 (10.2)	W	IG: RT CG: Active Structured Controls (stretching)	12 weeks 2 days/week	FAQ	IG Pre: 36.4 ± 19.2 Post: 36.1 ± 20.6 CG Pre: 41.0 ± 21.1 Post: 44.8 ± 21.0
Schmidt et al., 2015 [57]	Germany	Breast	GRT: 21 GET: 20 CG: 26	RT: 53 (12.55) ET: 56 (10.15) CG: 54 (11.19)	W	RT: RT ET: AT CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	12 weeks 2 days/week	MFI	GRT Pre: 9.25 ± 3.09 Post: 10.55 ± 3.22 GET Pre: 8.76 ± 4.31 Post: 12.35 ± 4.37 CG Pre: 9.54 ± 3.35 Post: 12.38 ± 3.50
Travier et al., 2015 [58]	Netherlands	Breast	IG: 102 CG: 102	IG: 49.7 (8.2) CG: 49.5 (7.9)	W	IG: Mixed CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	18 weeks 2 days/week	MFI	IG Pre: 10.1 ± 4.3 Δ change IC95% 1.9 [1.0 to 2.8] CG Pre: 10.6 ± 4.1 Δ change IC95% 2.3 [1.4 to 3.3]
Van Waart et al., 2015 [59]	Netherlands	Breast	IG:76 CG:77	IG: 49.9 (8.4) CG: 51.6 (8.8)	W	CI: Mixed CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	20 weeks 2 days/week	MFI y FQL	IG Pre: 10.6 ± 4.1 Post: 13.1 ± 3.9 CG Pre: 11.7 ± 4.4 Post: 14.7 ± 4.2
Mijwel et al., 2018 [60]	Sweden	Breast	GRT/HIIT: 74 GAT/HIIT:72 CG: 60	RT/HIIT: 52.7 (10.3) AT/HIIT: 54.4 (10.3) CG: 52.6 (10.2)	W	GRT/HIIT + RT GAT/HIIT +AT CG: Usual Care with General Recommendations (ACSM, WHO, healthy lifestyle advice)	16 weeks 2 days/week	PFS	GRT/HIIT Pre: 3.09 ± 3.17 Post: 3.16 ± 2.9 GAT/HIIT Pre: 2.10 ± 2.63 Post: 3.16 ± 2.6 CG Pre: 2.30 ± 2.81 Post: 3.94 ± 2.95
Ammitzbøll et al., 2019 [29]	Denmark	Breast	IG: 82 CG: 76	IG: 53 (33–73) CG: 52 (30–74)	W	IG: RT CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	20 weeks 2 days/week	FACIT-F	IG Δ change IC95% 2.71 [−0.1 to 5.5] CG Δ change IC95% 0.00 Reference
Baglia et al., 2019 [61]	USA	Breast	IG: 61 CG: 60	IG: 61.2 (7.09 CG: 62.0 (7.0)	W	IG: RT + AT CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	52 weeks 2 days/week	Facit-F	IG Pre: 37.9 ± 10.6 Post: 43.6 ± 10.6 CG Pre: 36.2 ± 10.8 Post: 36.7 ± 10.8
Mijwel et al., 2019 [36]	Sweden	Breast	GRT/HIIT: 74 GAT/HIIT: 72 CG: 60	GRT/HIIT: 52.7 (10.3) GAT/HIIT: 54.4 (10.3) CG: 52.6 (10.2)	W	RT: HIIT + RT AT HIIT: HIIT + AT CG: Usual Care with General Recommendations (ACSM, WHO, healthy lifestyle advice)	16 weeks 2 days/week	PFS	GRT/HIIT Pre: 3.09 ± 3.17 Post: 3.12 ± 3.03 GAT/HIIT Pre: 2.10 ± 2.63 Post: 3.18 ± 2.77 CG Pre: 2.30 ± 2.81 Post: 3.98 ± 3.05
Hojan et al., 2020 [62]	Poland	Prostate	IG: 36 CG: 36 ITT	IG: 65.7 (6.2) CG: 67.9 (4.9)	M	IG: Mixed CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	8 weeks 5 days/week	FACT-F	IG Pre: 113.4 ± 3.5 Post: 117.9 ± 9.7 CG Pre: 112.9 ± 3.9 Post: 81.5 ± 9.7

Table 2. *Cont.*

Author/Year	Country	Cancer Type	Sample Size	Age (SD)	Sex	Intervention Characteristics	Duration of Intervention	Measurement Tool	Results
Ndjavera et al., 2020 [63]	UK	Prostate	IG: 24 CG: 26 ITT	IG: 71.4 (5.4) CG: 72.5 (4.2)	M	IG: Mixed CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	12 weeks 2 days/week	Facit-F	IG Pre: 41.8 ± 10.2 Post: 41.8 ± 11.2 CG Pre: 42.9 ± 8.4 Post: 38.5 ± 11.9
Pereira et al., 2020 [64]	Mexico	Breast	GMICT: 80 GHIIT: 70 CG: 66	GMICT: 51 (4) GHIIT: 55 (5) CG: 53 (7)	W	MICT: Mixed HIIT: HIIT + RT CG: Usual Care with General Recommendations (ACSM, WHO, healthy lifestyle advice)	36 weeks 3 days/week	FACT-F	GMICT Pre: 18.6 ± 9.5 Post: 8.0 ± 4.2 GHIIT Pre: 20.4 ± 5.6 Post: 5.1 ± 3.6 CG Pre: 16.6 ± 5.6 Post: 16.9 ± 4.6
Piraux et al., 2020 [65]	Belgium	Prostate	GHIIT: 24 GRES: 24 CG: 24	GHIIT: 67.4 (8.9) GRES: 67.9 (7.1) CG: 71.9 (8.1)	M	HIIT: HIIT RT: RT CG: Usual Care with General Recommendations (ACSM, WHO, healthy lifestyle advice)	5–8 weeks 3 days/week	Facit-F	GHIIT Pre: 43.1 ± 6.9 Post: 42.1 ± 10.3 GRES Pre: 41.2 ± 7.7 Post: 40.5 ± 9.8 CG Pre: 41.1 ± 9.0 Post: 40.5 ± 9.8
Scott et al., 2020 [66]	USA	Breast	GLET: 58 GNLET: 59 CG: 57	GLET: 58 (9) GNLET: 59 (9) CG: 58 (9)	W	LET: AT NLET: AT + HIIT CG: Active Structured Controls (stretching)	16 weeks 3–4 days/week	Facit-F	GLET Pre: 36.7 ± 11.9 Post: 39.5 ± 12.2 GNLET Pre: 42.8 ± 8.9 Post: 44.8 ± 9.0 CG Pre: 39.6 ± 10.9 Post: 39.9 ± 10.7
Gal et al., 2021 [67]	Netherlands	Breast	IG: 68 CG: 114	IG: 58.0 (9.8) CG: 58.3 (9.5)	W	IG: Mixed CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	12 weeks 2 days/week	MFI	IG Pre: 11.6 ± 4.7 Δ change IC95% −1.0 [−1.8 to −0.1] CG Pre: 10.6 ± 4.3 Δ change IC95% −0.3 [−1.0 to 0.4]
Moraes et al., 2021 [68]	Brazil	Breast	IG: 13 CG: 13	IG: 55.0 (5.8) CG: 54.3 (5.2)	W	IG: RT CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	8 weeks 1 day/week	PFS	IG Pre: 5.1 ± 2.7 Post: 2.3 ± 1.4 CG Pre: 3.9 ± 2.0 Post: 3.0 ± 2.4
Harrison et al., 2022 [34]	USA	Prostate	IG: 13 CG: 13	IG: 65.7 (8.1) CG: 64.4 (8.3)	M	IG: Mixed CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	16 weeks 3 days/week	Facit-F	IG vs. CC Δ change IC95% +4.0 [−3.2 to 11.1]
Kang et al., 2022 [35]	Canada	Prostate	IG: 26 CG: 26	IG-CG: 63.4 (7.1)	M	IG: HIIT CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	12 weeks 3 days/week	FACT-F	IG Pre: 43.6 ± 6.6 Post: 46.0 ± 4.3 CG Pre: 45.3 ± 4.7 Post: 44.6 ± 6.0
Koevoets et al., 2022 [69]	Netherlands	Breast	IG: 91 CG: 90	IG: 52.1 (8.6) CG: 52.5 (8.7)	W	IG: Mixed CG: Passive Usual Care (no exercise/maintain habitual activity/no specific advice)	6 months 4 days/week	MFI	IG vs. CC Δ change IC95% +2.22 [1.11 to 3.32]

IG = Intervention Group; CG = Control Group; PFS = Piper Fatigue Scale; Facit-F = Functional Assessment of Chronic Illness Therapy-Fatigue; FACT-F = Functional Assessment of Cancer Therapy: Fatigue; MFI = Multidimensional Fatigue Inventory; RT = Resistance Training; AT = Aerobic Training; HIIT = High-Intensity Interval Training; MICT = Moderate-Intensity Continuous Training; FAQ = Fatigue Assessment Questionnaire; ET = Endurance Training; LET = Linear Exercise Therapy; NLET = Non-Linear Exercise Therapy; FQL = Fatigue Quality List; M = Men; UC = Usual Care; W = WomenGeneral.

3.1.3. Characteristics of Included Studies

The randomized controlled trials included in this systematic review evaluated the effects of supervised exercise programs compared to unsupervised exercise or usual care in patients diagnosed with breast or prostate cancer. These studies were conducted in a

variety of countries including the United States, Germany, Mexico, Denmark, Belgium, Brazil, Canada, and the Netherlands, thus offering an international perspective.

A total of 19 randomized controlled trials were analyzed in this review, encompassing more than 2200 participants overall. Mean participant ages varied across studies but generally ranged from 40 to 70 years, reflecting the broad age spectrum at which these types of cancer may occur.

Supervised exercise interventions included aerobic training, resistance training, High-Intensity Interval Training (HIIT), and combined programs that incorporated aerobic and resistance exercise components. The duration of interventions also varied, ranging from 8 to 52 weeks, with training frequencies typically between two and three sessions per week, although some studies applied frequencies as low as once or as high as five times per week. Although the inclusion criteria allowed for studies with interventions conducted up to five years after cancer treatment, most of the included studies implemented exercise during active oncologic treatment (Supplementary Table S1).

Cancer-related fatigue was assessed using various validated measurement tools, including the Piper Fatigue Scale (PFS), Fatigue Assessment Questionnaire (FAQ), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Functional Assessment of Cancer Therapy: Fatigue (FACT-F), and the Multidimensional Fatigue Inventory (MFI).

3.1.4. Quality Assessment and Risk of Bias

Methodological quality was evaluated using the PEDro scale, with 5 of the 19 studies (26.3%) rated as "fair" and the remaining 14 studies (73.7%) rated as "good" (Table 3).

Table 3. Methodological quality as measured by PEDro scale.

Study	1	2	3	4	5	6	7	8	9	10	11	Total
Al-Madjid et al., 2015 [55]	+	+	-	+	-	-	-	+	-	+	+	5
Schmidt et al., 2015 [56]	+	+	+	-	-	-	-	-	-	+	+	5
Schmidt et al., 2015 [57]	+	+	-	+	-	-	-	+	+	+	+	6
Travier et al., 2015 [58]	+	+	+	+	-	-	+	+	+	+	+	8
Van Waart et al., 2015 [59]	+	+	-	+	-	-	-	+	+	+	+	6
Mijwel et al., 2018 [60]	+	+	-	+	-	-	-	-	-	+	+	4
Ammitzbøll et al., 2019 [29]	+	+	-	+	-	-	-	-	+	+	+	5
Baglia et al., 2019 [61]	+	+	+	+	-	-	-	+	+	+	+	7
Mijwel et al., 2019 [36]	+	+	-	+	-	-	-	+	+	+	+	6
Hojan 2020 [62]	+	+	+	+	-	-	-	+	+	+	+	7
Ndjavera et al., 2020 [63]	+	+	+	+	-	-	+	-	+	+	+	7
Pereira et al., 2020 [64]	+	+	+	+	-	-	+	-	-	+	+	6
Piraux et al., 2020 [65]	-	+	-	+	-	-	-	+	+	+	+	6
Scott et al., 2020 [66]	-	+	-	+	-	-	-	+	+	+	+	6
Gal et al., 2021 [67]	+	+	-	+	-	-	-	-	+	+	+	5
Moraes et al., 2021 [68]	+	+	-	+	-	-	-	+	+	+	+	6
Harrison et al., 2022 [34]	-	+	-	+	-	-	+	+	-	+	+	6
Kang et al., 2022 [35]	+	+	-	+	-	-	-	+	+	+	+	6
Koevoets et al., 2022 [69]	-	+	-	+	-	-	-	+	+	+	+	6

1. Eligibility criteria and source (this item does not contribute to the total score). 2. Random allocation. 3. Concealed allocation. 4. Baseline comparability. 5. Blinding of participants. 6. Blinding of therapists. 7. Blinding of assessors. 8. Adequate follow-up (>85%). 9. Intention-to-treat analysis. 10. Between-group statistical comparisons. 11. Reporting of point measures and measures of variability.

Risk of bias was assessed using the Cochrane Risk of Bias Tool (RoB 2.0). Among the 19 included studies, 7 studies (36.8%) were found to have a high risk of bias, 11 studies (57.9%) showed some concerns, and 1 study (5.3%) was rated as low risk of bias (Figures 2 and 3).

Figure 2. Risk of bias assessment: summary of individual studies.

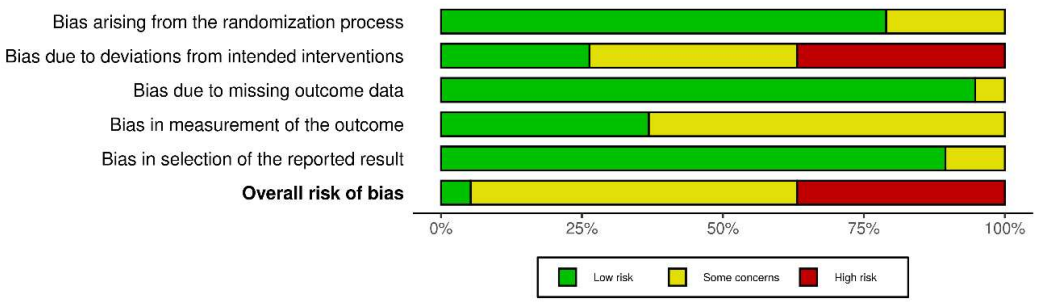

Figure 3. Risk of bias assessment: aggregate appraisal results.

3.2. Data Synthesis

3.2.1. Meta-Analysis

The pooled effect size for the impact of therapeutic exercise versus the CG on fatigue was 0.34 (95% CI: 0.22–0.47; I^2 = 56%, p = 0.00) (Figure 4).

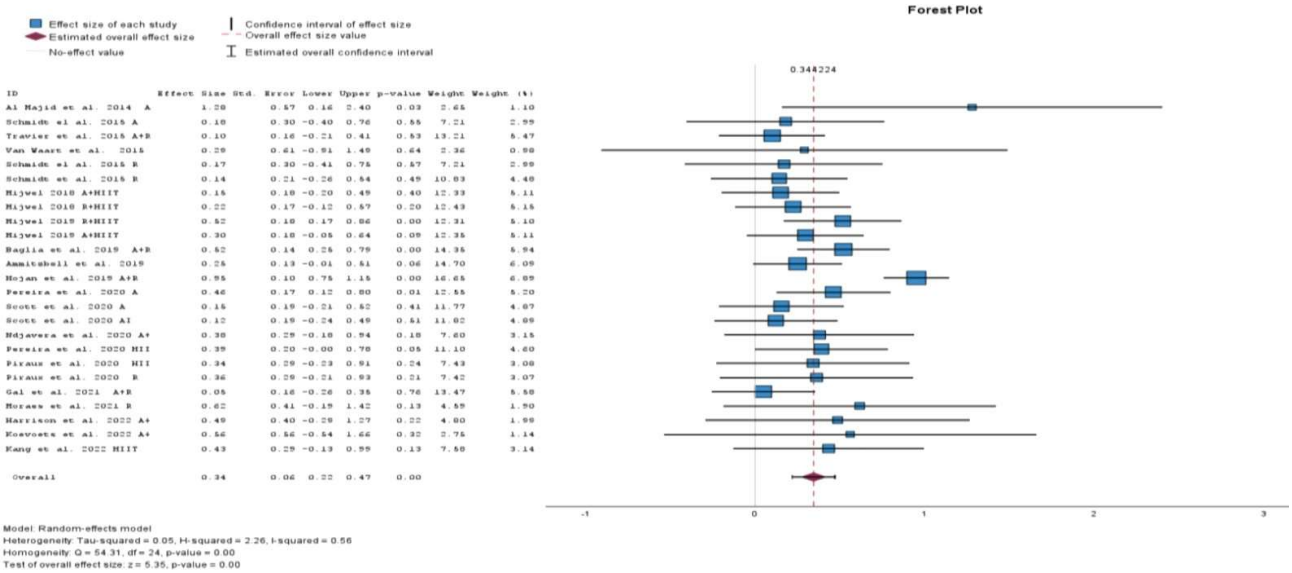

Figure 4. Meta-analysis for therapeutic exercise vs. control group (pooled ES analysis).

3.2.2. Sensitivity and Subgroup Analyses

The sensitivity analysis showed that removing individual studies from the meta-analysis did not substantially alter the pooled effect size estimate for therapeutic exercise vs. control group (Table 4).

Table 4. Sensitivity analyses.

Author, Year	ES	LL	UL	I^2
Ammitzbøll et al., 2019 [29] R	0.35	0.22	0.48	56.7
Harrison et al., 2022 [34] C	0.34	0.21	0.47	55.8
Kang et al., 2022 [35] H	0.34	0.21	0.47	57.6
Mijwel 2019 [36] R + HIIT	0.33	0.20	0.47	57.2
Mijwel 2019 [36] A + HIIT	0.35	0.21	0.48	57.4
Al Majid et al., 2015 [55] A	0.33	0.20	0.45	55.7
Schmidt el al. 2015 [56] A	0.34	0.22	0.47	57.3
Schmidt el al. 2015 [57] R	0.35	0.22	0.48	57.2
Schmidt et al., 2015 [57] R	0.35	0.22	0.48	56.5
Travier et al., 2015 [58] C	0.36	0.23	0.49	54.8
Van Waart et al., 2015 [59] C	0.34	0.22	0.47	57.6
Mijwel 2018 [60] A + HIIT	0.35	0.22	0.48	56.1
Mijwel 2018 [60] R + HIIT	0.35	0.21	0.48	56.9
Baglia et al., 2019 [61] C	0.33	0.20	0.46	56.9
Hojan et al., 2019 [62] C	0.28	0.19	0.36	0.0
Ndjavera et al., 2020 [63] C	0.34	0.21	0.47	57.7
Pereira et al., 2020 [64] A	0.33	0.20	0.47	57.5

Table 4. *Cont.*

Author, Year	ES	LL	UL	I^2
Pereira et al., 2020 [64] H	0.34	0.20	0.47	59.5
Piraux et al., 2020 [65] H	0.34	0.21	0.47	57.6
Piraux et al., 2020 [65] R	0.34	0.21	0.47	57.6
Scott et al., 2020 [66] A C	0.35	0.22	0.48	56.3
Scott et al., 2020 A I [66]	0.35	0.22	0.48	55.9
Gal et al., 2021 [67] C	0.36	0.23	0.48	53.3
Moraes et al., 2021 [68] R	0.33	0.21	0.46	57.4
Koevoets et al., 2022 [69] C	0.34	0.21	0.47	57.6

ES: Effect size; LL: lower limit; UL: upper limit.

Subgroup analyses based on exercise type, intervention duration, sex, and cancer type modified the pooled effect size estimate but did not affect the statistical significance of the comparison between therapeutic exercise and the control group (Tables 5–8).

Table 5. Subgroup analysis by type of exercise.

Exercise	ES	LL	UL	I^2
Endurance	0.258	0.052	0.518	26.4
Combined	0.421	0.095	0.747	80.0
HIIT	0.321	0.175	0.468	0.0
Resistance	0.250	0.062	0.439	0.0

ES: Effect size; LL: lower limit; UL: upper limit; HIIT: High-Intensity Interval Training.

Table 6. Subgroup analysis by duration of the exercise program.

Duration	ES	LL	UL	I^2
≤12 weeks	0.407	0.131	0.682	72.7
>12–24 weeks	0.234	0.131	0.682	0.0
>24 weeks	0.474	0.290	0.679	0.0

ES: Effect size; LL: lower limit; UL: upper limit; HIIT: High-Intensity Interval Training.

Table 7. Subgroup analysis by gender.

Gender	ES	LL	UL	I^2
Men	0.555	0.254	0.855	55.0
Women	0.274	0.190	0.362	0.0

ES: Effect size; LL: lower limit; UL: upper limit.

Table 8. Subgroup analysis by cancer type.

Cancer Type	ES	LL	UL	I^2
Prostate	0.555	0.254	0.855	55.0
Breast	0.274	0.186	0.362	0.0

ES: Effect size; LL: lower limit; UL: upper limit.

3.2.3. Publication Bias

No significant publication bias was found in the studies comparing therapeutic exercise to the control group, as indicated by funnel plot symmetry (Figure 5) and the results of Egger's test (p = 0.672) (Table 9).

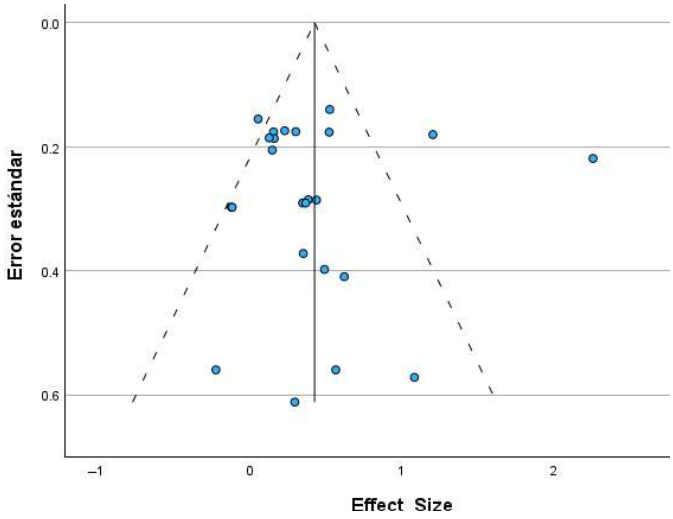

Figure 5. Funnel Plot.

Table 9. Publication bias by Egger's test.

Exercise vs. Control Group	Coefficient	p-Value
	0.284	0.672

4. Discussion

This systematic review and meta-analysis was conducted to determine the effectiveness of supervised therapeutic exercise on fatigue in oncology patients with breast or prostate cancer.

A total of 25 interventions from 19 randomized controlled trials were included, all demonstrating a positive effect of therapeutic exercise on fatigue in cancer patients. Although the magnitude of the effect falls within the range considered small by conventional standards, its clinical relevance is notable given that cancer-related fatigue is a highly prevalent, debilitating symptom that is difficult to manage pharmacologically. These results support the inclusion of therapeutic exercise as a safe and effective strategy to reduce fatigue, with the potential to improve quality of life, functional capacity, and recovery after cancer treatment. The consistency observed across studies also suggests that these programs can be flexibly adapted to different clinical profiles without compromising effectiveness.

These findings align with those reported in previous studies [37,38,46]. The improvements observed may be explained by exercise's protective effect against the decline in maximal oxygen uptake, which may help alleviate cancer-related fatigue [55]. In addition, physical training promotes progressive improvements in exercise tolerance and muscle strength, which may delay fatigue onset. Another relevant mechanism is the anti-inflammatory effect of physical activity, which, together with its cognitive benefits, could help counteract some treatment-related side effects, including fatigue [69].

These benefits are further enhanced by professional supervision, which helps patients overcome common barriers such as a lack of knowledge about exercise benefits or perceiving fatigue as a limitation. Supervision by trained professionals improves understanding

of exercise utility, thereby increasing adherence and intervention effectiveness [36]. Importantly, no serious adverse events or clinical complications directly attributable to the supervised exercise programs were reported. This finding, consistent with prior systematic reviews [24], reinforces the favorable risk–benefit profile of exercise prescription in cancer patients. The absence of major adverse effects strongly supports the integration of these non-pharmacological strategies into personalized care plans.

Beyond its direct impact on patients' daily functioning, cancer-related fatigue has been commonly associated with lower treatment adherence, reduced quality of life, and worse clinical outcomes [17]. Groenvold et al. [23] also demonstrated that fatigue is one of the most debilitating symptoms in cancer patients, significantly affecting overall health status and functional capacity, particularly in advanced or palliative stages. Moreover, persistent fatigue may reduce patients' ability to complete chemotherapy, radiotherapy, or hormonal therapy regimens, thereby compromising therapeutic efficacy and survival. Rock et al. [70] reported that modifiable lifestyle factors such as physical inactivity, poor diet, and obesity accounted for over 18% of cancer cases in the U.S. in 2014. Altogether, these data support the clinical importance of interventions targeting fatigue and related behaviors, as improvements may not only enhance patient well-being but also promote better adherence, treatment tolerance, and long-term clinical outcomes.

Subgroup analyses by exercise type showed that all supervised modalities were effective in reducing cancer-related fatigue, with statistically significant effect sizes. Combined aerobic and resistance training showed the largest effect size, although with considerable heterogeneity, suggesting variability in how these interventions are implemented. This could result from the combination of strength training—which affects fatigue through inflammatory and metabolic pathways and helps preserve muscle mass, function, and body composition [15,60,71,72], and aerobic training, which improves cardiorespiratory fitness and cardiovascular efficiency, thereby reducing fatigue perception [60]. HIIT programs, like resistance training (though with a slightly smaller effect size), also demonstrated consistent and significant effects with no heterogeneity, indicating a more uniform response to these interventions. HIIT has been shown to reduce inflammatory markers such as interleukins, improve body composition, and enhance cardiorespiratory fitness, notably increasing IL-15 levels, which may contribute to reduced fatigue and improved overall health in cancer survivors [73]. It is also highly effective in improving VO2 max, a key indicator of cardiorespiratory fitness [74], and provides significant benefits in a shorter time frame, allowing for higher training loads and improved adherence [75]. Moreover, HIIT positively impacts mitochondrial function, muscle capillarization, and fat oxidation capacity, all of which may lower fatigue during daily activities [76,77]. Conventional aerobic training showed a smaller but still significant effect, with low heterogeneity. These results suggest that while all exercise modalities are beneficial, combined interventions may offer the greatest clinical impact, although they require more standardized implementation. On the other hand, the consistent effects of HIIT and resistance training may facilitate their use in resource-limited clinical settings due to their structured format and more predictable outcomes.

Subgroup analysis based on program duration showed that all durations evaluated ($\leq$12 weeks, >12–24 weeks, and >24 weeks) were associated with significant reductions in fatigue, with moderate effect sizes. The greatest effect was seen in programs longer than 24 weeks, followed by those $\leq$12 weeks, while programs lasting 12–24 weeks had the smallest effect. Notably, substantial heterogeneity was observed among studies with $\leq$12-week programs, possibly reflecting variability in intensity, exercise type, or participant characteristics. In contrast, the absence of heterogeneity in longer-duration groups indicates more consistent outcomes, strengthening the evidence in favor of extended programs. The superior effectiveness of >24-week programs may be due to better physiological and

psychological adaptation occurring over time, resulting in more sustained benefits and fatigue reduction. These programs may also enhance adherence, which is crucial for long-term effects [78]. While brief interventions also show benefits, the high heterogeneity suggests the need for further research to optimize their effectiveness.

Subgroup analyses revealed differences in the magnitude of therapeutic exercise's effects on fatigue based on sex and cancer type. Among men, predominantly with prostate cancer, the effect size was notably higher, with moderate heterogeneity. Among women, primarily with breast cancer, the effect was more modest but more consistent across studies. These findings may reflect physiological or psychological differences or differences in exercise protocol implementation between men and women. Men in prostate cancer trials often received strength- or HIIT-focused interventions, while women with breast cancer typically participated in mixed programs with more varied frequencies or intensities. Clinically, these results suggest that therapeutic exercise is beneficial for both groups but may require tailoring to individual patient profiles to maximize effectiveness. Additionally, the greater heterogeneity in male-focused studies highlights the need to better standardize prostate cancer interventions, while the consistency in female-focused studies strengthens current recommendations in this population.

One of the main methodological challenges in exercise oncology trials is the lack of uniformity in the definition of control groups and the variability in intervention timing. In this meta-analysis, control conditions ranged from inactivity to light interventions, and most studies implemented exercise during active treatment, with few conducting it in later phases. These inconsistencies, together with the limited number of studies in certain categories and the absence of clear trends in the forest plot, precluded formal subgroup analyses. Altogether, these findings highlight the need for more precise and standardized reporting of both control group composition and intervention timing in future trials.

The analysis was performed using a random-effects model, appropriate for accounting for variability in study design, exercise type, intervention duration, and population characteristics. The heterogeneity observed was moderate, suggesting some variability in the results but not enough to compromise the validity of the pooled effect.

Sensitivity analyses demonstrated a high degree of stability in the exercise effect on cancer-related fatigue, with consistently significant results. Notably, heterogeneity dropped substantially when the study by Hojan et al. [62] was excluded, suggesting that this study may contribute to overall variability, possibly due to its large reported effect size. Nevertheless, the consistent effect across studies confirms the robustness and clinical applicability of therapeutic exercise, regardless of modality.

Potential publication bias was assessed via visual inspection of the funnel plot and Egger's test, with no significant asymmetry detected. The symmetrical distribution of studies and non-significant standard error coefficient support this conclusion. The comprehensive search strategy further reduces the risk of omitting relevant studies, reinforcing the validity and robustness of the meta-analysis and the reliability of the observed effects of therapeutic exercise on cancer-related fatigue.

This meta-analysis has some methodological limitations that should be considered. First, the impossibility of blinding participants in exercise interventions may introduce performance and detection biases. Additionally, several studies did not adequately describe the randomization process, limiting risk-of-bias assessment. Moderate statistical heterogeneity was observed, likely due to differences in participant characteristics, study designs, interventions, and fatigue measurement tools. This methodological variability affects comparability and external validity. While subgroup analyses by exercise type, cancer type, and sex were performed, the limited number of studies in each subgroup may have affected the robustness of these results. Lastly, the scarcity of long-term follow-up

data limits our understanding of the sustainability of exercise benefits. Therefore, although the results are promising, they should be interpreted with caution within the context of these limitations.

5. Conclusions

This meta-analysis confirms that supervised therapeutic exercise is an effective and safe intervention for reducing fatigue in patients with breast and prostate cancer, yielding clinically meaningful effects, with effect sizes exceeding established thresholds of clinical relevance. All exercise modalities were found to be beneficial, with combined interventions showing the greatest impact, and resistance or high-intensity protocols demonstrating the most consistent results. Despite moderate heterogeneity, the findings were robust, with no evidence of publication bias or adverse events. These results support the integration of therapeutic exercise into oncological care, with personalized interventions based on patient characteristics. Further studies are needed to identify the most effective and sustainable program components, particularly in relation to cancer type, sex, and clinical status.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app15158399/s1, Table S1: Timing of Exercise Interventions in Breast and Prostate Cancer Studies.

Author Contributions: Conceptualization, A.C.-U. and P.G.-F.; methodology, A.C.-U., J.L.M.-M. and P.G.-F.; software, A.C.-U. and P.G.-F.; validation, A.C.-U., P.G.-F. and J.L.M.-M.; formal analysis, A.C.-U., P.G.-F. and L.D.S.-D.S.; investigation, A.C.-U., P.G.-F., B.P.-R., A.M.C.-M., C.S.-M., C.L.-A. and L.D.S.-D.S.; resources, P.G.-F., C.L.-A. and J.L.M.-M.; data curation, A.C.-U., P.G.-F., C.S.-M. and A.M.C.-M.; writing—original draft preparation, A.C.-U. and P.G.-F.; writing—review and editing, A.C.-U., P.G.-F., B.P.-R., L.D.S.-D.S. and J.L.M.-M.; visualization, P.G.-F., A.C.-U., J.L.M.-M. and L.D.S.-D.S.; supervision, P.G.-F. and J.L.M.-M.; project administration, P.G.-F.; funding acquisition, not applicable. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The datasets used and/or analyzed during the current review and meta-analysis are available from the corresponding author upon reasonable request.

Conflicts of Interest: All authors state that they have no interests which might be perceived as posing a conflict with or bias with respect to the content of this article. This includes no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this article.

References

1. Torre, L.A.; Siegel, R.L.; Ward, E.M.; Jemal, A. Global cancer incidence and mortality rates and trends—An update. *Cancer Epidemiol. Biomark. Prev.* **2016**, *25*, 16–27. [CrossRef]
2. Siegel, R.L.; Miller, K.D.; Jemal, A. Cancer statistics, 2018. *CA Cancer J. Clin.* **2018**, *68*, 7–30. [CrossRef]
3. Ferlay, J.; Colombet, M.; Soerjomataram, I.; Parkin, D.M.; Piñeros, M.; Znaor, A.; Bray, F. Cancer statistics for the year 2020: An overview. *Int. J. Cancer* **2021**, *149*, 778–789. [CrossRef] [PubMed]
4. Bray, F.; Ferlay, J.; Soerjomataram, I.; Siegel, R.L.; Torre, L.A.; Jemal, A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.* **2018**, *68*, 394–424. [CrossRef] [PubMed]
5. Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J. Clin.* **2021**, *71*, 209–249. [CrossRef]
6. World Cancer Research Fund/American Institute for Cancer Research. *Diet, Nutrition, Physical Activity and Cancer: A Global Perspective*; World Cancer Research Fund/American Institute for Cancer Research: London, UK, 2018; Continuous Update Project Expert Report 2018. Available online: http://www.dietandcancerreport.org (accessed on 15 March 2025).

7. Clinton, S.K.; Giovannucci, E.L.; Hursting, S.D. The World Cancer Research Fund/American Institute for Cancer Research Third Expert Report on Diet, Nutrition, Physical Activity, and Cancer: Impact and Future Directions. *J. Nutr.* **2020**, *150*, 663–671. [CrossRef]
8. Solin, L.J. Breast Conservation Treatment With Radiation: An Ongoing Success Story. *J. Clin. Oncol.* **2010**, *28*, 709–711. [CrossRef] [PubMed]
9. Vera Donoso, C.D. El tratamiento del cáncer de próstata: Presente y futuro, realidades y posibilidades. *Actas Urol. Esp.* **2007**, *31*, 575–579. [CrossRef]
10. He, Y.; Tan, P.; He, M.; Hu, L.; Ai, J.; Yang, L.; Wei, Q. The primary treatment of prostate cancer with high-intensity focused ultrasound: A systematic review and meta-analysis. *Medicine* **2020**, *99*, e22610. [CrossRef]
11. Waks, A.G.; Winer, E.P. Breast Cancer Treatment. *JAMA* **2019**, *321*, 288. [CrossRef]
12. Montero, A.; Hervás, A.; Morera, R.; Sancho, S.; Córdoba, S.; Corona, J.A.; Rodríguez, I.; Chajón, E.; Ramos, A. Control de síntomas crónicos: Efectos secundarios del tratamiento con Radioterapia y Quimioterapia. *Oncología* **2005**, *28*, 41–50. [CrossRef]
13. Ruiz-Schutz, V.C.; Gomes, L.M.; Mariano, R.C.; de Almeida, D.V.; Pimenta, J.M.; Molin, G.Z.D.; Kater, F.R.; Yamamura, R.; Neto, N.F.C.; Maluf, F.C.; et al. Risk of fatigue and anemia in patients with advanced cancer treated with olaparib: A meta-analysis of randomized controlled trials. In *Critical Reviews in Oncology/Hematology*; Elsevier Ireland Ltd.: Amsterdam, The Netherlands, 2019; Volume 141, pp. 163–173.
14. Schmidt, M.E.; Wiskemann, J.; Steindorf, K. Quality of life, problems, and needs of disease-free breast cancer survivors 5 years after diagnosis. *Qual. Life Res.* **2018**, *27*, 2077–2086. [CrossRef]
15. Wefel, J.S.; Saleeba, A.K.; Buzdar, A.U.; Meyers, C.A. Acute and late onset cognitive dysfunction associated with chemotherapy in women with breast cancer. *Cancer* **2010**, *116*, 3348–3356. [CrossRef]
16. Lawrence, D.P.; Kupelnick, B.; Miller, K.; Devine, D.; Lau, J. Evidence report on the occurrence, assessment, and treatment of fatigue in cancer patients. *J. Natl. Cancer Inst.* **2004**, *32*, 40–50. [CrossRef]
17. Mustian, K.M.; Alfano, C.M.; Heckler, C.; Kleckner, A.S.; Kleckner, I.R.; Leach, C.R.; Mohr, D.; Palesh, O.G.; Peppone, L.J.; Piper, B.F.; et al. Comparison of pharmaceutical, psychological, and exercise treatments for cancer-related fatigue: A meta-analysis. *JAMA Oncol.* **2017**, *3*, 961–968. [CrossRef]
18. NCCN Clinical Practice Guidelines in Oncology. Cancer-Related Fatigue Version 2.2025. 2025. Available online: www.nccn.org (accessed on 21 April 2025).
19. Bower, J.E. Cancer-related fatigue—Mechanisms, risk factors, and treatments. *Nat. Rev. Clin. Oncol.* **2014**, *11*, 597–609. [CrossRef] [PubMed]
20. Jacobsen, P.B.; Hann, D.M.; Azzarello, L.M.; Horton, J.; Balducci, L.; Lyman, G.H. Fatigue in Women Receiving Adjuvant Chemotherapy for Breast Cancer: Characteristics, Course, and Correlates. *J. Pain Symptom Manag.* **1999**, *18*, 233–242. [CrossRef] [PubMed]
21. Hickok, J.T.; Roscoe, J.A.; Morrow, G.R.; Mustian, K.; Okunieff, P.; Bole, C.W. Frequency, severity, clinical course, and correlates of fatigue in 372 patients during 5 weeks of radiotherapy for cancer. *Cancer* **2005**, *104*, 1772–1778. [CrossRef]
22. Phillips, K.M.; Pinilla-Ibarz, J.; Sotomayor, E.; Lee, M.R.; Jim, H.S.; Small, B.J.; Sokol, L.; Lancet, J.; Tinsley, S.; Sweet, K.; et al. Quality of life outcomes in patients with chronic myeloid leukemia treated with tyrosine kinase inhibitors: A controlled comparison. *Support. Care Cancer* **2013**, *21*, 1097–1103. [CrossRef]
23. Groenvold, M.; Petersen, M.A.; Idler, E.; Bjorner, J.B.; Fayers, P.M.; Mouridsen, H.T. Psychological distress and fatigue predicted recurrence and survival in primary breast cancer patients. *Breast Cancer Res. Treat.* **2007**, *105*, 209–219. [CrossRef] [PubMed]
24. Lipsett, A.; Barrett, S.; Haruna, F.; Mustian, K.; O'Donovan, A. The impact of exercise during adjuvant radiotherapy for breast cancer on fatigue and quality of life: A systematic review and meta-analysis. *Breast* **2017**, *32*, 144–155. [CrossRef] [PubMed]
25. Cano-Uceda, A.; Pareja-García, P.; Sánchez-Rodríguez, E.; Fraguas-Ramos, D.; Martín-Álvarez, L.; Asencio-Vicente, R.; Rivero-de la Villa, A.; Pérez-Pérez, M.d.M.; Obispo-Portero, B.M.; Morales-Ruiz, L.; et al. Effects of a Short-Term Supervised Exercise Program in Women with Breast Cancer. *Appl. Sci.* **2024**, *14*, 6553. [CrossRef]
26. Ramírez-vélez, R.; Zambom-ferraresi, F.; García-hermoso, A.; Kievisiene, J.; Rauckiene-michealsson, A.; Agostinis-sobrinho, C. Evidence-based exercise recommendations to improve mental wellbeing in women with breast cancer during active treatment: A systematic review and meta-analysis. *Cancers* **2021**, *13*, 264. [CrossRef]
27. Wolin, K.Y.; Schwartz, A.L.; Matthews, C.E.; Courneya, K.S.; Schmitz, K.H. Implementing the Exercise Guidelines for Cancer Survivors. *J. Support. Oncol.* **2012**, *10*, 171–177. [CrossRef] [PubMed]
28. Adams, S.C.; Segal, R.J.; McKenzie, D.C.; Vallerand, J.R.; Morielli, A.R.; Mackey, J.R.; Gelmon, K.; Friedenreich, C.M.; Reid, R.D.; Courneya, K.S. Impact of resistance and aerobic exercise on sarcopenia and dynapenia in breast cancer patients receiving adjuvant chemotherapy: A multicenter randomized controlled trial. *Breast Cancer Res. Treat.* **2016**, *158*, 497–507. [CrossRef]
29. Ammitzbøll, G.; Kjær, T.K.; Johansen, C.; Lanng, C.; Andersen, E.W.; Kroman, N.; Zerahn, B.; Hyldegaard, O.; Bidstrup, P.E.; Dalton, S.O. Effect of progressive resistance training on health-related quality of life in the first year after breast cancer surgery–results from a randomized controlled trial. *Acta Oncol.* **2019**, *58*, 665–672. [CrossRef] [PubMed]

30. Midtgaard, J.; Hammer, N.M.; Andersen, C.; Larsen, A.; Bruun, D.M.; Jarden, M. Cancer survivors' experience of exercise-based cancer rehabilitation-A meta-synthesis of qualitative research. *Acta Oncol.* **2015**, *54*, 609–617. [CrossRef]
31. Gómez-Redondo, P.; Valenzuela, P.L.; Morales, J.S.; Ara, I.; Mañas, A. Supervised Versus Unsupervised Exercise for the Improvement of Physical Function and Well-Being Outcomes in Older Adults: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Sports Med.* **2024**, *54*, 1877–1906. [CrossRef]
32. Ligibel, J.A.; Bohlke, K.; May, A.M.; Clinton, S.K.; Demark-Wahnefried, W.; Gilchrist, S.C.; Irwin, M.L.; Late, M.; Mansfield, S.; Marshall, T.F.; et al. Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline. *J. Clin. Oncol.* **2022**, *40*, 2491–2507. [CrossRef]
33. An, K.Y.; Morielli, A.R.; Kang, D.W.; Friedenreich, C.M.; McKenzie, D.C.; Gelmon, K.; Mackey, J.R.; Reid, R.D.; Courneya, K.S. Effects of exercise dose and type during breast cancer chemotherapy on longer-term patient-reported outcomes and health-related fitness: A randomized controlled trial. *Int. J. Cancer* **2020**, *146*, 150–160. [CrossRef]
34. Harrison, M.R.; Davis, P.G.; Khouri, M.G.; Bartlett, D.B.; Gupta, R.T.; Armstrong, A.J.; McNamara, M.A.; Zhang, T.; Anand, M.; Onyenwoke, K.; et al. A randomized controlled trial comparing changes in fitness with or without supervised exercise in patients initiated on enzalutamide and androgen deprivation therapy for non-metastatic castration-sensitive prostate cancer (EXTEND). *Prostate Cancer Prostatic Dis.* **2022**, *25*, 58–64. [CrossRef]
35. Kang, D.W.; Fairey, A.S.; Boulé, N.G.; Field, C.J.; Wharton, S.A.; Courneya, K.S. A Randomized Trial of the Effects of Exercise on Anxiety, Fear of Cancer Progression and Quality of Life in Prostate Cancer Patients on Active Surveillance. *J. Urol.* **2022**, *207*, 814–822. [CrossRef] [PubMed]
36. Mijwel, S.; Jervaeus, A.; Bolam, K.A.; Norrbom, J.; Bergh, J.; Rundqvist, H.; Wengström, Y. High-intensity exercise during chemotherapy induces beneficial effects 12 months into breast cancer survivorship. *J. Cancer Surviv.* **2019**, *13*, 244–256. [CrossRef] [PubMed]
37. Reverte-Pagola, G.; Sánchez-Trigo, H.; Saxton, J.; Sañudo, B. Supervised and Non-Supervised Exercise Programs for the Management of Cancer-Related Fatigue in Women with Breast Cancer: A Systematic Review and Meta-Analysis. *Cancer* **2022**, *14*, 3428. [CrossRef] [PubMed]
38. Meneses-Echávez, J.F.; González-Jiménez, E.; Ramírez-Vélez, R. Effects of supervised exercise on cancer-related fatigue in breast cancer survivors: A systematic review and meta-analysis. *BMC Cancer* **2015**, *15*, 77. [CrossRef]
39. Zhou, H.-J.; Wang, T.; Xu, Y.-Z.; Chen, Y.-N.; Deng, L.-J.; Wang, C.; Chen, J.-X.; Tan, J.-Y. Effects of exercise interventions on cancer-related fatigue in breast cancer patients: An overview of systematic reviews. *Support. Care Cancer* **2022**, *30*, 10421–10440. [CrossRef]
40. VAN Vulpen, J.K.; Sweegers, M.G.; Peeters, P.H.M.; Courneya, K.S.; Newton, R.U.; Aaronson, N.K.; Jacobsen, P.B.; Galvão, D.A.; Chinapaw, M.J.; Steindorf, K.; et al. Moderators of Exercise Effects on Cancer-related Fatigue: A Meta-analysis of Individual Patient Data. *Med. Sci. Sports Exerc.* **2020**, *52*, 303–314. [CrossRef]
41. de Moura Ferraz Barbosa, M.P.; de Jesus, N.T.; Bergmann, A.; da Silva Alves Gomes, V.M.; Sacomori, C.; Dantas, D. Efficacy of supervised exercise on sleep of women who survived breast cancer: A systematic review with meta-analysis. *J. Cancer Surviv.* **2024**, *52*, 303–314. [CrossRef]
42. Herranz-Gómez, A.; Cuenca-Martínez, F.; Suso-Martí, L.; Varangot-Reille, C.; Prades-Monfort, M.; Calatayud, J.; Casaña, J. Effectiveness of Therapeutic Exercise Models on Cancer-Related Fatigue in Patients with Cancer Undergoing Chemotherapy: A Systematic Review and Network Meta-analysis. *Arch. Phys. Med. Rehabil.* **2023**, *104*, 1331–1342. [CrossRef]
43. Hilfiker, R.; Meichtry, A.; Eicher, M.; Nilsson Balfe, L.; Knols, R.H.; Verra, M.L.; Taeymans, J. Exercise and other non-pharmaceutical interventions for cancer-related fatigue in patients during or after cancer treatment: A systematic review incorporating an indirect-comparisons meta-analysis. *Br. J. Sports Med.* **2018**, *52*, 651–658. [CrossRef]
44. Penna, G.B.; Otto, D.M.; da Silva, T.C.; Pedroni, A.S.; Macagnan, F.E. Physical rehabilitation for the management of cancer-related fatigue during cytotoxic treatment: A systematic review with meta-analysis. *Support. Care Cancer* **2023**, *31*, 129. [CrossRef]
45. Gray, L.; Sindall, P.; Pearson, S.J. Does resistance training ameliorate cancer-related fatigue in cancer survivors? A systematic review with meta-analysis. *Disabil. Rehabil.* **2024**, *46*, 2213–2222. [CrossRef]
46. Cramp, F.; Byron-Daniel, J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database Syst. Rev.* **2012**, *11*, CD006145. [CrossRef]
47. Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *BMJ* **2009**, *8*, 336–341.
48. Higgins, J.P.T.; Green, S. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (Updated March 2011)*; The Cochrane Collaboration: London, UK, 2011.
49. Sterne, J.A.C.; Savović, J.; Page, M.J.; Elbers, R.G.; Blencowe, N.S.; Boutron, I.; Cates, C.J.; Cheng, H.-Y.; Corbett, M.S.; Eldridge, S.M.; et al. RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ* **2019**, *366*, 14898. [CrossRef]
50. Sherrington, C.; Herbert, R.D.; Maher, C.G.; Moseley, A. PEDro. A database of randomized trials and systematic reviews in physiotherapy. *Man. Ther.* **2000**, *5*, 223–226. [CrossRef] [PubMed]

51. Thalheimer, W.; Cook, S. How to Calculate Effect Sizes from Published Research: A Simplified Methodology. *Work. Learn. Res.* **2002**, *1*, 1–9.
52. Sutton, A.J.; Sheldon, T.; Song, F.; Abrams, K.R.; Jones, D.R.; Sheldon, T.A.; Song, F. *Methods for Meta-Analysis in Medical Research*; Wiley: Hoboken, NJ, USA, 2000.
53. Higgins, J.P.T.; Thompson, S.G. Quantifying heterogeneity in a meta-analysis. *Stat. Med.* **2002**, *21*, 1539–1558. [CrossRef] [PubMed]
54. Sterne, J.A.C.; Egger, M.; Smith, G.D. Systematic reviews in health care Investigating and dealing with publication and other biases in meta-analysis. *BMJ* **2001**, *323*, 101–105. [CrossRef]
55. Al-Majid, S.; Wilson, L.D.; Rakovski, C.; Coburn, J.W. Effects of Exercise on Biobehavioral Outcomes of Fatigue During Cancer Treatment: Results of a Feasibility Study. *Biol. Res. Nurs.* **2015**, *17*, 40–48. [CrossRef]
56. Schmidt, M.E.; Wiskemann, J.; Armbrust, P.; Schneeweiss, A.; Ulrich, C.M.; Steindorf, K. Effects of resistance exercise on fatigue and quality of life in breast cancer patients undergoing adjuvant chemotherapy: A randomized controlled trial. *Int. J. Cancer* **2015**, *137*, 471–480. [CrossRef]
57. Schmidt, T.; Weisser, B.; Dürkop, J.; Jonat, W.; Van Mackelenbergh, M.; Röcken, C.; Mundhenke, C. Comparing endurance and resistance training with standard care during chemotherapy for patients with primary breast cancer. *Anticancer Res.* **2015**, *35*, 5623–5629.
58. Travier, N.; Velthuis, M.J.; Bisschop, C.N.S.; Buijs, B.v.D.; Monninkhof, E.M.; Backx, F.; Los, M.; Erdkamp, F.; Bloemendal, H.J.; Rodenhuis, C.; et al. Effects of an 18-week exercise programme started early during breast cancer treatment: A randomised controlled trial. *BMC Med.* **2015**, *13*, 121. [CrossRef]
59. van Waart, H.; Stuiver, M.M.; van Harten, W.H.; Geleijn, E.; Kieffer, J.M.; Buffart, L.M.; de Maaker-Berkhof, M.; Boven, E.; Schrama, J.; Geenen, M.M.; et al. Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: Results of the PACES randomized clinical trial. *J. Clin. Oncol.* **2015**, *33*, 1918–1927. [CrossRef]
60. Mijwel, S.; Backman, M.; Bolam, K.A.; Jervaeus, A.; Sundberg, C.J.; Margolin, S.; Browall, M.; Rundqvist, H.; Wengström, Y. Adding high-intensity interval training to conventional training modalities: Optimizing health-related outcomes during chemotherapy for breast cancer: The OptiTrain randomized controlled trial. *Breast Cancer Res. Treat.* **2018**, *168*, 79–93. [CrossRef]
61. Baglia, M.L.; Lin, I.; Cartmel, B.; Sanft, T.; Ligibel, J.; Hershman, D.L.; Harrigan, M.; Ferrucci, L.M.; Li, F.; Irwin, M.L. Endocrine-related quality of life in a randomized trial of exercise on aromatase inhibitor–induced arthralgias in breast cancer survivors. *Cancer* **2019**, *125*, 2262–2271. [CrossRef]
62. Hojan, K.; Milecki, P. Does regular physical exercises during radiotherapy influence fatigue and physical endurance in high-risk prostate cancer patients? *Med. Rehabil.* **2019**, *23*, 21–27. [CrossRef]
63. Ndjavera, W.; Orange, S.T.; O'DOherty, A.F.; Leicht, A.S.; Rochester, M.; Mills, R.; Saxton, J.M. Exercise-induced attenuation of treatment side-effects in patients with newly diagnosed prostate cancer beginning androgen-deprivation therapy: A randomised controlled trial. *BJU Int.* **2019**, *125*, 28–37. [CrossRef] [PubMed]
64. Eliécer, P.-R.J.; Geesel, P.-F.D.; Ricardo, P.-R.; Pedro, P.-R.; Ximena, V.-B.; Alberto, C.-P.Y. Fatiga asociada al cáncer de mama luego de un programa de entrenamiento. *Acta Méd. Costarric.* **2020**, *62*, 18–25.
65. Piraux, E.; Caty, G.; Renard, L.; Vancraeynest, D.; Tombal, B.; Geets, X.; Reychler, G. Effects of high-intensity interval training compared with resistance training in prostate cancer patients undergoing radiotherapy: A randomized controlled trial. *Prostate Cancer Prostatic Dis.* **2021**, *24*, 156–165. [CrossRef] [PubMed]
66. Scott, J.M.; Thomas, S.M.; Peppercorn, J.M.; Herndon, J.E., 2nd; Douglas, P.S.; Khouri, M.G.; Dang, C.T.; Yu, A.F.; Catalina, D.; Ciolino, C.; et al. Effects of Exercise Therapy Dosing Schedule on Impaired Cardiorespiratory Fitness in Patients with Primary Breast Cancer: A Randomized Controlled Trial. *Circulation* **2020**, *141*, 560–570. [CrossRef]
67. Gal, R.; Monninkhof, E.M.; van Gils, C.H.; Groenwold, R.H.H.; Elias, S.G.; van den Bongard, D.H.J.G.; Peeters, P.H.M.; Verkooijen, H.M.; May, A.M. Effects of exercise in breast cancer patients: Implications of the trials within cohorts (TwiCs) design in the UMBRELLA Fit trial. *Breast Cancer Res. Treat.* **2021**, *190*, 89–101. [CrossRef]
68. Moraes, R.F.; Ferreira-Júnior, J.B.; Marques, V.A.; Vieira, A.; Lira, C.A.B.; Campos, M.H.; Freitas-Junior, R.; Rahal, R.M.S.; Gentil, P.; Vieira, C.A. Resistance training, fatigue, quality of life, anxiety in breast cancer survivors. *J. Strength Cond. Res.* **2021**, *35*, 1350–1356. [CrossRef]
69. Koevoets, E.W.; Schagen, S.B.; de Ruiter, M.B.; Geerlings, M.I.; Witlox, L.; van der Wall, E.; Stuiver, M.M.; Sonke, G.S.; Velthuis, M.J.; Jobsen, J.J.; et al. Effect of physical exercise on cognitive function after chemotherapy in patients with breast cancer: A randomized controlled trial (PAM study). *Breast Cancer Res.* **2022**, *24*, 36. [CrossRef]
70. Rock, C.L.; Thomson, C.; Gansler, T.; Gapstur, S.M.; McCullough, M.L.; Patel, A.V.; Andrews, K.S.; Bandera, E.V.; Spees, C.K.; Robien, K.; et al. American Cancer Society guideline for diet and physical activity for cancer prevention. *CA Cancer J. Clin.* **2020**, *70*, 245–271. [CrossRef]
71. Strasser, B.; Steindorf, K.; Wiskemann, J.; Ulrich, C.M. Impact of resistance training in cancer survivors: A meta-analysis. *Med. Sci. Sports Exerc.* **2013**, *45*, 2080–2090. [CrossRef]

72. Champ, C.E.; Carpenter, D.J.; Diaz, A.K.; Rosenberg, J.; Ackerson, B.G.; Hyde, P.N. Resistance Training for Patients with Cancer: A Conceptual Framework for Maximizing Strength, Power, Functional Mobility, and Body Composition to Optimize Health and Outcomes. *Sports Med.* **2023**, *53*, 75–89. [CrossRef]
73. Farley, M.J.; Boytar, A.N.; Adlard, K.N.; Salisbury, C.E.; Hart, N.H.; Schaumberg, M.A.; Jenkins, D.G.; Skinner, T.L. Interleukin-15 and high-intensity exercise: Relationship with inflammation, body composition and fitness in cancer survivors. *J. Physiol.* **2024**, *602*, 5203–5215. [CrossRef] [PubMed]
74. Toohey, K.; Pumpa, K.; McKune, A.; Cooke, J.; Welvaert, M.; Northey, J.; Quinlan, C.; Semple, S. The impact of high-intensity interval training exercise on breast cancer survivors: A pilot study to explore fitness, cardiac regulation and biomarkers of the stress systems. *BMC Cancer* **2020**, *20*, 787. [CrossRef] [PubMed]
75. Reljic, D.; Herrmann, H.J.; Jakobs, B.; Dieterich, W.; Mougiakakos, D.; Neurath, M.F.; Zopf, Y. Feasibility, Safety, and Preliminary Efficacy of Very Low-Volume Interval Training in Advanced Cancer Patients. *Med. Sci. Sports Exerc.* **2022**, *54*, 1817–1830. [CrossRef] [PubMed]
76. Little, J.P.; Safdar, A.; Wilkin, G.P.; Tarnopolsky, M.A.; Gibala, M.J. A practical model of low-volume high-intensity interval training induces mitochondrial biogenesis in human skeletal muscle: Potential mechanisms. *J. Physiol.* **2010**, *588*, 1011–1022. [CrossRef] [PubMed]
77. Schlüter, K.; Schneider, J.; Sprave, T.; Wiskemann, J.; Rosenberger, F. Feasibility of Two High-Intensity Interval Training Protocols in Cancer Survivors. *Med. Sci. Sports Exerc.* **2019**, *51*, 2443–2450. [CrossRef] [PubMed]
78. Wender, C.L.A.; Manninen, M.; O'Connor, P.J. The Effect of Chronic Exercise on Energy and Fatigue States: A Systematic Review and Meta-Analysis of Randomized Trials. *Front. Psychol.* **2022**, *13*, 907637. [CrossRef] [PubMed]