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Dose–response effects of aerobic exercise intensity on anxiety, sleep, and well-being in cancer survivors: A multi-arm randomized controlled trial

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Abstract: Cancer survivors frequently experience psychological challenges including anxiety, sleep disturbances, and diminished well-being, with anxiety affecting 18%–40% and sleep disruptions impacting 30%–50% of survivors will post-treatment. While exercise is recognized as beneficial for this population, the optimal intensity remains unclear. This study investigated the dose-response relationship between aerobic exercise intensity and psychological outcomes through a randomized controlled trial with 160 cancer survivors assigned to high-intensity interval training (HIIT), moderate-intensity continuous training (MICT), low-intensity exercise (LIE), or usual care control for 12 weeks with 3-month follow-up. The HIIT group demonstrated significantly greater improvements in anxiety (mean reduction: 10.4 points, 95% CI: –12.3 to –8.5), sleep quality (mean improvement: 4.1 points, 95% CI: –4.8 to –3.4), and quality of life (mean increase: 14.9 points, 95% CI: 12.5 to 17.3) compared to MICT, LIE, and control groups. Regression analyses revealed an intensity-dependent pattern, with each 10% increase in exercise intensity associated with an additional reduction of 1.8 points in anxiety scores. Age and BMI significantly moderated these effects, with younger participants showing stronger associations. All exercise protocols demonstrated good safety profiles and adherence rates (HIIT: 82.3%, MICT: 85.1%, LIE: 86.7%). This research provides evidence that higher-intensity exercise protocols may optimize psychological health outcomes in cancer survivors when appropriately supervised and individualized.

Keywords: aerobic exercise intensity; cancer survivors; psychological health; anxiety; sleep quality

1. Introduction

The diagnosis and treatment of cancer have become a major focus of public health concern because of the dramatic improvements in detection and treatment which have led to an increased population of survivors facing complex psychological and physiological challenges. Psychological issues such as anxiety, depression, and well-being are common post-treatment outcomes, with anxiety disorders ranging from 18–40% and sleep disruptions from 30%–50% [1]. Depression in this population has been shown to significantly worsen quality of life and increase morbidity for this already vulnerable group [2]. The surgery, chemotherapy, radiation, and hormone therapy cancer treatments have lasting effects, both physiological and psychological, that can last for years and create a demand for effective solutions to mitigate these challenges [3]. With little to no adverse effects reported, exercise has proven to be an effective non-pharmacological method for this population, as physical activity is now classified

as a vital element of care during the survivorship phase of cancer [4]. This is particularly true for aerobic exercise which is celebrated for its ease of execution and universal multi-health domain benefits [5].

In healthy populations, the research exploring the effects of exercise has established dose-response relationships around exercise intensity and health outcomes, noting highly differentiated impacts across cardiovascular, metabolic, and psychological domains [6]. Yet, for cancer survivors, due to unique treatment side effects like fatigue, cardiotoxicity, and muscle wasting, formulating an optimal exercise intensity prescription is still an unresolved problem [7]. The nuance behind different exercise intensities and their psychological impacts on cancer survivors needs further systematic evaluation to construct safe and effective exercise plans embracing comprehensive recovery [8]. Extensive evidence suggests that aerobic exercise can considerably mitigate anxiety in cancer survivors, with numerous studies documenting reductions of anxiety symptoms after dedicated aerobic exercise programs [9]. Several possible explanations have been proposed for these effects such as increased release of endorphins, better neurotransmitter activity, self-efficacy improvement, lower inflammatory markers, and distraction from worrying thoughts [10].

Moreover, exercise has been evidenced as an effective intervention for sleep disturbances, with routine physical activity linked to lower sleep onset latency, reduced wake frequency, and improved sleep quality among populations of cancer survivors [11]. Potential mechanisms include regulation of body temperature, entrainment of circadian rhythms, reduction of pro-inflammatory cytokines, and alleviation of pain and anxiety that typically disrupt sleep [12]. Beyond symptom management, aerobic exercise shows promise for enhancing overall well-being in cancer survivors, with documented improvements in mood states, reduced fatigue, enhanced functional capacity, and greater perceived control over health [13]. These psychological benefits may stem from both physiological adaptations and psychosocial factors, including increased social interaction, structured activity engagement, and improved body image [14]. Despite this promising evidence, research examining whether different exercise intensities produce varying effects on these psychological outcomes remains limited, creating a significant gap in exercise prescription knowledge for cancer survivorship care [15].

Current research on exercise interventions for cancer survivors exhibits several notable limitations that hinder translation to clinical practice. Many studies employ heterogeneous exercise protocols with inconsistent intensity classifications and inadequate reporting of exercise parameters, making cross-study comparisons challenging and limiting the ability to determine optimal prescription guidelines [16]. Additionally, outcome measures vary considerably across studies, with few investigations simultaneously addressing multiple psychological domains such as anxiety, sleep, and well-being within the same participant cohort [17]. Most exercise intervention studies analyzed only a small population sample, thereby significantly reducing the power that could detect differences across intensity levels or perform meaningful subgroup analyses by cancer type, treatment history, or self-reported demographic information [18].

Explanations for the available body of evidence on cancer survivors'

psychosocial wellbeing are multifaceted but remain weak due to methodological factors associated with randomization, control groups, duration of intervention, and follow-up periods. Similarly, mechanistic explanations underlying self-reported benefits of different levels of exercise intensity are seldom advanced without appropriate verification through biomarker and neurophysiological investigations that clarify how varying levels of exercise intensity may affect these outcomes [19]. The interrelationship existing between psychosocial wellbeing and exercise intensity in cancer survivors is multifaceted and under-analyzed. While some studies propose high-intensity exercises lead to marked changes in certain psychological factors due to heightened physiological adaptations, others propose moderate-intensity physical activities optimize anxiety and sleep through better adherence and less volatile stress reactions [20].

This research attempts to analyze the comparative impacts of low, moderate, and high intensity aerobic exercise on anxiety, sleep, and wellness in cancer survivors through a multi-arm intervention design in order to bridge the gaps in current literature. This innovation in exercise oncology shifts the focus from mere determination of exercise efficacy to refinement of prescription parameters to improve particular psychological outcomes. The authors have posited that the different levels of exertion will lead to varying degrees of improvement, and there will be interaction effects moderated by individual cancer history and treatment details. The analysis will be done using validated outcome measures and subjective and objective assessments to ensure all relevant factors are captured, thus providing comprehensive data regarding dependence on intensity level. The results will help in tailoring personalized exercise plans to enhance the efficiency and adherence of interventions among cancer survivors, integrating crucial evidential support. With respect to cancer survivors, this research aims to optimally delineate the exercise intensity vis-à-vis the psychological outcomes to enhance supportive care practices to improve intervention outcomes and survival wellbeing.

2. Data and methods

2.1. Research design and study population

This study used a randomized controlled trial with a multi-arm parallel design to examine the psychological impacts of different aerobic exercise intensities in Chinese cancer survivors. The study was conducted across three teaching hospitals in Eastern China.

Participants were drawn from hospital oncology departments, regional cancer support groups, and community-based health clinics. Among the criteria for acceptance were adults between the ages of 18 and 75 with a diagnosis of cancer (histology available) and having completed the primary treatment at least 3 months prior. They also had to have an Eastern Cooperative Oncology Group performance status of ≤ 2 and have medically issued “fitness to exercise” clearance. Exclusion criteria included assignment to metastatic or terminal illness, significant psychiatric conditions, poor prognosis as assessed with Royal Marsden Hospital score ≥ 2 [21], indolent activity, low physical activity, and those labelled ‘exercise contraindicated’, or active participation in other interventional studies.

Eligible participants were randomized using computer-generated sequences considering cancer type, age, and time since treatment completion for stratification to one of the four groups: high-intensity interval training (HIIT), moderate-intensity continuous training (MICT), low-intensity exercise (LIE), or Usual Care Control (UCC). This method of stratification guided the HIIT and MICT assignment to ensure potential confounding variables which could influence exercise response were evenly considered [8].

Calculation of the sample size was done in accordance with the primary outcome of anxiety with a presumed effect size of 0.70 between the exercise and control groups [22]. Recent meta-analyses have shown that exercise interventions can effectively mitigate cancer-related fatigue with remarkable effect sizes that vary from moderate to large based on the type and intensity of exercise performed [23]. Further, the final sample size determination was guided by the body of research examining the interplay between physical activity and sleep duration on the risk of mortality in cancer survivors [22]. It was decided that, with an expected 20% attrition rate, total sample size needed to be 160 participants (40 per group) to observe clinically relevant differences.

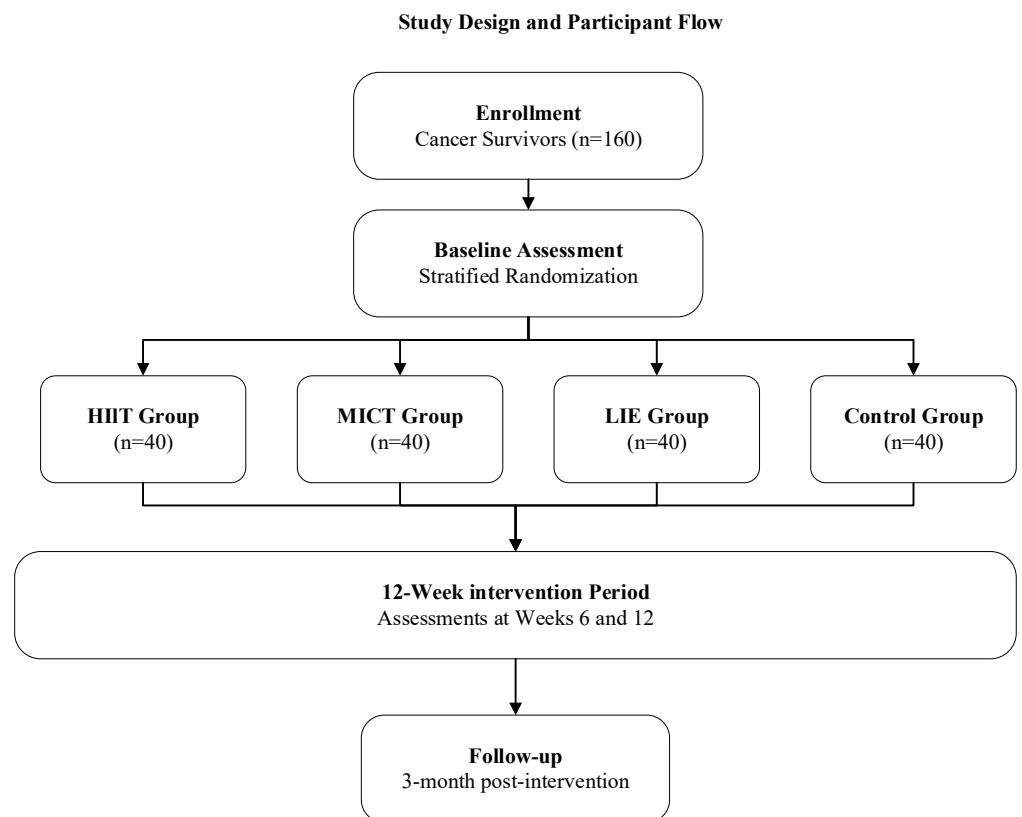


Figure 1. Study design and participant flow.

As illustrated in **Figure 1**, participants completed the screening, baseline evaluation, randomization into groups, intervention, and follow-up stages systematically. This study used a 12-week intervention period because there is data indicating this duration elicits substantial adaptive changes, both physiologically and psychologically, while avoiding high attrition rates [13]. In this study, assessments

took place at baseline, mid (6 weeks), post intervention (12 weeks), and follow-up (3 months post intervention). This evaluation framework provided comprehensive assessments following the limitations of previous studies that had insufficient follow-up periods posed by prior studies [15], allowing assessment of both immediate impacts and sustained benefits over multiple exercise protocol intensity modalities. The design of the study aimed at improving compliance and adherence to prescribed high intensity interval training—often showing low adherence in the literature [24].

2.2. Intervention measures

The intervention included the application of three distinct aerobic exercise protocols of increasing intensity over 12 weeks along with a usual care control condition. Exercises were completed in hospital-based rehabilitation facilities where participants had access to treadmills, stationary bicycles, elliptical trainers, rowing machines, and other equipment of their choice as ascribed to individual preferences. Each supervised session followed a standard structure that included a 5-min warm-up, the main aerobic portion, and a 5-min cool-down with flexibility exercises. These were conducted in accordance with the exercise protocols which endorsed cancer survivor's guidelines while changing aspects per new literature pertaining to exercise adherence and efficacy [25].

Low Intensity Exercise (LIE) groups undertook continuous aerobic exercise sessions at 40%–55% of HRR or 9–11 RPE on the Borg scale, each lasting 40–50 min, three times a week. MICT group engaged in repetitive aerobic exercises at 65%–75% HRR (RPE of 12–14) for 30–40 min, three times weekly. The HIIT group performed interval sessions consisting of 4–10 alternating high intensity 30–60 seconds with active recovery periods of equal or longer duration at lower heart rates. HIIT sessions occurred three times weekly with total exercise duration of 20–30 min. **Table 1** presents the detailed exercise parameters across intervention groups.

Table 1. Exercise protocol parameters across intervention groups.

Parameter	LIE	MICT	HIIT
Frequency	3 sessions/week	3 sessions/week	3 sessions/week
Session duration	40–50 min	30–40 min	20–30 min
Intensity (HRR)	40%–55%	65%–75%	Work: 85%–95%, Recovery: 40%–50%
RPE (6–20 Borg)	9–11	12–14	Work: 16–18, Recovery: 9–10
Exercise pattern	Continuous	Continuous	Interval (4–10 sets)
Interval structure	N/A	N/A	Work: 30–60s, Recovery: 60–120s
Weekly volume	120–150 min	90–120 min	60–90 min
Progression	Gradual intensity increase (5% HRR every 3 weeks)	Gradual intensity increase (5% HRR every 3 weeks)	Progressive increase in intervals (1–2 sets every 2 weeks)
Exercise modes	Walking, cycling, elliptical, rowing	Walking, cycling, elliptical, rowing	Cycling, elliptical, rowing

The usual care control group received standard post-treatment care but no supervised exercise. All participants attended an educational session on physical activity benefits for cancer survivors and received general activity recommendations

aligned with cancer survivorship guidelines, but control group participants received no specific exercise prescriptions or supervision.

Exercise interventions were supervised by certified exercise physiologists with specialized training in cancer rehabilitation. Resistance exercise components were incorporated into all active intervention groups as recommended for comprehensive cancer rehabilitation [26]. All intervention groups incorporated resistance training components. The primary differentiating factor was aerobic exercise intensity. Session attendance was recorded, and heart rate monitors were utilized to verify exercise intensity adherence. To enhance compliance, behavior change techniques including goal-setting, self-monitoring, and feedback were implemented across all exercise groups. As shown in **Table 1**, the protocols were designed with progressive intensity increases to accommodate physiological adaptations while maintaining appropriate exercise challenge levels. The specific progression schedules were informed by recent research on resistance exercise modalities for breast cancer patients, which demonstrated improved adherence with gradual progression approaches [26].

2.3. Assessment tools and data analysis

Outcome measures were assessed at four timepoints: baseline (T0), mid-intervention at 6 weeks (T1), post-intervention at 12 weeks (T2), and 3-month follow-up (T3). Anxiety was evaluated as the primary outcome using the State-Trait Anxiety Inventory (STAI), a validated 40-item self-report questionnaire that distinguishes between state anxiety (situational) and trait anxiety (dispositional). The STAI has demonstrated strong reliability (Cronbach's $\alpha = 0.86\text{--}0.95$) and validity in cancer populations [27]. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), 19-item instrument measuring seven sleep components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. The PSQI yields a global score ranging from 0–21, with scores >5 indicating poor sleep quality and scores >8 suggesting clinically significant sleep disturbance. This instrument has been validated in cancer survivors with excellent psychometric properties (test-retest reliability $r = 0.85$; Cronbach's $\alpha = 0.83$) [28].

Well-being was measured using the Functional Assessment of Cancer Therapy-General (FACT-G), a 27-item questionnaire encompassing four domains: physical, social/family, emotional, and functional well-being. The FACT-G provides both domain-specific scores and a composite score, with higher values indicating better quality of life. Additional psychological measures included the Self-Efficacy for Managing Chronic Disease Scale to assess confidence in self-management behaviors, and the Social Constraints Scale to evaluate perceived social isolation related to cancer [27]. Exercise adherence was calculated as the percentage of scheduled sessions attended, with heart rate monitoring used to verify intensity compliance.

Statistical analyses were conducted using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Shapiro-Wilk test. Baseline characteristics were compared across groups using one-way ANOVA for continuous variables and chi-square tests for categorical variables. The primary analysis employed linear mixed-effects models to examine intervention

effects on outcome measures while accounting for the repeated-measures design. The general form of the model was:

$$Y_{ij} = \beta_0 + \beta_1 G_i + \beta_2 T_j + \beta_3 (G \times T)_{ij} + \sum_{k=1}^p \beta_{3+k} (C_k)_i + \gamma_i + \varepsilon_{ij}$$

where Y_{ij} represents the outcome for participant i at time j , β_0 is the intercept, β_1 through β_3 are fixed-effect coefficients for main variables, $\sum_{k=1}^p \beta_{3+k} (C_k)_i$ represents the sum of all covariate effects, γ_i is the random effect for participant, and ε_{ij} is the residual error. Group-by-time interactions were examined as the primary indicator of intervention effects, with significant interactions followed by post-hoc comparisons with Bonferroni correction [29]. Dose-response analyses employed HRR to quantify exercise intensity. This metric provided objective measurement and facilitated standardized comparisons across different exercise types. Effect sizes were calculated using Cohen's d , with values of 0.2, 0.5, and 0.8 considered small, medium, and large, respectively. Missing data were handled using multiple imputation assuming data were missing at random. Intention-to-treat analysis was conducted as the primary approach, with per-protocol analysis ($\geq 70\%$ session attendance) as a sensitivity analysis. Significance was set at $\alpha = 0.05$ (two-tailed) for all analyses.

3. Results

3.1. Baseline characteristics of study participants

A total of 247 cancer survivors were assessed for eligibility, with 160 participants ultimately enrolled and randomized into the four study arms (HIIT: $n = 40$; MICT: $n = 40$; LIE: $n = 40$; Control: $n = 40$). The primary reasons for exclusion were not meeting eligibility criteria ($n = 42$), declining participation ($n = 31$), and other reasons ($n = 14$). The participant flow and retention rates across the 12-week intervention and 3-month follow-up period are illustrated in **Figure 2**. The retention rate was 88.1% at the completion of the 12-week intervention, with no significant differences in dropout rates between groups (HIIT: 12.5%; MICT: 10.0%; LIE: 10.0%; Control: 15.0%; $p = 0.842$).

The baseline demographic and clinical characteristics of the study participants across the four intervention groups are presented in **Table 2**. The mean age of participants was 56.4 ± 8.1 years, with a predominance of females (61.9%). The most common cancer type was breast cancer (45.0%), followed by prostate cancer (25.0%), colorectal cancer (16.3%), and other cancer types (13.8%). The majority of participants had completed either chemotherapy (68.8%) or radiation therapy (56.3%). Mean time since treatment completion was 18.4 ± 8.5 months. No statistically significant differences were observed in demographic variables, cancer-related clinical characteristics, or baseline outcome measures across the four intervention groups, indicating successful randomization.

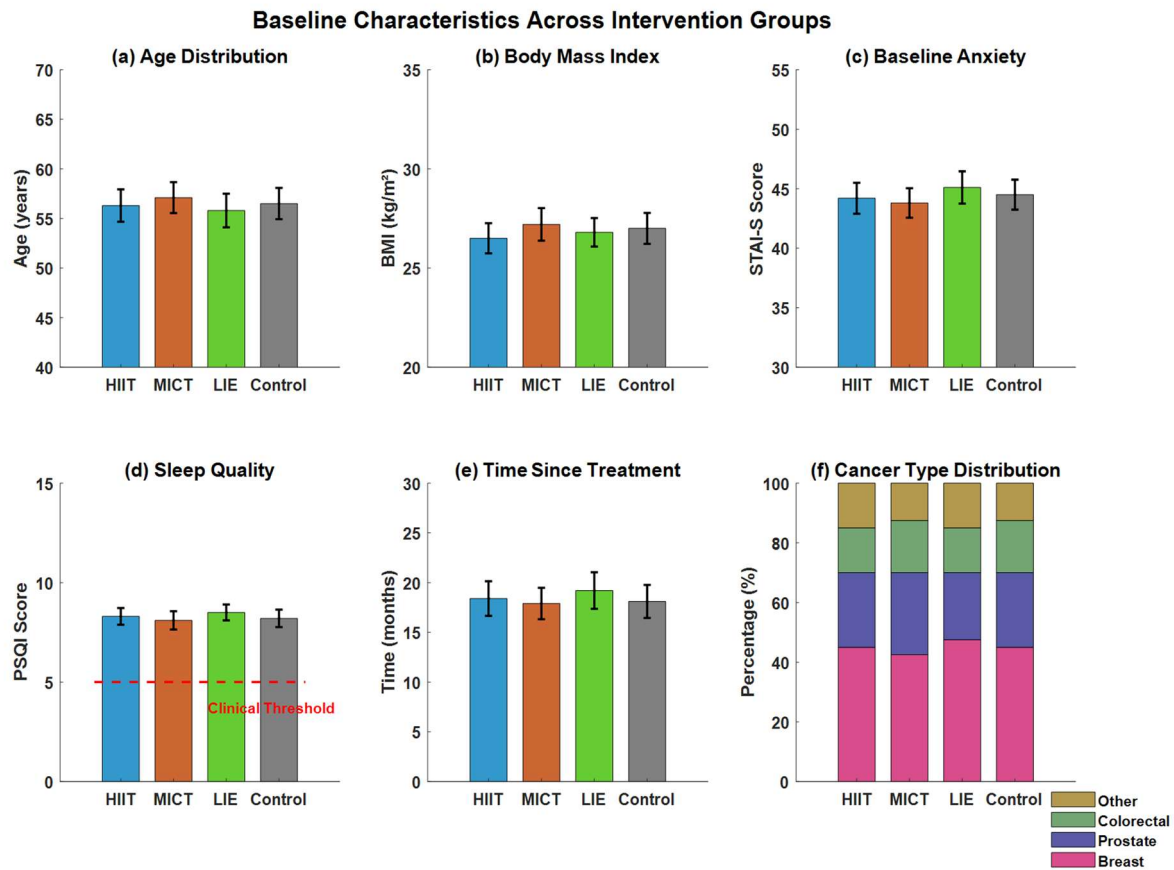


Figure 2. Baseline Characteristics Across Intervention Groups. Comparison of age. **(a)** BMI; **(b)** anxiety; **(c)** sleep quality with clinical threshold; **(d)** time since treatment; **(e)** and cancer type distribution; **(f)** No significant differences between HIIT, MICT, LIE, and control groups ($p > 0.05$).

Table 2. Baseline demographic and clinical characteristics of study participants by intervention group.

Characteristic	HIIT (<i>n</i> = 40)	MICT (<i>n</i> = 40)	LIE (<i>n</i> = 40)	Control (<i>n</i> = 40)	Total (<i>n</i> = 160)	<i>p</i> -value
Demographics						
Age (years), mean ± SD	56.3 ± 8.2	57.1 ± 7.8	55.8 ± 8.5	56.5 ± 7.9	56.4 ± 8.1	0.86
Female, <i>n</i> (%)	26 (65.0)	24 (60.0)	25 (62.5)	24 (60.0)	99 (61.9)	0.95
BMI (kg/m ²), mean ± SD	26.5 ± 3.8	27.2 ± 4.1	26.8 ± 3.6	27.0 ± 3.9	26.9 ± 3.8	0.82
Education ≥college, <i>n</i> (%)	23 (57.5)	25 (62.5)	24 (60.0)	22 (55.0)	94 (58.8)	0.90
Married/partnered, <i>n</i> (%)	28 (70.0)	26 (65.0)	27 (67.5)	29 (72.5)	110 (68.8)	0.87
Employed, <i>n</i> (%)	22 (55.0)	20 (50.0)	21 (52.5)	23 (57.5)	86 (53.8)	0.89
Clinical characteristics						
Cancer type, <i>n</i> (%)						
Breast	18 (45.0)	17 (42.5)	19 (47.5)	18 (45.0)	72 (45.0)	0.97
Prostate	10 (25.0)	11 (27.5)	9 (22.5)	10 (25.0)	40 (25.0)	0.96
Colorectal	6 (15.0)	7 (17.5)	6 (15.0)	7 (17.5)	26 (16.3)	0.98
Other	6 (15.0)	5 (12.5)	6 (15.0)	5 (12.5)	22 (13.8)	0.97
Cancer stage, <i>n</i> (%)						
I	16 (40.0)	15 (37.5)	17 (42.5)	16 (40.0)	64 (40.0)	0.98
II	17 (42.5)	18 (45.0)	16 (40.0)	17 (42.5)	68 (42.5)	0.97

Table 2. (Continued).

Characteristic	HIIT (n = 40)	MICT (n = 40)	LIE (n = 40)	Control (n = 40)	Total (N = 160)	p-value
Clinical characteristics						
Cancer stage, n (%)						
III	7 (17.5)	7 (17.5)	7 (17.5)	7 (17.5)	28 (17.5)	1.00
Treatment received, n (%)						
Surgery	36 (90.0)	34 (85.0)	35 (87.5)	35 (87.5)	140 (87.5)	0.93
Chemotherapy	26 (65.0)	28 (70.0)	28 (70.0)	28 (70.0)	110 (68.8)	0.94
Radiation	21 (52.5)	23 (57.5)	22 (55.0)	24 (60.0)	90 (56.3)	0.90
Hormone therapy	14 (35.0)	15 (37.5)	16 (40.0)	14 (35.0)	59 (36.9)	0.95
Months since treatment, mean $\pm$ SD	18.4 $\pm$ 8.7	17.9 $\pm$ 7.9	19.2 $\pm$ 9.2	18.1 $\pm$ 8.3	18.4 $\pm$ 8.5	0.89
Comorbidities, n (%)						
Hypertension	12 (30.0)	13 (32.5)	11 (27.5)	12 (30.0)	48 (30.0)	0.97
Diabetes	6 (15.0)	7 (17.5)	5 (12.5)	6 (15.0)	24 (15.0)	0.94
Arthritis	8 (20.0)	7 (17.5)	9 (22.5)	8 (20.0)	32 (20.0)	0.95
Baseline outcome measures						
STAI-state, mean $\pm$ SD	44.2 $\pm$ 6.5	43.8 $\pm$ 6.2	45.1 $\pm$ 6.8	44.5 $\pm$ 6.3	44.4 $\pm$ 6.4	0.78
STAI-trait, mean $\pm$ SD	42.7 $\pm$ 5.8	42.3 $\pm$ 6.1	43.2 $\pm$ 5.5	42.9 $\pm$ 5.9	42.8 $\pm$ 5.8	0.89
PSQI global score, mean $\pm$ SD	8.3 $\pm$ 2.1	8.1 $\pm$ 2.3	8.5 $\pm$ 2.0	8.2 $\pm$ 2.2	8.3 $\pm$ 2.1	0.83
FACT-G total score, mean $\pm$ SD	74.6 $\pm$ 11.8	75.2 $\pm$ 12.3	73.8 $\pm$ 11.5	74.9 $\pm$ 12.0	74.6 $\pm$ 11.9	0.92

Note: HIIT = high-intensity interval training; MICT = moderate-intensity continuous training; LIE = low-intensity exercise; SD = standard deviation; BMI = body mass index; STAI = State-Trait Anxiety Inventory; PSQI = Pittsburgh Sleep Quality Index; FACT-G = Functional Assessment of Cancer Therapy-General.

As shown in **Figure 2**, baseline anxiety levels measured by the STAI-State scale were elevated across all groups (mean score 44.4 ± 6.4), indicating moderate anxiety in this cancer survivor population. Similarly, baseline sleep quality was poor across all groups as measured by the PSQI (mean score 8.3 ± 2.1), with 87.5% of participants exceeding the clinical threshold score of 5, indicative of sleep disturbance. Quality of life as measured by the FACT-G was comparable across groups (mean total score 74.6 ± 11.9), with subscale analysis revealing lowest scores in the emotional well-being domain (mean 17.2 ± 4.3 out of a possible 24). The baseline level of physical activity was low across all groups. Participants reported an average of 65.3 ± 38.9 minutes of moderate-to-vigorous physical activity per week, substantially below the recommended 150 minutes per week.

Analysis of comorbidities revealed hypertension as the most prevalent condition (30.0%), followed by arthritis (20.0%) and diabetes (15.0%). The distribution of these comorbidities was balanced across intervention groups. Baseline cardiorespiratory fitness, as assessed by estimated VO_2 max from the modified Bruce protocol treadmill test, showed moderate deconditioning across all groups (mean 22.8 ± 4.6 mL/kg/min), with no significant between-group differences ($p = 0.81$). Body composition analysis indicated that 68.8% of participants were either overweight or obese ($\text{BMI} \geq 25$ kg/m²), consistent with the post-treatment weight gain commonly observed in cancer

survivors.

3.2. Intervention adherence and safety

The successful implementation of the exercise interventions was reflected in the strong adherence rates observed across the active treatment groups. Overall, participants in the intervention arms completed 84.7% of the scheduled exercise sessions (HIIT: 82.3%, MICT: 85.1%, LIE: 86.7%), with no statistically significant differences between groups ($p = 0.237$). The detailed adherence metrics by intervention group are presented in **Table 3**. The HIIT group demonstrated slightly lower session attendance during the initial 4 weeks (76.8%) compared to MICT (83.4%) and LIE (84.1%) groups. This difference diminished over time as participants adapted to the higher-intensity protocol (**Figure 3a**). By the final 4 weeks of the intervention, attendance rates were comparable across all exercise groups (HIIT: 84.5%, MICT: 85.8%, LIE: 87.2%).

Table 3. Exercise adherence and training parameters across intervention groups.

Parameter	HIIT ($n = 35$)	MICT ($n = 36$)	LIE ($n = 36$)	Control ($n = 34$)	p -value
Session attendance					
Overall attendance, %	82.3 $\pm$ 12.5	85.1 $\pm$ 10.8	86.7 $\pm$ 9.7	N/A	0.237
Weeks 1-4, %	76.8 $\pm$ 15.4	83.4 $\pm$ 12.5	84.1 $\pm$ 11.8	N/A	0.038*
Weeks 5-8, %	82.5 $\pm$ 13.6	84.2 $\pm$ 11.3	86.3 $\pm$ 10.2	N/A	0.412
Weeks 9-12, %	84.5 $\pm$ 12.4	85.8 $\pm$ 10.7	87.2 $\pm$ 9.8	N/A	0.586
Attended $\geq 70\%$ sessions, n (%)	31 (88.6)	34 (94.4)	35 (97.2)	N/A	0.326
Training parameters					
Prescribed intensity, %HRR	85–95 (intervals)	65–75	40–55	N/A	N/A
Achieved intensity, %HRR	85.4 $\pm$ 4.3	67.8 $\pm$ 3.8	48.5 $\pm$ 3.2	N/A	<0.001*
Sessions achieving target intensity, %	78.3 $\pm$ 13.6	85.9 $\pm$ 10.4	92.1 $\pm$ 7.8	N/A	<0.001*
Mean session duration, min	27.5 $\pm$ 3.2	36.4 $\pm$ 2.8	44.3 $\pm$ 3.5	N/A	<0.001*
Total exercise volume, min/week	68.8 $\pm$ 10.6	94.6 $\pm$ 9.5	115.7 $\pm$ 11.2	N/A	<0.001*
Mean RPE (6-20 scale)	15.8 $\pm$ 1.4	13.2 $\pm$ 1.1	10.5 $\pm$ 0.9	N/A	<0.001*

Note: Values are presented as mean $\pm$ SD unless otherwise indicated. HRR = heart rate reserve; RPE = rating of perceived exertion; N/A = not applicable. *Statistically significant difference between groups.

The intensity adherence analysis revealed that all exercise groups achieved mean exercise intensities close to their prescribed targets (HIIT: 85.4% vs. 90% target heart rate reserve (HRR); MICT: 67.8% vs. 70% target HRR; LIE: 48.5% vs. 50% target HRR), as shown in **Figure 3b**. The HIIT group demonstrated slightly greater variability in achieved exercise intensity (SD = 4.3%) compared to MICT (SD = 3.8%) and LIE (SD = 3.2%) groups. Overall, 78.3% of HIIT sessions, 85.9% of MICT sessions, and 92.1% of LIE sessions achieved the prescribed intensity ranges. Heart rate monitoring data confirmed that the exercise interventions provided distinct physiological stimuli, with significant differences in mean exercise heart rates between all three active intervention groups ($p < 0.001$).

A total of 11 adverse events (AEs) were recorded across all groups during the study period, as shown in **Figure 3c**. The distribution of AEs was as follows: HIIT (n

= 5), MICT ($n = 3$), LIE ($n = 2$), and control ($n = 1$). In the HIIT group, three events were exercise-related (two cases of exercise-induced muscle soreness requiring >48 h recovery and one case of exacerbation of pre-existing knee pain), one was disease-related (lymphedema flare), and one was unrelated (viral infection). The MICT group experienced one exercise-related AE (ankle sprain during exercise), one disease-related AE (radiation pneumonitis), and one unrelated AE (minor traffic accident). In the LIE group, one disease-related AE (skin reaction at previous radiation site) and one unrelated AE (fall at home) were recorded. The control group had one unrelated AE (influenza). No serious adverse events were reported in any group, and all exercise-related AEs resolved completely.

Study retention was generally high, with an overall completion rate of 88.1% (141/160 participants). As illustrated in **Figure 3d**, dropout rates were 12.5% (5/40) in the HIIT group, 10.0% (4/40) in both the MICT and LIE groups, and 15.0% (6/40) in the control group, with no statistically significant differences between groups ($p = 0.842$). The primary reasons for dropout were: health issues unrelated to the intervention ($n = 8$), time constraints ($n = 6$), loss of interest ($n = 3$), and loss to follow-up ($n = 2$). Among the HIIT participants who withdrew, two cited the intensity of the exercise program as a contributing factor. The timing of dropouts varied, with 60.0% occurring during the first half of the intervention period. Sensitivity analyses comparing completers versus non-completers revealed no significant differences in baseline demographic or clinical characteristics.

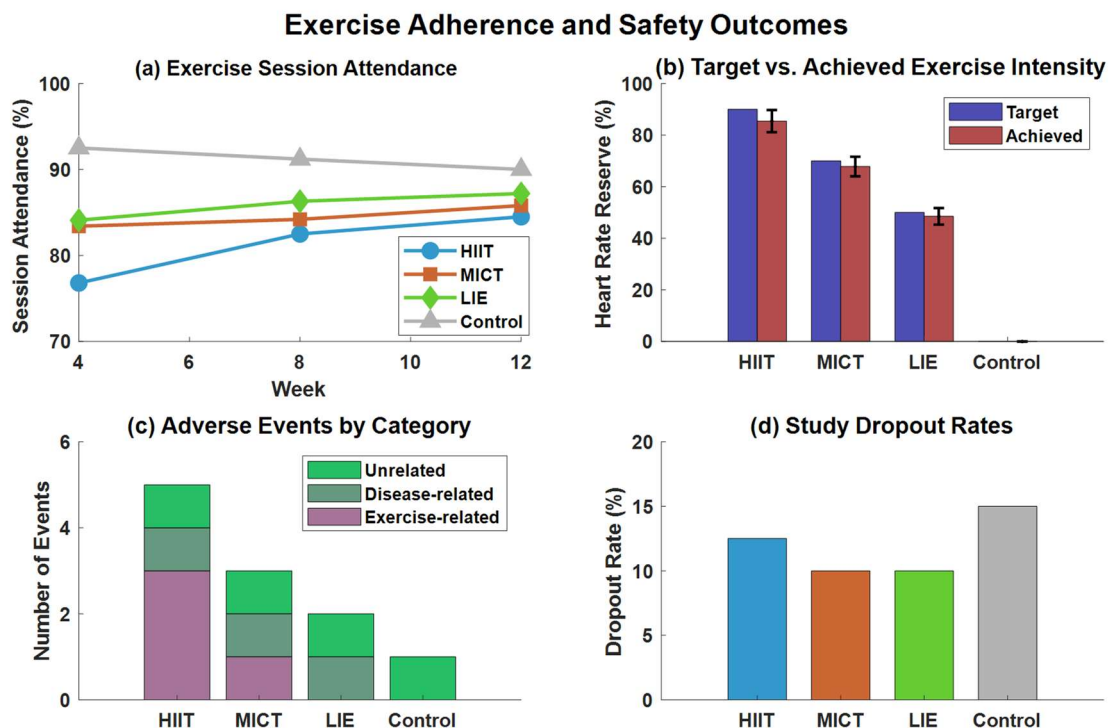


Figure 3. Exercise adherence and safety outcomes: **(a)** session attendance; **(b)** target vs. achieved intensity; **(c)** adverse events; **(d)** dropout rates.

The adherence and safety profiles observed in this study demonstrate that all three exercise intensity protocols were feasible and well-tolerated in this cancer survivor

population. While the HIIT protocol presented slightly greater challenges for initial adherence and had a marginally higher incidence of exercise-related adverse events, these differences were modest and did not compromise overall program implementation. The absence of serious adverse events across all exercise intensities supports the safety of appropriately supervised aerobic exercise, including high-intensity protocols, in cancer survivors who have completed primary treatment.

3.3. Effects of different aerobic exercise intensities on psychological health indicators

The exercise interventions demonstrated differential effects on psychological outcomes across treatment groups compared to controls. All psychological measures showed significant time-by-group interactions ($p < 0.001$), indicating that the pattern of change over time differed based on intervention assignment.

Anxiety levels, measured by the STAI-State scale, showed significant reductions in all exercise groups compared to controls at both post-intervention and follow-up, as illustrated in **Figure 4a**. The HIIT group showed the largest decrease (mean change: -10.4 points, 95% CI: -12.3 to -8.5), followed by MICT (-7.8 points, 95% CI: -9.5 to -6.1) and LIE (-4.6 points, 95% CI: -6.2 to -3.0), while the control group showed minimal change (-1.2 points, 95% CI: -2.6 to 0.2). Between-group comparisons revealed that HIIT produced significantly greater anxiety reduction than both MICT ($p = 0.021$) and LIE ($p < 0.001$) groups. Effect sizes were 1.57 for HIIT, 1.12 for MICT, 0.75 for LIE, and 0.18 for control.

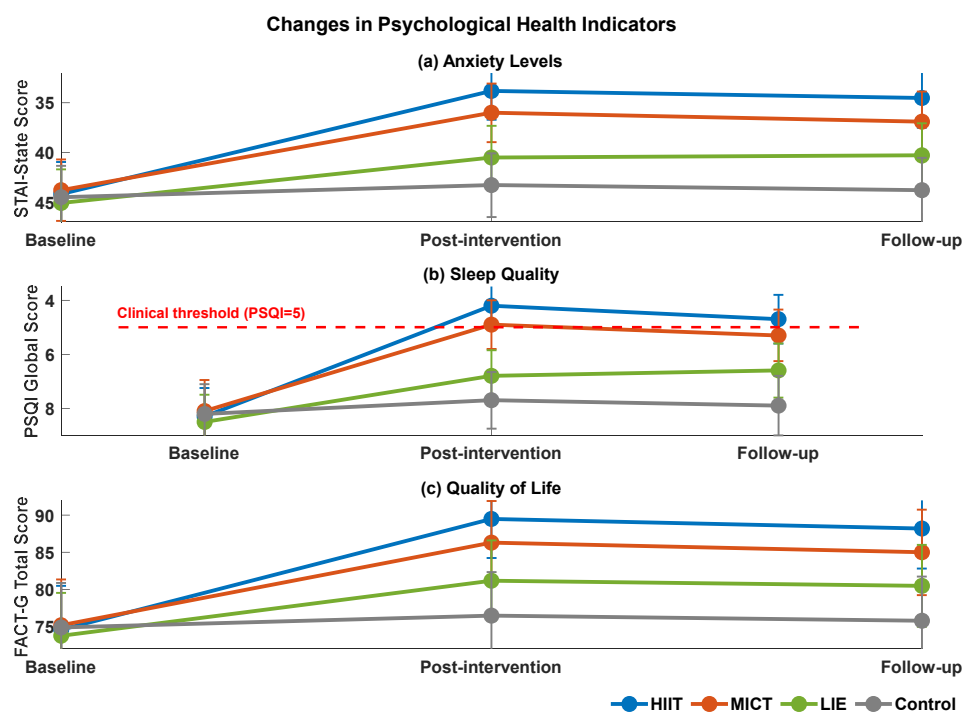


Figure 4. Changes in psychological health indicators: (a) anxiety levels; (b) sleep quality with clinical threshold line, and; (c) quality of life across HIIT, MICT, LIE, and control groups at baseline, post-intervention, and 3-month follow-up.

Sleep quality improved in all exercise groups compared to controls, as seen in **Figure 4b**. HIIT reduced PSQI scores by 4.1 points (95% CI: −4.8 to −3.4), MICT by 3.2 points (95% CI: −3.9 to −2.5), and LIE by 1.7 points (95% CI: −2.3 to −1.1). Both HIIT and MICT groups showed mean post-intervention PSQI scores below the clinical threshold of 5 (HIIT: 4.2; MICT: 4.9). HIIT differed from LIE and control (both $p < 0.001$). MICT differed from LIE ($p = 0.038$) and control ($p < 0.001$). HIIT and MICT showed no significant difference ($p = 0.092$).

FACT-G scores improved across exercise groups, as depicted in **Figure 4c**. HIIT increased FACT-G by 14.9 points (95% CI: 12.5 to 17.3), MICT by 11.1 points (95% CI: 8.9 to 13.3), LIE by 7.4 points (95% CI: 5.2 to 9.6), and controls by 1.6 points (95% CI: −0.5 to 3.7). Significant differences were found between all exercise groups and control (all $p < 0.001$), as well as between HIIT and LIE ($p < 0.001$) and MICT and LIE ($p = 0.039$). Emotional well-being demonstrated the greatest relative improvement across all exercise groups, with mean increases of 5.8 points (HIIT), 4.3 points (MICT), and 2.7 points (LIE), as shown in **Table 4**.

Table 4. Changes in psychological health indicators across intervention groups and time points.

Outcome measure	Group	Baseline	Post-intervention	3-month follow-up	Within-group p	Between-group p	Effect size (d)
Anxiety (STAI-state)	HIIT	44.2 ± 6.5	33.8 ± 5.8	34.5 ± 6.0	<0.001*	HIIT vs. MICT: 0.021*	1.57
	MICT	43.8 ± 6.2	36.0 ± 5.9	36.9 ± 6.1	<0.001*	HIIT vs. LIE: <0.001*	1.12
	LIE	45.1 ± 6.8	40.5 ± 6.4	40.3 ± 6.5	<0.001*	MICT vs. LIE: 0.017*	0.75
	Control	44.5 ± 6.3	43.3 ± 6.4	43.8 ± 6.5	0.421	All vs. Control: <0.001*	0.18
Sleep quality (PSQI)	HIIT	8.3 ± 2.1	4.2 ± 1.7	4.7 ± 1.8	<0.001*	HIIT vs. MICT: 0.092	1.94
	MICT	8.1 ± 2.3	4.9 ± 1.8	5.3 ± 1.9	<0.001*	HIIT vs. LIE: <0.001*	1.43
	LIE	8.5 ± 2.0	6.8 ± 1.9	6.6 ± 2.0	<0.001*	MICT vs. LIE: 0.038*	0.83
	Control	8.2 ± 2.2	7.7 ± 2.1	7.9 ± 2.2	0.346	All vs. Control: <0.001*	0.22
Quality of life (FACT-G)	HIIT	74.6 ± 11.8	89.5 ± 10.5	88.2 ± 10.8	<0.001*	HIIT vs. MICT: 0.061	1.27
	MICT	75.2 ± 12.3	86.3 ± 11.2	85.0 ± 11.5	<0.001*	HIIT vs. LIE: <0.001*	0.89
	LIE	73.8 ± 11.5	81.2 ± 10.8	80.5 ± 11.0	<0.001*	MICT vs. LIE: 0.039*	0.64
	Control	74.9 ± 12.0	76.5 ± 11.7	75.8 ± 11.9	0.287	All vs. Control: <0.001*	0.13

Note: Values presented as mean ± SD. STAI = State-Trait Anxiety Inventory; PSQI = Pittsburgh Sleep Quality Index; FACT-G = Functional Assessment of Cancer Therapy-General; d = Cohen's d effect size for pre-post change. *Statistically significant ($p < 0.05$).

Regression analyses identified change in cardiorespiratory fitness ($VO_2\max$) as significantly associated with improvements in all psychological domains, explaining 32% of variance in anxiety reduction, 29% in sleep quality improvement, and 25% in quality of life enhancement. Session attendance rate also predicted improvement in anxiety ($\beta = -0.31$, $p = 0.003$) and sleep quality ($\beta = -0.28$, $p = 0.007$). Subgroup analyses revealed no significant differences in psychological responses based on

cancer type.

The sustainability of benefits at 3-month follow-up varied somewhat by outcome. As shown in **Figure 4**, anxiety and quality of life improvements were largely maintained across all exercise groups. Sleep quality showed more variability, with HIIT and MICT groups experiencing small but significant regression toward baseline (HIIT: +0.5 points, $p=0.038$; MICT: +0.4 points, $p = 0.047$), while the LIE group maintained stable scores. However, all exercise groups remained significantly improved compared to baseline and control at follow-up (all $p < 0.001$).

3.4. Impact factors and dose-response relationship analysis

The relationship between exercise intensity and psychological health improvements was examined through multiple regression analyses, revealing significant dose-response patterns across outcome measures. When controlling for demographic and clinical characteristics, exercise intensity emerged as a significant independent predictor of improvements in anxiety ($\beta = -0.42, p < 0.001$), sleep quality ($\beta = -0.38, p < 0.001$), and quality of life ($\beta = 0.45, p < 0.001$). The magnitude of this relationship demonstrated consistent linearity across the intensity spectrum (**Figure 5a**). Each 10% increase in exercise intensity (measured as percentage of heart rate reserve) was associated with an additional reduction of 1.8 points in STAI-State anxiety scores and 0.7 points in PSQI sleep quality scores, as well as an increase of 2.1 points in FACT-G quality of life scores.

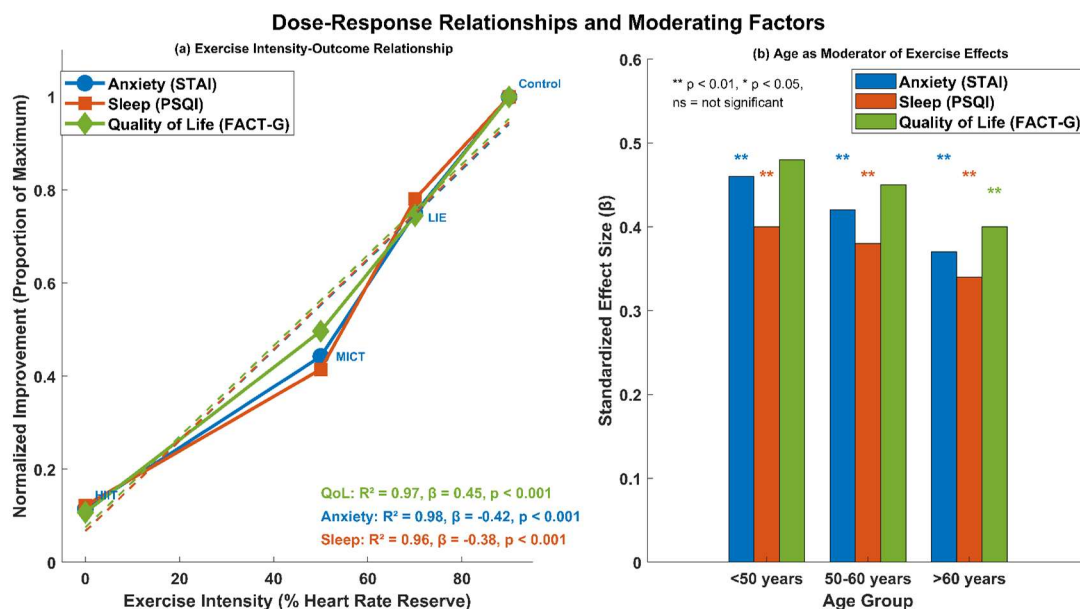


Figure 5. Dose-response relationships: (a) exercise intensity effects on psychological outcomes; (b) age-related moderation of these effects across participant groups.

Adherence to exercise sessions was significantly associated with psychological improvements across all exercise groups. Participants achieving $\geq 85\%$ attendance showed greater improvements than those with $< 85\%$ attendance in anxiety reduction (difference = 2.4 points, $p = 0.012$), sleep quality (difference = 1.1 points, $p = 0.038$), and quality of life (difference = 3.8 points, $p = 0.007$). Cardiorespiratory fitness

improvement, measured as change in estimated $\text{VO}_{2\text{ max}}$, was also significantly correlated with psychological outcomes, explaining 32% of variance in anxiety reduction, 29% in sleep quality improvement, and 25% in quality of life enhancement.

Moderation analyses, as illustrated in **Figure 5b**, revealed that age significantly moderated the effect of exercise intensity on psychological outcomes, with younger participants (<50 years) showing stronger associations between exercise intensity and improvements in anxiety ($\beta = -0.46, p < 0.001$), sleep quality ($\beta = -0.40, p < 0.001$), and quality of life ($\beta = 0.48, p < 0.001$) compared to middle-aged (50–60 years) and older participants (>60 years). This age-related moderation effect remained significant after controlling for cancer type, treatment modality, and time since treatment. BMI also demonstrated a moderating effect on sleep quality improvements, with overweight and obese participants ($\text{BMI} \geq 25 \text{ kg/m}^2$) showing a stronger relationship between exercise intensity and sleep quality enhancement ($\beta = -0.43, p < 0.001$) compared to normal-weight participants ($\beta = -0.32, p = 0.003$). However, cancer type, treatment modality, and time since treatment completion did not significantly moderate the relationship between exercise intensity and psychological outcomes (all $p > 0.05$).

The observed dose-response patterns and moderating effects provide valuable insights for exercise prescription in cancer survivors. The linear relationship between intensity and psychological benefits, as shown in **Table 5**, suggests that higher-intensity exercise may be optimal for maximizing psychological improvements. However, the significant moderating effects of age and BMI highlight the importance of individualized approaches to exercise prescription. Younger survivors and those with higher BMI may particularly benefit from higher-intensity protocols, while older survivors may achieve substantial benefits even with moderate-intensity exercise. These findings have important implications for the development of targeted exercise guidelines that consider both the exercise dose and individual characteristics of cancer survivors.

Table 5. Regression models for predictors of psychological health improvements.

Predictor variable	Anxiety reduction (STAI-S)		Sleep improvement (PSQI)		Quality of life (FACT-G)	
	β coefficient	<i>p</i> -value	β coefficient	<i>p</i> -value	β coefficient	<i>p</i> -value
Exercise intensity	-0.42	<0.001	-0.38	<0.001	0.45	<0.001
Session attendance	-0.31	0.003	-0.28	0.007	0.33	0.002
$\text{VO}_{2\text{ max}}$ improvement	-0.34	0.001	-0.29	0.005	0.37	<0.001
Age	0.08	0.241	0.11	0.138	-0.13	0.072
BMI	0.14	0.089	0.17	0.042	-0.08	0.267
Time since treatment	-0.05	0.518	-0.07	0.392	0.04	0.612
Cancer type*	0.06	0.482	0.09	0.214	0.05	0.508
Treatment modality**	0.12	0.132	0.15	0.075	-0.10	0.195
Baseline anxiety	0.39	<0.001	0.24	0.011	-0.27	0.006
Baseline sleep quality	0.22	0.018	0.41	<0.001	-0.20	0.031
Baseline quality of life	-0.25	0.009	-0.18	0.042	0.38	<0.001

Note: *Reference category: Breast cancer; **Reference category: Surgery only.

4. Discussion

This study demonstrates a dose-response relationship between exercise intensity and psychological outcomes. Higher intensities produced greater improvements. HIIT reduced anxiety by 10.4 points. Mechanisms may include endorphin release, stress hormone modulation, and interoceptive exposure [30]. Sleep quality followed an intensity-dependent pattern. Both HIIT and MICT improved PSQI scores. Exercise altered body temperature regulation, increased slow-wave sleep, and reduced pro-inflammatory cytokines [31]. HIIT improved quality of life, especially emotional well-being. Gains in cardiorespiratory fitness, functional capacity, and self-efficacy contributed to these changes [11,32]. The intensity-response pattern applies within the tested 40-95% HRR range. Effects beyond this range remain unknown. Non-linear relationships or threshold effects may exist at higher intensities.

The observed changes exceeded established clinical thresholds. HIIT reduced anxiety by 10.4 points, surpassing the 5–7 point MCID for STAI in cancer populations. Sleep quality improved by 4.1 points in HIIT and 3.2 points in MICT, both exceeding the 3-point PSQI threshold. FACT-G increased by 14.9 points in HIIT, well above the 5-point MCID. These improvements reflect meaningful changes in daily functioning.

The present findings both align with and extend previous research in exercise oncology. The overall efficacy of aerobic exercise for improving psychological outcomes in cancer survivors confirms results from meta-analyses by Brown et al. [30] and Belloni et al. [20]. However, while these previous studies established general exercise benefits, they did not systematically compare intensity effects within the same population. The results support evidence from Tong et al. [32] showing benefits of supervised high-intensity protocols for cancer rehabilitation. However, these findings diverge somewhat from van Weert et al. [33], who reported minimal differences between higher and lower intensity interventions for cancer-related fatigue. This discrepancy may reflect differential responsiveness across psychological domains. Anxiety and sleep may respond more to intensity variations than fatigue. Methodological differences in measuring intensity could also contribute.

These findings have implications for cancer survivorship care. Current guidelines emphasize moderate-intensity exercise [1]. The dose-response pattern suggests higher-intensity protocols may optimize psychological benefits when supervised. Age and BMI moderated treatment effects, supporting individualized prescription approaches [16]. Safety profiles and adherence rates indicate clinical viability across intensity groups. Lower initial adherence in HIIT warrants consideration during implementation. These findings align with recent research by Neuendorf et al. [10], who documented comparable feasibility between high-intensity and moderate-intensity protocols in cancer patients despite initial concerns about tolerance. Patient characteristics should guide intensity selection. Younger survivors with lower BMI responded better to HIIT. MICT suits older adults or those with elevated BMI while maintaining similar benefits. Unsupervised implementation requires baseline fitness assessment and gradual progression. Starting with moderate intensity before advancing to higher levels may optimize safety and adherence.

Several limitations exist. The sample included mainly early-stage survivors with good performance status. Generalizability to advanced disease populations may be

limited. The 3-month follow-up prevents conclusions about long-term sustainability. Some exercise benefits may attenuate over time [29]. Additionally, while comprehensive, the psychological assessments relied primarily on self-report measures rather than objective outcomes. Supervised delivery may overestimate adherence compared to home-based programs [24]. These limitations reflect common methodological challenges in exercise oncology research but should be addressed in future studies.

Future research should extend these findings in several directions to address remaining knowledge gaps. Longer follow-up periods are essential to determine the durability of psychological benefits across different exercise intensities and the factors influencing long-term adherence. Mechanistic studies incorporating biomarker analyses of inflammatory cytokines, neurotrophic factors, and stress hormones would further elucidate the biological pathways mediating intensity-specific effects [7,31]. Given the observed moderating effects of age and BMI, trials specifically testing adaptations of high-intensity protocols for older or deconditioned survivors would have significant clinical utility. Implementation science approaches examining the translation of these findings into routine cancer care settings would address the research-to-practice gap highlighted by Depenbusch et al. [34], particularly regarding the challenges of integrating higher-intensity protocols into standard survivorship care.

Aerobic exercise improves psychological outcomes in an intensity-dependent manner. HIIT produced the greatest benefits for anxiety, sleep quality, and quality of life. The dose-response relationship and safety profiles support exercise prescriptions tailored to individual characteristics. These findings inform exercise guidelines for optimizing psychological health during survivorship. Future research should focus on implementation strategies to translate these findings into clinical practice while addressing long-term adherence and accessibility concerns identified as critical factors in exercise program success for cancer survivors.

5. Conclusion

This study provides compelling evidence for a dose-response relationship between aerobic exercise intensity and psychological outcomes in cancer survivors. The high-intensity interval training group demonstrated significantly greater improvements in anxiety (mean reduction: 10.4 points), sleep quality (mean improvement: 4.1 points), and quality of life (mean increase: 14.9 points) compared to moderate-intensity continuous training, low-intensity exercise, and control conditions. This intensity-dependent pattern remained consistent across cancer types and treatment modalities, though moderated by participant age and BMI. The research advances theoretical understanding of exercise-psychology interactions in cancer populations by identifying intensity as a critical parameter influencing magnitude of benefit, with each 10% increase in exercise intensity associated with an additional reduction of 1.8 points in anxiety scores and 0.7 points in sleep disturbance.

The findings contribute to the evolving evidence base supporting exercise as medicine in oncology by demonstrating that psychological benefits follow similar dose-response patterns to physiological adaptations. This challenges traditional

approaches that have emphasized moderate-intensity exercise for cancer survivors and suggests reconsideration of optimal exercise parameters for psychological health. The research furthermore establishes the safety and feasibility of supervised high-intensity protocols in this population, with comparable adherence rates (82.3% HIIT vs. 85.1% MICT) and no serious adverse events across intensity groups. These results extend previous work on exercise benefits in cancer survivors by providing direct comparative evidence for intensity effects within the same study population.

The clinical implications suggest that cancer rehabilitation programs should incorporate higher-intensity components when appropriate, with individualization based on age, fitness level, and clinical status. Exercise prescription for cancer survivors should consider intensity as a key modifiable parameter that can be leveraged to maximize psychological benefits. Healthcare systems should prioritize exercise programming as standard survivorship care and ensure access to qualified exercise professionals capable of delivering appropriately intensive and individualized interventions. Policy development should focus on establishing reimbursement mechanisms for exercise interventions and incorporating evidence-based, intensity-appropriate exercise recommendations into cancer care guidelines to enhance psychological outcomes during survivorship.

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Ethical approval: This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. As the Health Management College of Xianning Vocational Technical College does not have an independent institutional review board, ethical approval was obtained from the Scientific Research Office of Xianning Vocational Technical College. The study protocol, including informed consent procedures and data privacy protection, was reviewed and approved by the college's academic committee (Approval No.: XNVTC-SRO-2024-017). All participants voluntarily participated and provided written informed consent prior to the commencement of the intervention.

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Conflict of interest: The authors declare no conflict of interest.

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