

REVIEW

The effects of exercise on sleep disturbances and cancer-related fatigue for female breast cancer survivors receiving adjuvant hormone therapy: A systematic review

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Abstract

Background: Breast cancer is the most common type of cancer, accounting for 15% of all new cases. Hormone therapy (HT) is extremely effective in reducing breast cancer recurrence. However, adherence to HT medication is often poor due to negative side effects such as fatigue and sleep disturbances. Physical activity has been identified as a possible intervention to improve quality of life and reduce side effects of HT.

Objective: The objective of this systematic review was to summarise evidence of exercise interventions for women being treated with HT for breast cancer.

Method: Electronic searches were conducted from inception to March 2022 using Medline, SPORTdiscus, Embase, Scopus, PsycINFO and Web of Science databases. Searches included a combination of terms related to breast cancer, exercise, sleep disturbances, fatigue and HT.

Results: Ten eligible papers were identified, and their quality was assessed. Type, frequency, duration and intensity of exercise interventions varied. Exercise types included aerobics, strength/resistance training, walking and yoga. Heterogeneity of data made it difficult to draw conclusions. However, aerobic exercise interventions provide clear improvements in fatigue and sleep disturbances.

Conclusions: This review identified a lack of consistency in exercise recommendations for women being treated for breast cancer. It identifies that aerobic exercise can successfully improve fatigue and sleep disturbances, consistent with existing literature. Exercise has a range of benefits for this population, including improving psychological well-being and quality of life. Clinicians should strongly advocate for engagement in exercise to promote overall physical and psychological well-being in women being treated for breast cancer.

KEYWORDS

breast cancer, cancer-related fatigue, physical activity, sleep disturbances

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1 | BACKGROUND

Breast cancer is one of the most common forms of cancer,¹ with 2.26 million cases of breast cancer in women reported in 2020, and 685,000 deaths reported globally.² Around 80% of breast cancers are hormone receptor positive, meaning that the cancer cells have oestrogen or progesterone receptors or both.³ This means that they respond to hormone therapy (HT) which stops or slows the growth of tumours by blocking/interfering with the body's ability to produce these two hormones.⁴ The most commonly prescribed HTs are selective oestrogen receptor modulators such as tamoxifen or aromatase inhibitors such as anastrozole and exemestane.^{5,6}

Adjuvant HT is prescribed to maximise the positive impacts of primary treatments such as surgery, chemotherapy or radiation.⁷ It aims to prevent breast cancer recurrence by interfering with the effects of oestrogen and is usually prescribed for a 5-year period.⁸ Research has shown that taking HT as prescribed significantly reduces the risk of breast cancer recurrence and death.⁹ After 5 years of HT, the risk of recurrence is halved, with this reducing to only one third after a further 5 years.¹⁰ Yet, rates of adherence to HT are sub-optimal.¹¹ A study of 4178 women with breast cancer found that 23% discontinued their medication early.¹² Poor adherence is often attributed to the adverse side effects associated with HT.¹³ The most reported side effects include fatigue, sleep disturbances, hot flashes and joint pain.^{14,15}

Cancer related fatigue (CRF) is extremely common for women with breast cancer and has been defined as 'a distressing, persistent, subjective sense of tiredness or exhaustion related to cancer or cancer treatment'.¹⁶ As many as 99% of women experience fatigue during breast cancer treatment, as a result of HT depriving the body of oestrogen.^{17,18} Patients undergoing HT are at a heightened risk of CRF, with 60% experiencing CRF throughout their treatment.^{19,20} CRF is strongly associated with deterioration in women's quality of life and has a significant impact on their treatment adherence.²¹ Research has also evidenced a link between CRF levels and emotional upset, muscle weakness, pain and concentration problems.²² Breast cancer patients have reported that experiences of CRF have affected their ability to work and attend social events, suggesting a significant negative impact on their day-to-day life.²³ Sleep disturbances are also a common side effect for women receiving HT for breast cancer.²⁴ Fortner et al.²⁵ reported that 61% of breast cancer patients had a noticeable decline in sleep quality. Poor sleep quality can significantly reduce the quality of life of women being treated for breast cancer and is related to increased fatigue.²⁶ For example, research has shown that women with poorer sleep quality were less able to function generally due to less energy, greater bodily pain and more mental health problems.²⁵ Sleep quality is strongly associated with mental disorders (e.g., depression) in women with breast cancer.²⁷ Sleep disturbances can also impact on women's adherence to HT medication.²⁸ This is extremely concerning as poor sleep is associated with greater breast cancer mortality.²⁹

Researchers have investigated possible methods (both pharmacological and non-pharmacological) of stopping or reducing sleep disturbances that occur in women because of HT. One study found that 42%

of women had used medication for sleep in the past month.³⁰ Sleep medication may be effective in managing sleep disturbances for a short period of time but is not recommended as a long-term solution, due to associated side effects and potential harms.³¹ Furthermore, sleep medications should be used with caution by breast cancer patients as they have the potential to interact with other treatment.³² Therefore, non-pharmacological methods for addressing sleep disturbances should be prioritised.

Numerous studies have investigated various interventions to target CRF and sleep disturbances related to HT.³³⁻³⁷ The most prominent of these interventions discussed within the literature is exercise. Physical activity is defined as any movement that results in the utilisation of energy.³⁸ Exercise is a subcategory of physical activity which is planned, structured, repetitively and purposefully focused on improvement or maintenance of physical fitness.³⁹ However, the terms physical activity and exercise may be used interchangeably. There is an increasing wealth of evidence to support exercise as an effective non-pharmacological intervention throughout the course of cancer treatment.^{40,41} Research findings have suggested that engagement in exercise may have the potential to reduce many of the negative side effects of cancer treatment thus, benefitting cancer patients and their treatment adherence. For example, research has provided evidence to suggest that exercise can improve symptoms and side effects including physical functioning,⁴² sleep quality,⁴³ quality of life^{44,45} and pain levels in cancer patients.⁴⁶ Exercise has also been associated with reductions in recurrence and mortality of some cancers.⁴⁷

Among these benefits, there is extensive evidence to indicate that exercise can also reduce CRF and which can consequently improve patients' overall quality of life.^{48,49} Exercise has been suggested to reduce CRF due to instigating adaptive changes, including 'gains in muscle mass and plasma volume, improved lung ventilation and perfusion, increased cardiac reserve and a higher concentration of oxidative muscle enzymes'.⁵⁰ A decrease in physical activity (e.g., due to illness) can reverse this process, resulting in individuals becoming more prone to muscle fatigue.^{51,52} For women receiving HT, reducing physical activity levels due to feelings of fatigue can negatively impact their exercise capacity and fatigue resistance, creating a continuous cycle.⁵³ Research has shown that this cycle can be reversed through gradually increasing physical activity levels.⁵⁴ Whilst previous findings have suggested this effect of exercise on CRF in breast cancer patients, there are limited findings specific to patients undergoing HT. Therefore, research is needed to bring clarity to this relationship and advance the intervention guidelines surrounding this type of treatment.

Findings about the most appropriate type, intensity, frequency and duration of physical activity for reducing CRF are unclear. One study suggested that moderate intensity aerobic exercises were related to improvements in fatigue during treatment.⁵⁵ Another found that a mixture of cardiovascular activity, stretching and resistance training reduced CRF in women with breast cancer.⁵⁶ A 2013 study also suggested that deep water aquatic exercise can reduce CRF.³⁴ Carayol et al.⁵⁷ argued that lower doses (90-120 min weekly) of moderate intensity exercise are more beneficial for improving CRF than higher doses. In contrast, a systematic review found non-significant

improvements in CRF for women in exercise intervention groups compared with control groups.⁵⁸ Clearly, the volume of research around physical activity and CRF is extensive. However, there is little consensus on the optimal type (e.g., aerobic, resistance), mode and dose (frequency, intensity and duration) of physical activity for reducing symptoms of fatigue.⁵⁹ The current review aimed to determine the most effective exercise interventions for reducing CRF and sleep disturbances in breast cancer patients receiving HT. It will do this through synthesising existing information about the effects of different types, modes and doses of exercise interventions. This will have practical implications for research and practice through identifying clearer exercise recommendations for women with breast cancer.

2 | METHODOLOGY

The process of the current review was conducted in accordance with the PRISMA statement guidelines.⁶⁰ A protocol was developed in advance and registered as a preprint through PsyArXiv (<https://doi.org/10.31234/osf.io/q7tm3>).

2.1 | Eligibility criteria

Studies were included if their participants were women of 18+ years who were prescribed adjuvant HT, were randomised controlled trials or had a control/comparison group and reported the effectiveness of exercise interventions on CRF and/or sleep measures. Studies which used participants who had a previous diagnosis of insomnia disorders were excluded. Only studies with female participants were included, due to the scale of literature around females compared with males with breast cancer. Full details of inclusion/exclusion criteria are provided in Table 1.

2.2 | Information sources

Online searches were conducted from February to March 2022. The databases used were Medline, SPORTdiscus, Embase, Scopus, PsycINFO and Web of Science. Databases were searched from the year of inception to March 2022.

2.3 | Search strategy

A combination of search terms relating to breast cancer, physical activity, sleep disturbances/fatigue and HT were developed. Search terms can be seen in the [supporting file](#).

2.4 | Study selection

Search results from each database were uploaded into a folder on EndNote (Version 20). Duplicates were removed. Titles and abstract screening was conducted by five reviewers, based on the agreed inclusion/exclusion criteria. Each paper was screened independently by

TABLE 1 Pre-determined selection criteria.

Inclusion criteria	Exclusion criteria
Female participants who are 18 years or older, who have been prescribed adjuvant hormone therapy for breast cancer	Studies which do not investigate using human subjects
Studies must be randomised controlled trials or have a control/comparison group	Studies which do not include HT
Studies reporting the effectiveness of interventions on fatigue/sleep measures	Studies which use participants who have had previous insomnia diagnosis before breast cancer
	Studies which do not include primary data (e.g., systematic reviews and meta-analyses)
	Studies in which the full text was not available
	Studies which are not published in English

Abbreviation: HT, Hormone therapy,

two authors. Where information from abstracts was unclear, papers were retained for review during the full-text screening stage. Full-text screening of each paper was conducted independently by two authors and subsequently crosschecked by the team of researchers. Upon screening, it became clear that some studies ($n = 8$) had used a combination of participants with and without HT. This was considered, and the decision was made to accept those where the majority of participants were receiving HT ($n = 5$) due to the value of the data in these studies. Any screening conflicts were resolved through discussion.

2.5 | Data extraction

The task of data extraction was split up between the research group, with each member independently extracting data from their share of the studies. A data extraction form was produced, following the guidelines from the *Cochrane Handbook for Systematic Reviews of Interventions*.⁶¹ Relevant data were extracted from the method and results sections of the included studies to obtain details of the sample size, participant demographics, study design, HT, exercise intervention, measures of sleep and fatigue, method of analysis, effect size and the overall result. The extracted data were entered into the form, which was an online, shared document, that only the research group members had access to. Reasons for inclusion and exclusion were also recorded in the shared document and disagreements surrounding inclusion were resolved through discussion.

2.6 | Quality appraisal

Each study that met the criteria during the screening stages was selected for quality assessment. The Quality Assessment Tool for

Quantitative Studies, developed by the Effective Public Health Practice Project, was utilised.⁶² This is a valid and reliable tool which assesses selection bias, study design, confounders, blinding, data collection methods, withdrawals and dropouts, intervention integrity and analysis.⁶³ The methodological quality is assessed for each of these characteristics, and researchers are required to score each section as 'strong', 'moderate', or 'weak'. Studies receive a global rating, taking account of their score for each section. A global rating of 'weak' is given if two or more categories are rated as weak. Studies are rated as 'moderate' if one category is rated as weak, and a global rating of 'strong' is given to studies with no weak ratings. Each researcher individually assessed five of the 10 studies and scored them on the Quality Assessment Tool for Quantitative Studies. Researchers then discussed any scoring discrepancies and agreed on a final score for each study.

2.7 | Data analysis

Data extracted from each of the 10 included studies were placed in a shared Microsoft Excel (2022) document. Due to heterogeneity of the data for exercise interventions and measures used in the included studies, it was not possible for a meta-analysis to be carried out. Therefore, a narrative synthesis was conducted. The focus of the narrative synthesis was to summarise key information from the papers, which were pertinent to the current research question.⁶⁴ Data on the type, intensity, frequency, and duration of exercise intervention and the effects of these were synthesised.

3 | RESULTS

3.1 | Study selection

A total of 1070 records were identified. After the removal of duplicates, 614 remained. After title and abstract screening, 140 were retained for full-text review. Ten papers met the inclusion criteria. The number of papers at each stage of screening and reasons for exclusion are shown in the PRISMA flow diagram in Figure 1.

3.2 | Study characteristics

The study characteristics are shown in Table 2. All studies included are randomised controlled trials. Sample sizes range from 18 to 500. The total number of participants included is 1136 (excluding Penttinen et al.⁶⁴ as this is a follow-up on the participants used by Saarto et al.⁶⁵). Included studies were published from 2008 to 2020. Studies were published in six countries including the USA ($n = 3$), Finland ($n = 3$), Germany ($n = 1$), South America ($n = 1$), Korea ($n = 1$) and Denmark ($n = 1$). Participants in included studies were receiving a variety of HT medication, including tamoxifen and letrozole. Specific medications taken by participants in each study are shown in Table 2, except for five studies which did not specify HT medication.

The majority of included studies investigated CRF ($n = 9$). Two measured sleep disturbances in addition to CRF, and one focused only on sleep disturbances. All studies used self-report measures for CRF. Five studies relied on a single scale, and five used two or more scales to measure CRF. Scales used include the Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT [$n = 4$]), the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30 [$n = 3$]) and the breast cancer-specific adaptation of this ($n = 1$), the Piper Fatigue Scale ($n = 2$) and the Cancer Fatigue Scale (CFS [$n = 1$]).

3.3 | Quality assessment

Table 3 shows ratings for each study on the Quality Assessment Tool for Quantitative Studies. One study was given a global rating of 'strong'. Five were given the rating of 'moderate', and four were rated 'weak'.

3.4 | Exercise interventions

As shown in Table 2, the types of interventions used include aerobic combined with strength/resistance training ($n = 4$), walking ($n = 3$), yoga ($n = 1$) and step aerobics combined with circuit training ($n = 2$, including Saarto et al.⁶⁵ and Penttinen et al.⁶⁴ follow up).

Four studies combined aerobic and strength/resistance training interventions.⁶⁶⁻⁶⁹ These differed in length and delivery of the interventions. For example, Baglia et al.⁶⁶ intervention included two strength sessions, and 150 min of aerobic training weekly, over a period of 12 months. Paulo et al.⁶⁹ intervention was 40 min of aerobic, and 30 min of resistance training weekly, for 9 months. In comparison, Møller et al.⁶⁸ intervention included two 6-week phases. Phase one involved 9 h of exercise weekly (strength training sessions and restorative cardio). Phase two involved 6 h weekly of sports games, dancing and circuit training at moderate-high intensity. Kim et al.⁶⁷ also included two 6-week phases. Phase one involved one weekly aerobic and strength training session, and phase two increased to twice weekly. These were of low, moderate and high intensities. Each of these studies combined aerobic and resistance training but delivered these programmes in different ways.

Three studies used walking interventions. Payne³³ intervention involved 20 min of walking four times weekly. This was completed at a moderate intensity for a 12-week period. Another study included 12 individual sessions with an exercise specialist within the first 6 weeks, aiming to help participants gradually increase their intensity over a 12-week period.⁷⁰ They aimed to reach 150 min of walking per week by the final week. This intervention is described as moderate intensity. The intervention set by Baruth et al.⁷¹ started with participants walking 3 days per week for 20 min each. By week 8, this increased to 5 days for 30–40 min each. Week 1 was moderate intensity, reaching vigorous intensity from weeks 8–12. Therefore, all three walking interventions lasted for 12 weeks. Two aimed to gradually increase walking duration, whereas one remained the same for 12 weeks.

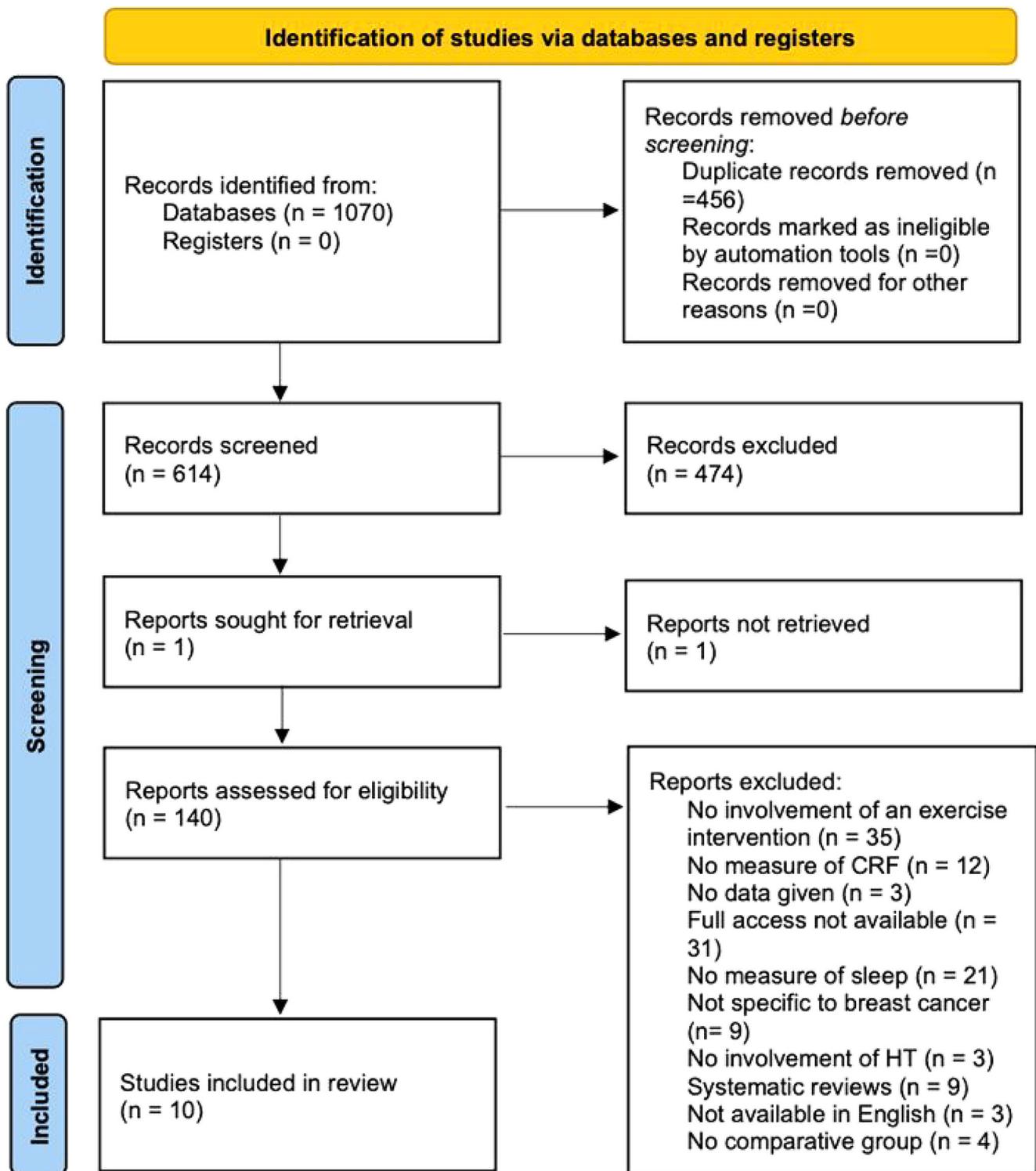


FIGURE 1 PRISMA flow diagram of study selection. CRF, cancer-related fatigue; HT, hormone therapy.

One study compared Iyengar-Yoga to a physical exercise intervention.⁷² Iyengar-Yoga involves traditional elements of yoga (e.g., positions and breath control) but is unique as it uses ‘probs’ (e.g., belts, robes or blankets) to help individuals perform and hold positions. It has been suggested that this is useful for cancer patients who may have less stamina as it can minimise exertions.⁷³ The yoga group

completed a 60-min session weekly for 12 weeks. The control group completed a physical exercise intervention for 60 min each week for 12 weeks. Both the yoga and physical exercise groups also performed home-based workouts twice weekly for 20 min each.

Saarto et al.⁶⁵ and the follow-up by Penttinen et al.⁶⁴ used a step aerobics and circuit training exercise intervention, lasting 12 months.

TABLE 2 Characteristics of included studies.

Study	Country	Sample size recruited/analysed	Mean age	Hormone therapy	Exercise type	Exercise frequency	Exercise intensity	Exercise duration	Investigating fatigue or sleep disturbances	Measurement of fatigue/sleep disturbances	Findings
Baglia et al. (2019)	USA	121/121	61.2 (SD = 7.0)	Als	Aerobic and strength training	2x weekly strength training, 150 min aerobic exercise/week (split in any way)	Moderate	Aerobic: 150 min per week, Strength: two sessions per week	Fatigue	FACIT	Significant improvement in CRF
Baruth et al. (2015)	Columbia	33/32	Intervention group: 57.4 (SD = 6.1), control group: 54.9 (SD = 6.5)	21 receiving HT	Walking	Week 1: 3 days/week, by week 8: 5 days/week	Moderate, progressing to moderate to vigorous	Week 1: 20 min, week 8 onwards: 30–40 min	Fatigue	FACIT	Significant reduction in fatigue
Kim et al. (2020)	Korea	66/58	Intervention group: 49.91 (SD = 7.62), control group: 48.48 (SD = 6.75)	23 receiving HT	Aerobic and strength training	First phase: 1x weekly, Second phase: 2x weekly	Low, moderate and high	2 h each session	Fatigue and sleep disturbances	PSQI and Piper Fatigue Scale	Not significant
Lötzke et al. (2016)	Germany	119/92	Intervention group: 51.0 (SD = 11.0), control group: 51.4 (SD = 11.1)	Combination of HT and radiation or chemotherapy	Iyengar-Yoga	1x weekly session, encouraged to do 2 more each week at home	Moderate and high	60/min week in person, encouraged to do 2x 20 min at home	Fatigue	EORTC-C30 and CFS-D	Significant change in CRF for comparison group
Møller et al. (2020)	Denmark	711/153	51.7	77.1% receiving HT (41% tamoxifen, 29% letrozole and 8% other)	Resistance and aerobic	First 6 weeks: three sessions per week and one restorative session. Second six weeks frequency not specified	Moderate and high	9 h/s for 6 weeks, then 6 h for next 6 weeks	Fatigue	EORTC-C30	Not significant

(Continues)

TABLE 2 (Continued)

Study	Country	Sample size recruited/analysed	Mean age	Hormone therapy	Exercise type	Exercise frequency	Exercise intensity	Exercise duration	Investigating fatigue or sleep disturbances	Measurement of fatigue/sleep disturbances	Findings
Paulo et al. (2019)	Finland	124/36	Intervention group: 63.2 (SD = 7.1), control group: 66.5 (SD = 9.6)	AIs	Resistance and aerobic	3x weekly	Not specified	40 min aerobic, 30 min resistance aerobic 3x week for 9 months	Fatigue	EORTC-QLQ-C30 and EORTC QLQ-BR23	Significant improvement in CRF and sleep disturbances
Payne et al. (2008)	USA	20/18	64.7 (SD = 6.3)	Tamoxifen, anastrozole or letrozole	Walking	4x weekly	Moderate	20 min	Fatigue and sleep disturbances	PFS and PSQI	Significant improvement in sleep disturbances
Penttinen et al. (2019)	Finland	444/444	Intervention group: 52.8 (SD = 7.2), control group: 53.3 (SD = 7.7)	419 receiving HT (150 taking AIs, 261 taking Tamoxifen)	Step aerobics and circuit training	1x weekly supervised, recommended 2–3 times at home	'hard' and 'somewhat hard'	60 min	Fatigue	FACIT	Not significant
Rogers et al. (2009)	USA	41/36	53 (SD = 9)	27% on an oestrogen receptor modulator, 73% on an AI	Walking	12 individual exercise sessions with a specialist in the first 6 weeks	Moderate	Progressed to 150 min by the final week of a 12-week programme	Sleep disturbances	PSQI	Not significant
Saarto et al. (2012)	Finland	573/500	Intervention group: 52.3, control group: 52.4	419 receiving HT (150 taking AIs, 261 taking tamoxifen)	Step aerobics and circuit training	1x weekly supervised, recommended 2–3 times at home	Somewhat hard' or 'hard'	60 min	Fatigue	FACIT	Not significant

Note: Measurement methods used: Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT); European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30); European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire for Breast Cancer (EORTC-QLQ-BR23); Cancer Fatigue Scale (CFS-D); Pittsburgh Sleep Quality Index (PSQI); Piper Fatigue Scale (PFS).

Abbreviations: AIs, aromatase inhibitors; CRF, cancer-related fatigue; HT, hormone therapy

TABLE 3 Quality assessment ratings.

Author	Section A: selection bias	Section B: study design	Section C: confounders	Section D: blinding	Section E: data collection methods	Section F: withdrawals and dropouts	Global rating
Baglia et al.	Moderate	Strong	Strong *	Weak	Strong	Strong	Moderate
Baruth et al.	Moderate	Strong	Strong	Weak	Strong	Strong	Moderate
Lotzke et al.	Weak	Strong	Weak	Moderate	Strong	Weak	Weak
Møller et al.	Weak	Strong	Weak	Moderate	Weak	Moderate	Weak
Paulo et al.	Moderate	Weak *	Strong *	Weak	Strong	Weak	Weak
Payne et al.	Weak	Strong	Weak	Weak	Strong	Strong	Weak
Penttinen et al.	Strong	Strong	Strong *	Weak	Strong	Moderate	Moderate
Saarto et al.	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Kim et al.	Strong	Strong	Strong	Weak	Strong	Strong	Moderate
Rogers et al.	Strong	Strong	Strong	Weak	Strong	Strong	Moderate

Note: * = There was a disagreement between researchers about the rating for this item, which was then resolved through discussion.

The exercise group completed supervised training led by an experienced physical therapist once weekly. This alternated weekly between step aerobics and circuit training, for 60 min per session. The intensity target was 'somewhat hard' or 'hard' as rated on the 'Rating of Perceived Exertion Scale'.

Participants were also encouraged to complete home training 2–3 times per week. The type of home training was optional but was encouraged to be endurance based (e.g., walking) or jumps and leaps-like step aerobics.

3.5 | Effectiveness of exercise interventions

Of the four studies that combined aerobic and resistance training, two had significant positive effects on sleep disturbances or CRF. Baglia et al.⁶⁶ 12-month intervention saw significant effects on CRF at follow-up. The exercise intervention group showed greater improvement (of approximately 10%) in CRF compared with the usual care group. Paulo et al.⁶⁹ also saw an improvement in both sleep disturbances and CRF from their 9-month exercise intervention. The exercise group showed a decrease in both CRF symptoms and sleep disturbances at 3, 6 and 9 months compared to baseline and the control group. However, two of the four studies found no significant improvement in CRF or sleep disturbances after aerobic/resistance interventions. Møller et al.⁶⁸ found no significant difference between groups for CRF symptoms after the 12-week intervention. Similarly, Kim et al.⁶⁷ saw a slight improvement in sleep disturbances for the intervention group but this was not statistically significant. They also found no significant effect of the exercise intervention on CRF. Each of these two interventions only lasted 12 weeks, compared to 12 and 9 months for the previous two. This difference in duration could potentially explain the difference in findings.

Of the three studies that implemented walking interventions, one found significant effects on sleep disturbances but not CRF,³³ and one found a significant effect on CRF symptoms.⁷¹ One found no significant effect of walking on sleep disturbances, other than a significant effect on sleep latency.⁷⁰ Both Rogers et al.⁷⁰ and Baruth et al.⁷¹ increased the frequency and duration of walking throughout the intervention, but their findings differ noticeably. Whilst not statistically significant, Baruth et al. reported changes in CRF whereas Rogers et al. found no changes in sleep disturbances. Whilst this difference in findings is interesting to consider, it is hard to draw real conclusions as the studies are not directly comparable due to having investigated different outcome measures.

The 12-week Iyengar-Yoga intervention which was compared to a physical exercise intervention initially found that neither significantly improved CRF.⁶⁸ At a 3-month follow-up post-intervention the physical exercise group saw improvement in CRF, whereas the Iyengar-Yoga group did not show improvements at the follow-up. As this is the only included study using a yoga intervention, no direct comparisons are possible.

The 12-week step aerobics intervention by Saarto et al.⁶⁵ found a significant linear relationship between higher levels of physical activity and recovery from CRF, regardless of the intervention group. At 5 years follow-up, findings suggest that participants with increased levels of physical activity were likely to have improved symptoms of CRF.⁶⁴ These findings suggest that physical activity in general, regardless of whether this was step aerobics, had a significant effect on CRF.

The effects of different intensities and durations of exercise interventions from the included studies were also taken into consideration. However, there were no common trends in relation to the effectiveness of specific intensities or durations for influencing CRF or sleep disturbances.

4 | DISCUSSION

4.1 | Summary of findings

The aim of this review was to investigate the effects of exercise interventions on CRF and sleep disturbances in women with breast cancer who are receiving HT, in order to provide more clarity on the most appropriate exercise recommendations for reducing side effects of HT. Despite the importance of HT for reducing cancer recurrence, adherence remains sub-optimal due to the impact of adverse side effects.¹⁴ Some of the most common side effects experienced by breast cancer survivors include CRF and sleep disturbances.¹⁵ Exercise has potential benefits for reducing the impact or helping to manage these side effects, which in turn could reduce non-adherence. However, there is little consensus in the literature about the most appropriate type, intensity, frequency and duration of exercise for women taking HT. Clear guidance on exercise recommendations that could help manage the side effects of HT is needed to improve overall quality of life and medication adherence.

Due to the heterogeneity of the reviewed studies and their interventions, it is difficult to draw strong conclusions and recommendations surrounding the main principles of physical activity interventions. Overall, many of the included studies did not report statistically significant changes in CRF or sleep disturbances, yet many did show slight improvements, with small to moderate effect sizes. These findings are in line with previous research,⁷⁴ which found a small to moderate improvement in CRF for female breast cancer patients participating in a physical activity intervention. The current findings also suggest that aerobic exercise can elicit larger effects on CRF and sleep disturbances, which is also consistent with previous results.^{75,76} Previous research has reported that aerobic exercise is associated with reduced symptoms of anxiety and depression, and enhanced quality of life in patients with chronic kidney diseases and has had beneficial effects on sleep disorders among the elderly.⁷⁷ Researchers have suggested that this is because aerobic exercise differs from other types of exercise, as it is dependent on the aerobic energy-generating process (the use of oxygen to meet energy demands).⁷⁸ It has been suggested that this unique process may reduce pain sensitisation through activating pain inhibitory mechanisms, which will likely improve sleep quality and, therefore, also improve quality of life and CRF.^{79,80} Thus, aerobic exercise interventions should be considered during the treatment process of breast cancer patients for more effective management of CRF and sleep disturbances.

Whilst the findings of this review give support only for moderate improvements, physical activity should continue to be recommended for breast cancer patients undergoing HT. There is an increasing field of evidence, including some of the reviewed studies, which give support for a wide range of benefits for cancer patients, elicited by physical activity interventions. Results have suggested physical activity interventions can reduce many cancer-related treatment side effects, including physical functioning,⁸¹ quality of life,^{45,82} mental health disorders, for example, anxiety,⁸³ and pain.⁸⁴ Additionally, it is known that long-term use of HT can affect women's bone health and increase the

risk of developing osteoporosis.⁸⁵ Research has shown that combined aerobic and resistance training is a safe and feasible way to improve bone health after cancer treatment.^{86,87} Researchers have also found that women receiving HT who participated in combined resistance and impact training-maintained bone mass density.⁸⁸ As physical activity interventions have been shown to be beneficial in reducing the extent of numerous side effects, they should, in turn, improve the likelihood of treatment adherence and outcomes for breast cancer patients.

Physical activity interventions have also been shown to increase overall physical performance in cancer patients.^{89,90} Physical performance can benefit one's self-esteem, self-confidence and self-efficacy, which can consequently be beneficial in aspects of social interaction, and reducing symptoms of anxiety.^{50,91} It has also been suggested that improved self-confidence and mood can boost physical independence⁸⁹ and increase the likelihood of repeating the behaviour.⁹² Therefore, it could be presumed that physical activity interventions could be beneficial in the likelihood of treatment adherence and outcomes and should be recommended in clinical guidelines.

The additional benefits of physical activity for mental health are extremely important and are particularly relevant to cancer patients due to the bidirectional relationship between mental and physical health.⁹³ Research has evidenced that breast cancer patients have a high risk of developing mental health conditions, with frequent reports of anxiety and sleep disturbances which are described as distressing and significantly interfere with women's quality of life.⁹⁴ This emphasises the importance of an intervention which can improve multiple side effects – including mental health symptoms. Physical activity can influence secondary benefits in addition to CFR improvements. Thus, the use of physical activity interventions is of clinical interest.

4.2 | Recommendations for future studies

The most considerable variations between the studies were the frequency and duration of the interventions. Based on previous findings, it was expected that a period of 6 weeks of aerobic exercise may show a greater improvement in CRF and sleep disturbances.⁹⁵ However, due to the heterogeneity of the intervention frequencies and duration periods of the selected studies it is difficult to compare them. This makes it difficult to determine whether longer duration interventions or those with a greater frequency of sessions are more effective. To better optimise physical activity interventions for breast cancer patients, it is important to understand FITT principles of the interventions⁹⁶ and how they influence adherence and side effects. FITT principles stand for frequency, intensity, time and type of physical activity. These are important aspects to consider when analysing physical activity interventions. From the current results, it is clear to see that the type of physical activity which is most beneficial in the management of CRF and sleep disturbances, is aerobic exercise. However, due to the heterogeneity between the frequency and time periods of the interventions and a lack of detail in reporting the intensities, recommendations cannot be drawn based on these principles of physical activity. This

highlights the need for future research to utilise high-quality reporting methods, to ensure results are valid and replicable. Future research may consider investigating these using more standardised procedures, in which participants are assessed over varying time periods or varying session frequency, to draw conclusions and recommendations about the frequency and duration of intervention. It would also be beneficial to further research the effects of intensity on intervention efficacy.

4.3 | Study limitations

This review focused specifically on women with breast cancer. Approximately 350 men are diagnosed with breast cancer annually in the United Kingdom, and whilst this is considerably less than the number of women, it is an important issue that should be considered. This review was also limited to studies which were published in English and used resources and databases available to the university, meaning some studies were excluded for not having access to full texts due to paywalls. This highlights the importance of open science in making research free and accessible in order to allow reproducibility and replicability of findings.⁹⁷ A grey literature search could have been conducted to identify information not produced by commercial publishers; however, due to time and resource limitations, this was not possible.⁹⁸ In addition to a grey literature search, hand searches of the reference lists of included studies could have been searched for relevant papers.

4.4 | Conclusions and clinical implications

The current review aimed to synthesise literature to determine the most successful exercise interventions on reducing sleep disturbances and CRF in women with breast cancer undergoing HT. Despite the heterogeneity of the selected studies making drawing conclusions difficult, this review has important implications for future research and practice. Findings suggest that aerobic exercise interventions can successfully improve CRF and sleep disturbances, which is consistent with existing literature. Beyond the benefits of CRF and sleep, physical activity interventions can improve other treatment side effects, including positive impacts on psychological well-being and perceived quality of life. Therefore, clinicians should advocate strongly for engagement in exercise for promoting overall physical and psychological well-being in women being treated for breast cancer.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Not applicable.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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