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Can improving quality of sleep reduce the symptoms of cancer-related fatigue in adults?: A systematic review

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Abstract

Purpose: Cancer-related fatigue (CRF) results in reduced quality of life for cancer patients. The relationship between tiredness and fatigue has been established in cancer patients and has been shown to be reciprocal, meaning the relationship is somewhat 'chicken or the egg' with tiredness influencing fatigue and vice versa. The aim of this study is to determine whether an improvement in sleep quality can ease the symptoms of CRF and whether this can support the theory that CRF symptoms stem from the effect of tiredness.

Method: Three databases were searched producing 259 papers. The papers were filtered using several inclusion criteria, resulting in a final list of 20 papers for analysis. The remaining papers (20) were critically appraised using the Critical Appraisals Skills Programme (CASP) randomised control trial checklist and assessed for bias using the Cochrane Collaboration's tool for assessing risk of bias in randomised trials.

Results: Fourteen papers showed an increase in sleep quality that also resulted in an improvement in fatigue symptoms. Cognitive behavioural therapy was shown to be the most effective intervention with a statistically significant decrease in fatigue alongside significant improvement in sleep quality shown in six of the papers ($p < 0.05$). Sleep education also had a positive impact on both sleep and fatigue scores with three papers showing significant improvements. Three papers focusing on exercise interventions produced a significant improvement in fatigue symptoms and quality of sleep.

Conclusion: Improving quality of sleep does ease the symptoms of CRF; however, the 'chicken or the egg' question regarding CRF and tiredness cannot be answered at this stage.

KEYWORDS
cancer, cancer-related fatigue, fatigue sleep, tiredness

1 | INTRODUCTION

Cancer-related fatigue (CRF) is defined as 'a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning' (Berger et al., 2015) and affects between 59% and 100% of cancer patients (Weis, 2011). CRF can affect patients before, during and after therapy (Charalambous et al., 2019). The cause of CRF is a subject of debate. It often occurs as a consequence of radiotherapy and chemotherapy (Yang et al., 2019), but it is also hypothesised that CRF comes from a combination of interrelated cytokine, muscular, neurotransmitter and neuroendocrine changes (O'Higgins et al., 2018). It is a debilitating condition for patients. Patients say that because of CRF that they *'live [their] life at half energy and [are] very tired and depressed on a daily basis'* and that *'fatigue rules [their] life'* (n/a, 2018). CRF presents with symptoms such as weakness, difficulty concentrating, depression, a lack of energy and tiredness/sleepiness that is not relieved with rest (Ancoli-Israel et al., 2001; Jean-Pierre et al., 2007).

It is a misconception that fatigue and tiredness are the same. Tiredness is 'the state of wishing for sleep or rest', whereas fatigue is 'extreme tiredness resulting from mental or physical exertion, or illness' (Lexico, n.d.-a; n/a, n.d.-b). Tiredness can be alleviated by sleep, but to alleviate fatigue, the causes must be treated. Despite the difference, the two are closely linked. Poor sleep is positively correlated with fatigue. Patients who get less sleep report much higher on fatigue assessments; additionally, poor sleep is a predictor of CRF (Peoples et al., 2017; Roscoe et al., 2007). Fatigue and insomnia have been shown to be reciprocally related suggesting the possibility that treatment for one may impact the other (Roscoe et al., 2007). As well as poor sleep being a contributor to the symptoms of CRF, there is evidence showing that CRF can impact the quality of sleep via interaction with the hypothalamic–pituitary–adrenal (HPA) axis and disrupting circadian rhythms (Innominato et al., 2010; Wu et al., 2012). In this proposed mechanism, cancer acts as a stressor for the HPA axis, resulting in a constant amount of cortisol production instead of the peak and dip experienced at morning and night. Cortisol is needed to inform the body when to wake up; therefore, high levels at night prevent sleep (Bush, 2014). This interconnection between sleep and CRF creates an almost 'chicken or the egg' scenario; does the poor sleep cause the CRF or does the CRF result in poor sleep? If it is the case that poor sleep leads to CRF, then improving how cancer patients sleep may be a viable solution to address the symptom burden of CRF.

Current treatments for CRF include both pharmacological and nonpharmacological options (Mustian et al., 2017). Pharmacological treatments include the use of erythropoietin-stimulating agents (ESAs), psychostimulants, Modafinil, L-carnitine, dexamethasone and herbal remedies, whereas nonpharmacological treatments rely on exercise, nutrition, rest and sleep and the use of alternative and complementary medicine (Mohandas et al., 2017). Any pharmaceutical intervention has its downsides, such as any adverse events, other drug interactions and cost so the solution may lie in these nonpharmacological treatment options. However, exercise can be difficult in patients struggling with the lack of energy associated with CRF and the nausea that can result from the cancer itself or the cancer treatment can make the thought of eating daunting for cancer patients (n/a, n.d.-c; n/a, n.d.-d). Trying to improve sleep in cancer patients may therefore be the most accessible treatment options for patients. The aim of this systematic review is to investigate whether improving sleep is an effective treatment for improving the symptoms of CRF, with the secondary aim being to determine if this can be used to infer whether lack of sleep causes CRF. This will be achieved by reviewing studies that attempted to improve sleep in cancer patients and looking at what effect this had on their levels of fatigue. The information will then be used to assess whether fatigue improved with improved sleep and whether this means that CRF is caused by poor sleep.

2 | METHODS

2.1 | Literature search

Electronic databases search in May 2020 included PubMed, CENTRAL (Cochrane Central Register of Controlled Trials) and OVID databases. The search terms used for the databases are outlined in Table 1. This generated 259 papers, of which 31 duplicates were removed. The remaining papers were then read to exclude studies based upon the inclusion criteria. Literature search was performed by one, independent reviewer.

TABLE 1 Search terms used

Database	Search terms	Yield
PubMed	((Cancer OR neoplasm) AND fatigue AND (sleep* OR sleep quality OR sleep disturbance OR insomnia OR sleep deprivation OR sleep loss OR insufficient sleep OR inadequate sleep OR sleep duration) AND (randomised control trial OR RCT))	214
Cochrane	1. MeSH descriptor: [Sleep] explode all trees 2. MeSH descriptor: [Neoplasms] explode all trees 3. MeSH descriptor: [Fatigue] explode all trees 4. #1 AND #2 AND #3	38
OVID	1. MeSH descriptor: [Sleep] explode all trees 2. MeSH descriptor: [Neoplasms] explode all trees 3. MeSH descriptor: [Fatigue] explode all trees 4. #1 AND #2 AND #3 *filtered by publication type: randomised controlled trial	7

2.2 | Inclusion criteria

Papers were only considered for the systematic review if they met several criteria. The papers had to be written and published in English. The study participants had to be over 18 years old. The study participants had to be cancer patients or cancer survivors suffering from fatigue. The studies had to measure both sleep and fatigue as outcome measures and use a nonsurgical intervention to improve sleep quality. Randomised control trials (RCTs) were prioritised as they are considered to be reliable sources of data and rank highly on the hierarchy of evidence they will be focused on (Burns et al., 2011; n/a, 2009). The use of RCTs will also reduce sources of bias. Studies with any conflict of interest or no details of ethical approval were excluded. This excluded 98 papers leaving 130 remaining. Papers were further excluded based on whether improvement of sleep was the primary outcome of the intervention. Two further studies were excluded as they had used the same patient population from another study, and another two were excluded as the full paper could not be accessed. This excluded a further 110 papers leaving 20 papers. No additional papers were added from the references.

2.3 | Critical appraisal and risk of bias assessment

All papers were critically appraised using the 'critical appraisal skills programme (CASP) RCT checklist' (Critical appraisal skills programme, 2019). The papers were then assessed for the risk of bias using the 'Cochrane Collaboration's tool for assessing risk of bias in randomised trials' (Higgins et al., 2011). The result of this assessment is outlined in Figure 2 and Table 2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were also followed. Critical appraisal and risk of bias assessment was performed by one, independent reviewer.

3 | RESULTS

The search produced 259 papers and is outlined in Figure 1. After applying inclusion and exclusion criteria, a total of 20 papers were selected for this systematic review (Barsevick et al., 2010; Berger et al., 2009; Chaoul et al., 2018; Cohen et al., 2004; Dirksen & Epstein, 2008; Espie et al., 2008; Garland et al., 2019; Heckler

TABLE 2 Summary of risk of bias analysis using the Cochrane Collaboration's tool for the studies (total of 20) that met the inclusion and exclusion criteria

Author	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Barsevick et al. (2010)	+	+	?	?	+	+	+
Berger et al. (2009)	+	+	?	?	+	+	+
Chaoul et al. (2018)	+	?	-	-	+	+	?
Cohen et al. (2004)	+	+	?	?	+	+	+
Dirksen and Epstein (2008)	+	?	-	-	+	+	?
Espie et al. (2008)	+	?	-	-	+	+	+
Garland et al. (2010)	+	+	?	-	+	+	+
Heckler et al. (2016)	?	?	?	?	+	+	+
Irwin et al. (2017)	+	+	+	+	+	+	+
Kröz et al. (2017)	+	-	-	-	+	+	-
Lin et al. (2019)	+	+	?	?	+	+	?
McQuade et al. (2017)	+	?	?	?	+	+	+
Poier et al. (2018)	+	?	-	-	?	+	-
Ritterband et al. (2012)	+	+	?	?	+	+	?
Savard et al. (2005)	?	?	?	?	+	+	?
Savard et al. (2014)	+	+	?	?	+	+	+
Vargas et al. (2014)	?	+	?	?	+	+	?
Yeh and Chung (2016)	+	+	-	-	+	+	?
Zachariae et al. (2018)	?	+	?	?	+	+	+
Zengin and Aylaz (2019)	+	?	?	?	+	+	+

et al., 2016; Irwin et al., 2017; Kröz et al., 2017; Lin et al., 2019; McQuade et al., 2017; Poier et al., 2019; Ritterband et al., 2012; Savard et al., 2005; Savard et al., 2014; Vargas et al., 2014; Yeh & Chung, 2016; Zachariae et al., 2018; Zengin & Aylaz, 2019). Of these 20 papers, 15 were published between 2010 and 2020 (Barsevick et al., 2010; Chaoul et al., 2018; Garland et al., 2019; Savard et al., 2014; Vargas et al., 2014; Zengin & Aylaz, 2019) and the remaining five published between 2004 and 2009 (Berger et al., 2009; Cohen et al., 2004; Espie et al., 2008; Savard et al., 2005). The majority of the papers were RCTs (Berger et al., 2009; Cohen et al., 2004; Espie et al., 2008; Irwin et al., 2017; Lin et al., 2019; McQuade et al., 2017; Ritterband et al., 2012; Yeh & Chung, 2016) with the remaining papers being two randomised clinical intervention trials (Barsevick et al., 2010; Dirksen & Epstein, 2008), a three-armed pragmatic trial in a comprehensive cohort design (Kröz et al., 2017) and a pragmatic comprehensive cohort study (Poier et al., 2019).

3.1 | Quality assessment

Using the CASP tool, all papers included addressed a clearly focused issue, all of the patients who entered the trial were correctly accounted for at its conclusion, the groups were treated equally, the results could be applied to cancer patients, all clinically important outcomes were considered and the benefits were worth the harms and costs. All but one paper had similar groups at the start of the trial with the paper from Poier et al. showing an unequal distribution of patients to each intervention group (Poier et al., 2019). Due to the nature of the interventions, blinding of patients was not possible; however, some studies did blind the research personnel (Garland et al., 2019; Lin et al., 2019; Savard et al., 2014; Vargas et al., 2014; Zachariae et al., 2018). Blinding was not discussed in six of the papers (Barsevick et al., 2010; Berger et al., 2009; Cohen et al., 2004; McQuade et al., 2017; Ritterband et al., 2012; Zengin & Aylaz, 2019).

The results of the Cochrane Collaboration's tool for assessing risk of bias in randomised trials are outlined in Figure 2 and Table 2. In total, 16 of the papers discussed their methods of randomisation with all of them using an acceptable method (minimisation, stratified sampling and permuted-block procedure). Papers from Heckler et al., Savard et al. (2005), Vargas et al. and Zachariae et al. did not discuss their method of randomisation and therefore risk of bias cannot be assessed (Heckler et al., 2016; Savard et al., 2005; Vargas et al., 2014; Zachariae et al., 2018). Concealment of allocation was discussed in 12 of the papers. Eleven of these papers used acceptable methods of concealment; however, Kröz et al. used no form of concealment (Kröz et al., 2017). Allocation was not discussed in the remaining eight papers (Chaoul et al., 2018; Dirksen & Epstein, 2008; Espie et al., 2008; Heckler et al., 2016; McQuade et al., 2017; Poier et al., 2019; Savard et al., 2005; Zengin & Aylaz, 2019), and therefore, risk of bias could not be assessed. Two of the papers allowed participants to select the intervention group they wished to be a part of introducing a high risk of bias (Kröz et al., 2017; Poier et al., 2019). Other papers featured participant groups with limited ethnic diversity (Chaoul et al., 2018; Dirksen & Epstein, 2008; Ritterband et al., 2012;

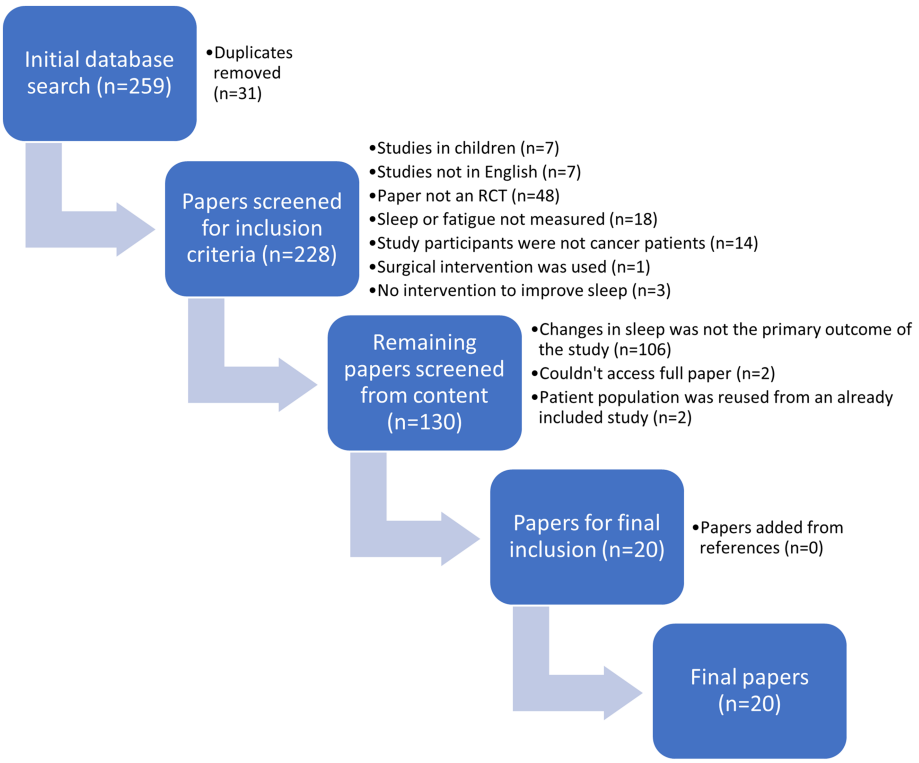

FIGURE 1 Flow diagram outlining the exclusion and inclusion criteria as well as the number of papers identified after each step

Savard et al., 2005; Vargas et al., 2014) or lacked a placebo control (Lin et al., 2019; Yeh & Chung, 2016).

3.2 | Study population

A total of 2981 patients were recruited across the 20 studies. Seven papers used cancer survivors (Garland et al., 2019; Irwin et al., 2017; Lin et al., 2019; Poier et al., 2019; Ritterband et al., 2012; Zachariae et al., 2018), with the remaining 13 using patients with active cancer treatment. Of the 13 papers using cancer patients, seven focused on breast cancer patients (Berger et al., 2009; Chaoul et al., 2018; Dirksen & Epstein, 2008; Kröz et al., 2017; Savard et al., 2014; Vargas et al., 2014), two focused on lymphoma patients (Cohen et al., 2004; Yeh & Chung, 2016), one focused on prostate cancer (McQuade et al., 2017) and three used multiple different cancer diagnoses (Barsevick et al., 2010; Espie et al., 2008; Zengin & Aylaz, 2019).

3.3 | Measures

Sleep can be measured both objectively and subjectively. Subjective methods use questionnaires or diaries that are short, can be done by the trial participants themselves and are inexpensive. Questionnaires feature a series of questions that ask patients to quantitatively rate their sleep. Sleep diaries are also done by the patient themselves and ask questions on how the patient slept over a couple of weeks. Objective methods require the participant to wear or be connected to a measuring device. The device measures changes that occur overnight to determine the quality, duration and so forth of sleep. Devices can be small so patients can take them home or advanced pieces of technology requiring trained personnel to operate (such as polysomnography [PSG]). This equipment is extremely precise, but it is also more expensive to run and requires specially trained staff. Smaller devices can be worn by the participant and commonly feature an actigraph that measures movement. These are cheaper than more advanced methods and can be operated by the participants; however, they still require trained staff and equipment to interpret the data (Ibáñez et al., 2018).

There were seven different methods used to measure sleep in the papers included. The subjective measures were the Pittsburgh Sleep Quality Index (PSQI), sleep diaries, Verran and Snyder-Halpern Sleep Scale (VSHSS), Insomnia Sleep Inventory (ISI) and Insomnia Sleep Scale (ISS) questionnaires. Actigraphy and PSG were the objective measures used to measure sleep. PSQI was the most common method used with 13 of the papers using it (Barsevick et al., 2010; Cohen et al., 2004; Garland et al., 2019; Irwin et al., 2017; Poier et al., 2019; Vargas et al., 2014; Zachariae et al., 2018; Zengin & Aylaz, 2019), followed by sleep diaries (Barsevick et al., 2010; Berger et al., 2009; Espie et al., 2008; Garland et al., 2019; Ritterband et al., 2012; Savard et al., 2005; Zachariae et al., 2018) and ISI (Dirksen & Epstein, 2008; Garland et al., 2019; Irwin et al., 2017; Ritterband et al., 2012; Savard et al., 2005; Zachariae et al., 2018) (eight papers), actigraphy (four papers) (Barsevick et al., 2010; Chaoul et al., 2018; Garland et al., 2019), IIS (Savard et al., 2005; Savard et al., 2014) and PSG (Irwin et al., 2017; Savard et al., 2005) (two papers) and VSHSS (one paper) (Yeh & Chung, 2016).

Fatigue can also be measured both objectively and subjectively. Subjective methods are more commonly used and rely on the use of questionnaires (Neuberger, 2003; Vries et al., 2003). Fatigue questionnaires ask patients to rate their fatigue based on different criteria.

In the papers featured in this review, fatigue was measured using 12 different questionnaires. Fatigue Inventory (FI), Multidimensional Fatigue symptom Index (MFSI), Piper Fatigue Scale (PFS), Brief Fatigue Inventory (BFI), Functional Assessment of Chronic Illness Therapy for Fatigue (FACIT-F), Profile of Mood States Fatigue/Inertia Subscale (POMSF/I), General Fatigue Scale (GFS), Profile Of Mood States - Fatigue symptom subscale (POMS-F), Cancer Fatigue Scale (CFS-D), Fatigue Symptom Inventory (FSI), Functional Assessment of Cancer Therapy (FACT-G) and Fatigue Severity Scale (FSS) were the

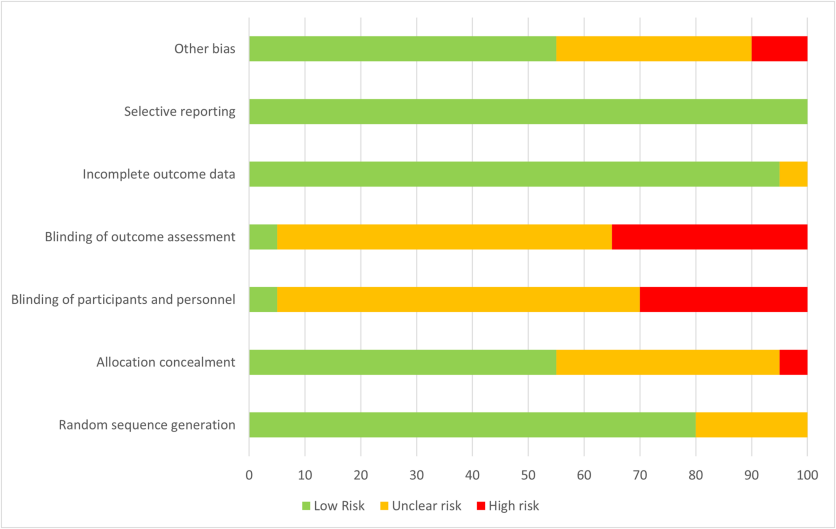

FIGURE 2 This graph demonstrates risk of bias for different studies investigated. Item presented as percentages across all included studies

12 questionnaires used. MFSI was the most commonly used with six papers using it (Garland et al., 2019; Irwin et al., 2017; Lin et al., 2019; Ritterband et al., 2012; Savard et al., 2005) followed by BFI (four papers) (Chaoul et al., 2018; Cohen et al., 2004; Heckler et al., 2016; McQuade et al., 2017), FACIT-F (Heckler et al., 2016; Zachariae et al., 2018), CFS-D (Kröz et al., 2017; Poier et al., 2019) and FSI (Espie et al., 2008; Vargas et al., 2014) (two papers) and FI (Yeh & Chung, 2016), PFS (Berger et al., 2009), POMSF/I (Dirksen & Epstein, 2008), GFS (Barsevick et al., 2010), POMS-F (Barsevick et al., 2010), FACT-G (Espie et al., 2008) and FSS (Espie et al., 2008) (one paper).

3.4 | Interventions

Nine of the papers included used a form of cognitive behavioural therapy (CBT) to improve sleep (Dirksen & Epstein, 2008; Irwin et al., 2017; Ritterband et al., 2012; Savard et al., 2005; Zachariae et al., 2018). Three papers used a sleep education programme (Kröz et al., 2017; Poier et al., 2019; Zengin & Aylaz, 2019). Eight papers used an exercise programme. Of these, three used a form of yoga (Chaoul et al., 2018; Cohen et al., 2004; Lin et al., 2019), two used aerobic training (Kröz et al., 2017; Poier et al., 2019) and three used Tai Chi or Qigong (Irwin et al., 2017; McQuade et al., 2017; Yeh & Chung, 2016). The remaining interventions used were 'energy and sleep enhancement' (EASE) intervention (Barsevick et al., 2010), Individualised Sleep Promotion Plan (ISPP) (Berger et al., 2009), acupuncture (Garland et al., 2019), armodafinil (Heckler et al., 2016), cognitive behavioural stress management (CBSM) intervention (Vargas et al., 2014) and reflexology (Zengin & Aylaz, 2019).

The EASE intervention used a research nurse to provide information to each participant as well as teach behavioural skills taught in three telephone sessions. The nurse engaged the participant in a discussion of his/her experience of fatigue and sleep disturbance. EASE group participants also received a handbook that included the information about symptoms and examples of energy conservation and sleep management strategies (Barsevick et al., 2010). The ISPP was a behavioural control method that included modified stimulus control, modified sleep restriction, relaxation therapy and sleep hygiene. The plan was developed with participants and a research nurse (Berger et al., 2009). Armodafinil is a drug used to promote wakefulness and is used to treat patients suffering from excessive sleepiness such as those with narcolepsy, sleep apnoea or shift work sleep disorder (n/a, n.d.).

3.5 | Findings

The general trend among the studies was that better sleep quality resulted in less fatigue, and no changes in sleep resulted in no changes in fatigue. Of the nine papers that used CBT, eight showed a statistically significant improvement in sleep quality or a reduction in insomnia scores ($p = <0.05$) (Espie et al., 2008; Heckler et al., 2016; Ritterband et al., 2012; Savard et al., 2005; Zachariae et al., 2018). Statistically significant decrease in fatigue was shown in six of these papers ($p = <0.05$). (Espie et al., 2008; Heckler et al., 2016; Ritterband et al., 2012; Savard et al., 2005; Zachariae et al., 2018). The study from Irwin et al. did also show a decrease in fatigue with the improvement in sleep quality; however, this change was not statistically significant ($p = > 0.5$) (Irwin et al., 2017). Dirksen and Epstein showed a decrease in ISI scores as a result of CBT treatment (23.91 to 14.38) which lead to a statistically significant decrease in fatigue ($p = <0.05$); however, no p-value was included for the change in ISI score so it cannot be determined whether this change is statistically significant. Of the studies using an exercise intervention, six of eight studies showed a significant increase in sleep quality or reduction in insomnia (Cohen et al., 2004; Irwin et al., 2017;Lin et al., 2019; Poier et al., 2019; Yeh & Chung, 2016); however, only three of those six showed significant reduction in fatigue (Lin et al., 2019; Poier et al., 2019; Yeh & Chung, 2016). The two papers that showed a lack of improvement in sleep quality, Chaoul et al. and McQuade et al., showed a lack of improvement in fatigue (Chaoul et al., 2018; McQuade et al., 2017). McQuade et al. did show an improvement in sleep duration but this had no impact on fatigue. Three of the studies showed an improvement in sleep quality, but this did not lead to a significant improvement in fatigue (Cohen et al., 2004; Irwin et al., 2017; Kröz et al., 2017). Irwin et al. showed an improvement with fatigue alongside sleep quality, but this improvement was not significant (Irwin et al., 2017). Similarly, when using aerobic therapy alone, Kröz et al. had patients that improved in both sleep quality and fatigue, but the improvement was not significant (Kröz et al., 2017). Cohen et al. had patients who, although sleeping better, showed no difference in fatigue (Cohen et al., 2004). Sleep education had a positive impact on both sleep and fatigue scores with all three papers showing significant improvements (Kröz et al., 2017; Poier et al., 2019; Zengin & Aylaz, 2019). The EASE intervention used by Barsevick et al. had no effect on sleep or fatigue (Barsevick et al., 2010). The ISPP used by Berger et al. improved sleep quality significantly but had no effect on fatigue (Berger et al., 2009).

To assess the treatment effect of the papers showing significant changes in both sleep quality and fatigue, Cohen's d values (d) were analysed. d values allow us to look at treatment effect sizes of the mean of the treatment group compared with the mean of the control group. d of 1 indicates that the groups differ by 1 standard deviation. A general rule is that a d of 0.2 is small, 0.5 is medium and 0.8 is large.

d values were provided by six papers (Dirksen & Epstein, 2008; Espie et al., 2008; Lin et al., 2019; Ritterband et al., 2012; Savard et al., 2014; Zachariae et al., 2018), and for one paper, a value can be calculated using other data provided in the paper (Zengin & Aylaz, 2019). Dirksen and Epstein showed medium treatment effects with their CBT for insomnia (ISI $d = 0.37$, fatigue scores $d = 0.43$) (Dirksen & Epstein, 2008). Espie et al. showed big treatment effects as a result of CBT therapy with a d of 1.09 for sleep efficiency and 0.81 on FSI scores (Espie et al., 2008). Ritterband et al. showed medium and large treatment effects with CBT treatment. d for sleep efficiency was 0.72, whereas fatigue scores had a d of 1.16

(Ritterband et al., 2012). Both methods of CBT (professionally delivered [PCBT] and video delivered [VCBT]) tested by Savard et al. (2014) showed large improvement in both ISI scores and sleep efficiency (ISI $d = 1.84$ [PCBT], 1.40 [VCBT]; SE $d = 1.03$ [PCBT], 0.83 [VCBT]); however, the PCBT intervention showed greater improvements in fatigue scores (PCBT $d = 0.80$, VCBT $d = 0.34$) (Savard et al., 2014). Zachariae et al. showed large improvements in PSQI sleep quality ($d = 0.90$) and medium improvements in fatigue scores ($d = 0.42$) by using CBT (Zachariae et al., 2018). Lin et al. showed medium improvements in both sleep quality and fatigue following their YOCAS intervention ($d = 0.24$ and 0.31, respectively) (Lin et al., 2019). Zengin and Aylaz did not include Cohen's *d* figures in their analysis; however, from the data provided, *d* was calculated as 3.30 for PSQI scores and 5.64 for the FSS scores (Zengin & Aylaz, 2019).

The remaining four papers did not provide *d* values or the data to calculate them, so other methods have been used to analyse treatment effects. Garland et al. did provide a *d* for ISI scores showing a medium treatment effect ($d = 0.31$). For PSQI scores, the between group difference was 1.51 points showing that, on average, patients who completed CBT-I scored higher on PSQI scores than those who completed 8 weeks of acupuncture. These patients also scored higher on MFSI scores (between group difference = 1.65) (Garland et al., 2019). Savard et al. (2005) showed that those who received CBT slept 14.93% more efficiently compared with 3.4% in the control group (between group difference = 11.59%). Patients who got more efficient sleep also had better fatigue scores (MFSI between group difference = 0.43). Yeh and Chung showed a difference in sleep efficiency of 7.07 on VSHSS, with those who did qigong scoring higher. This was reflected in fatigue scores with the qigong group scoring 2.25 points less (Yeh & Chung, 2016). Heckler et al. did not provide between group differences for ISI scores or the data to calculate this, but they did provide between group differences for BFI scores and FACIT-F scores. Patients who received CBT without armodafinil scored higher on both fatigue measures (1.09 [BFI], 5.84 [FACIT-F]) compared with patients who received no CBT or armodafinil. A pretreatment and posttreatment difference is given for ISI scores for the CBT group without armodafinil (difference = −5.13); however, this is not given for the control group, so it cannot be said how effective CBT was in reducing insomnia (Heckler et al., 2016). Studies have been summarised in Tables 3–5.

4 | DISCUSSION

This review set out to answer the questions: 'Is there enough literature evidence to support the hypothesis that improving sleep alleviates the symptoms of CRF?' and 'can this be used to infer whether lack of sleep causes CRF?'. The evidence shows that patients that report improvement in their sleep quality are less fatigued. This was the case in 14 of the papers (Dirksen & Epstein, 2008; Lin et al., 2019; Poier et al., 2019; Savard et al., 2005; Yeh & Chung, 2016; Zengin & Aylaz, 2019) of which the improvements in fatigue were shown to be significant in 12 of them (Dirksen & Epstein, 2008; Heckler et al., 2016; Lin et al., 2019; Poier et al., 2019; Savard et al., 2005; Yeh & Chung, 2016; Zengin & Aylaz, 2019). If sleep quality was not improved, then neither was fatigue as shown in two papers (Barsevick et al., 2010; Chaoul et al., 2018). The lack of improvement in the Barsevick et al. study may be due to the intervention used. The EASE intervention is a novel intervention and may be ineffective at improving sleep quality in cancer patients. The infrequency of the Tibetan yoga intervention by Chaoul et al. may have limited its effectiveness in improving sleep. There were four yoga sessions during the chemotherapy and a further three over 6 months. In comparison, other studies that used yoga, Cohen et al. and Lin et al., had weekly sessions for 7 weeks and two sessions per week for 4 weeks, respectively. In three papers, fatigue remained the same despite improvements in sleep quality (Berger et al., 2009; Cohen et al., 2004; Vargas et al., 2014). All these studies used cancer patients currently receiving treatment. Any improvements to fatigue from the interventions may have been cancelled out by fatigue caused by cancer treatments they were undertaking (Iop et al., 2004). In the study from McQuade et al., cancer patients in the qigong/tai chi group slept longer when compared with those in the light exercise and control groups; however, there was no change in fatigue or sleep quality. This suggests that the quality of sleep is more important when trying to treat fatigue. The association between sleep quality and fatigue in cancer survivors has been recently confirmed using actigraphy-derived sleep quality parameters (Martin et al., 2021). This makes sense when considering that CRF can affect the HPA axis. Interrupting the HPA axis prevents those suffering from CRF from falling into the third stage of the sleep cycle (delta sleep) resulting in fatigue, a greater need to sleep and a reduction in growth hormones that aid recovery (Wu et al., 2012). Without delta sleep, the amount of time spent sleeping would make little difference. This lends evidence to the theory that fatigue can cause poor sleep.

CBT was shown to be the most successful intervention. The benefits of CBT are that it requires no additional equipment or effort from the patient (Hofmann et al., 2012). Cancer patients may be too tired to perform exercise interventions limiting their widespread use. CBT avoids this problem by only requiring the use of a therapist as opposed to the patient's physical ability. Therapists and CBT sessions can be mobile allowing it to be used in both community and hospital settings in addition to psychiatric practices. This gives it the added benefit of being a service to those who may be bed bound or who lack the mobility to perform the exercise interventions. Additionally, CBT can be delivered digitally allowing CBT to be delivered when the patient cannot be accessed and has been shown to be at least as effective as face-to-face CBT (Luik et al., 2019; Luo et al., 2020). CBT can also be used in group settings which would allow cancer patients to interact with each other and form support networks (Daniels, 2015; n/a, 2017).

The main limitation of this review is the lack of consistency between papers. Many different ways of assessing sleep and fatigue are used which limits the number of direct comparisons that can be made. In addition, the papers use a mixture of cancer patients at various stages, including cancer survivors and those currently undergoing

TABLE 3 Summary table of the studies included (Barsevick et al., 2010; Zengin & Aylaz, 2019)

Author	Year	Type of study	Participants	Intervention	Data collection
Barsevick et al.	2010	Randomised clinical intervention trial	Breast, lung, colorectal, prostate, gynaecologic, bladder, or testicular cancer or lymphoma	'Energy and sleep enhancement' (EASE) intervention	GFS, POMS-F, PSQI, actigraphy, sleep diary
Berger et al.	2009	RCT	Stages I–IIIA breast cancer patients	Individualized sleep promotion plan (ISPP)	PSQI, daily diary, actigraphy, and PFS
Chaoul et al.	2018	RCT	Breast cancer patients undergoing chemotherapy	Tibetan yoga	PSQI, BFI, actigraphy
Cohen et al.	2004	RCT	Lymphoma patients	Tibetan yoga	PSQI, BFI
Dirksen and Epstein	2008	Randomised experimental design	Stages I, II or III breast cancer patients	CBT	ISI, POMSF/I
Espie et al.	2008	RCT	Breast, prostate, colorectal, or gynaecological cancer patients	CBT	Actigraphy, sleep diary, FSI, FACT-G
Garland et al.	2010	RCT	Cancer survivors	8 weeks of acupuncture, CBT-I	PSQI, sleep diary, ISI, MFSI
Heckler et al.	2016	RCT	Cancer survivors	CBT-I, armodafinil	BFI, FACIT-fatigue scale, ISI
Irwin et al.	2017	RCT	Breast cancer survivors w/insomnia	CBT, Tai Chi Chih	PSQI, ISI, PSG, MFSI
Kröz et al.	2017	Three-armed pragmatic trial in a comprehensive cohort design	Breast cancer patients w/CRF for more than 6 months	Multimodal therapy (sleep education, psychoeducation, eurythmy- and painting therapy), aerobic therapy, MT + AT	PSQI, CFS-D
Lin et al.	2019	RCT	Cancer survivors	Yoga therapy programme (yoga for cancer survivors [YOCAS])	MFS, PSQI
McQuade et al.	2017	RCT	Prostate cancer patients undergoing radiotherapy	Qigong/tai chi (QGTC)	PSQI, BFI
Poier et al.	2018	Pragmatic comprehensive cohort study	Breast cancer survivors	Multimodal therapy (MT; psychoeducation, eurythmy therapy, painting therapy, and sleep education/ restriction), or a combination therapy (CT; MT plus aerobic training [AT]), AT alone	PSQI, CFS-D
Ritterband et al.	2012	RCT	Cancer survivors with insomnia	Online CBT-I programme (SHUTi)	Sleep diary, ISI, MFSI
Savard et al.	2014	RCT	Breast cancer patients	PCBT-I (pro admin) composed of six weekly, individual sessions of approximately 50 min; VCBT-I (video) composed of 60-min animated video + six booklets	ISI, daily sleep diary, actigraphy, MFSI
Savard et al.	2005	RCT	Breast cancer patients	CBT	Sleep diary, ISI, IIS, PSG, MFSI
Vargas et al.	2014	RCT	Early-stage breast cancer patients	Cognitive behavioural stress management (CBSM) intervention	PSQI, FSI

TABLE 3 (Continued)

Author	Year	Type of study	Participants	Intervention	Data collection
Yeh and Chung	2016	RCT	Non-Hodgkin's lymphoma patients	Chan-Chuang qigong exercise 20-min twice daily for 21 days	Verran and Snyder-Halpern sleep scale, FI
Zachariae et al.	2018	RCT	Breast cancer survivors	iCBT-I (internet delivered CBT)	PSQI, sleep diary, ISI, FACIT-F
Zengin and Aylaz	2019	RCT	Phase II - IV lung and laryngeal, gynaecological, colorectal, Hodgkin's disease, breast, bladder and prostrate, gastric and oesophageal and pancreatic cancer patients	Sleep hygiene education and reflexology	PSQI, FSS

Abbreviations: CBT, cognitive behavioural therapy; CRF, cancer-related fatigue; FACT-G, functional assessment of cancer therapy; FSI, fatigue symptom inventory; FSS, fatigue severity scale; GFS, general fatigue scale; ISI, insomnia sleep inventory; MFSI, multidimensional fatigue symptom index; PCBT, professionally delivered CBT; POMS-F, profile of mood states fatigue/inertia subscale; PSG, polysomnography; PSQI, Pittsburgh sleep quality index; RCT, randomised control trial; VCBT, video delivered CBT.

TABLE 4 A table to summarise the results of the studies and display the *p*-values of the treatment effects (Barsevick et al., 2010; Zengin & Aylaz, 2019)

Author	Year	Summary of results	*P*-value (sleep scores)	*P*-value (fatigue scores)	Number of participants
Barsevick et al.	2010	EASE intervention did not improve fatigue or reduce sleep disturbance	Not given	Not given	292
Berger et al.	2009	Sleep quality improved in BT group but there was no difference in fatigue between groups	$p = <0.003$	$p = 0.253$	219
Chaoul et al.	2018	There were no group differences in total sleep disturbances or fatigue levels over time	$p = 0.16$	$p = 0.89$	227
Cohen et al.	2004	Better sleep quality, duration and less disturbances; however, there were no significant differences in fatigue	$p = <0.004$	$p = 0.93$	39
Dirksen and Epstein	2008	Patients scored lower on ISI and had significantly lower fatigue	Not given	$p = <0.05$	72
Espie et al.	2008	Standardised relative effect sizes were large for complaints of difficulty initiating sleep, waking from sleep during the night and for sleep efficiency (percentage of time in bed spent asleep). Significant reduction in daytime fatigue	$p = <0.001$	$p = <0.001$	150
Garland et al.	2010	Improvement in sleep scores and reduction in fatigue scores with both CBT-I and acupuncture. CBT-I showed better improvement than acupuncture	$p = <0.001$	$p = 0.53$	160
Heckler et al.	2016	CBT-I improved fatigue as measured by two separate scales. Positive effect on ISI. Armodafinil had no effect	$p = 0.002$	$p = 0.002$	96
Irwin et al.	2017	CBT-I and TCC groups showed improvements in sleep quality, sleep diary measures and related symptoms ($P < 0.01$). Improvement shown to fatigue scores; however, this was not significant ($P > 0.5$)	$p = 0.001$	$p = > 0.5$	90
Kröz et al.	2017	Sleep quality and fatigue significantly improved with MT. Changes in fatigue and sleep quality were not significant in the AT group. CT group showed significant improvement in sleep, but changes in fatigue were not significant	$p = <0.05$	$p = > 0.05$	126

(Continues)

TABLE 4 (Continued)

Author	Year	Summary of results	*P*-value (sleep scores)	*P*-value (fatigue scores)	Number of participants
Lin et al.	2019	YOCAS participants demonstrated significantly greater improvements in CRF compared with participants in standard survivorship care at postintervention ($P < 0.01$). YOCAS participants reported significantly better sleep quality and improvements in CRF	$p = <0.01$	$p = <0.01$	410
McQuade et al.	2017	QGTC group reported longer sleep duration but this difference did not persist over time. There were no group differences in other domains of sleep or fatigue	$p = <0.05$	$p = > 0.05$	90
Poier et al.	2018	Improvements shown for fatigue and insomnia at T1 and T2 in MT, CT and AT. Difference between AT and MT shown to be significant. Data use EORTC scores but do not include PSQI or CFS-D scores	$p = 0.019$	$p = 0.012$	126
Ritterband et al.	2012	CBT group showed improvements in overall insomnia severity, sleep efficiency, sleep onset latency, soundness of sleep, restored feeling upon awakening and general fatigue	$p = <0.01$	$p = <0.01$	28
Savard et al.	2014	Sleep improved more with CBT than the control. PCBT showed decreased fatigue compared with VCBT and control	$p = <0.001$	$p = <0.001$	242
Savard et al.	2005	Significant differences from pretreatment to posttreatment were observed for all sleep measures, except total sleep time. MFI scores decrease over time	$p = <0.05$	$p = <0.001$	57
Vargas et al.	2014	Women in CBSM reported greater improvements in PSQI sleep quality scores than controls. Women in CBSM also reported greater reductions in fatigue-related daytime interference than controls, though there were no significant differences in changes in fatigue intensity	$p = <0.03$	$p = > 0.3$	240
Yeh and Chung	2016	After intervention, the average fatigue, worst fatigue and overall sleep quality scores all improved in the Qigong group. This change compared with the control group was significant	$p = <0.001$	$p = <0.001$	108
Zachariae et al.	2018	Large effect sizes were found for improvements in insomnia severity (ISI), sleep quality (PSQI) and sleep efficiency; medium effect sizes for increased total sleep time, less time in bed and fewer EMAs; and small effect sizes for shorter SOL, fewer NAs, reductions in fatigue (FACIT-F) and less time spent awake after sleep onset (WASO)	$p = <0.001$	$p = <0.001$	255
Zengin and Aylaz	2019	Experimental group showed improvement in both PSQI scores and FSS scores. The difference between the mean scores of the groups was statistically significant ($p = 0.000$).	$p = 0.000$	$p = 0.000$	167

Abbreviations: AT, aerobic training; BT, behavioural therapy; CBT-I, cognitive behavioural therapy-I; CBSM, cognitive behavioural stress management; CRF, cancer-related fatigue; CT, combination therapy; EASE, energy and sleep enhancement; EORTC, European organisation for research and treatment of cancer; FACIT-F, functional assessment of chronic illness therapy for fatigue; FSS, fatigue severity scale; ISI, insomnia sleep inventory; MT, multimodal therapy; NA, nocturnal awakening; PSQI, Pittsburgh Sleep Quality Index; QGTC, Qigong/tai chi; SOL, Sleep Onset Latency; TCC, Tai Chi Chih; YOCAS, yoga for cancer survivors.

therapy. It is therefore hard to conclude whether the changes in fatigue are due to sleep or due to the individual circumstances of these cancer patient populations. It is also difficult to determine which cancer patient population should be targeted to get the most benefits from sleep improvement interventions. The studies included also have a limited scope. The patient populations lack diversity and have

TABLE 5 Summary of the data from the papers included (Barsevick et al., 2010; Zengin & Aylaz, 2019)

Author	Year	Summary of results	Effect on sleep	Effect on fatigue
Barsevick et al.	2010	EASE intervention did not improve fatigue or reduce sleep disturbance	PSQI results - EASE group before intervention: 8.01 (3.96), after intervention: 7.96 (3.59). Control group before intervention: 7.83 (4.37), after intervention: 8.24 (3.83)	POMS-F results - EASE group before intervention: 3.01 (1.13), after intervention: 2.85 (1.01). Control group before intervention: 3.00 (1.03), after intervention: 2.96 (1.12)
Berger et al.	2009	Sleep quality improved in BT group but there was no difference in fatigue between groups	Sleep quality improved significantly in the behavioural therapy group ([$F(2, 174) = 55.93$, $p < 0.003$]). Statistically significant differences over time on all sleep variables obtained by diary and actigraphy (all $p < 0.01$). Significantly lower number of awakenings [$F(1, 196)$ 54.66, p50.032], fewer WASO-M [$F(1,186)$54.95, p50.027] and higher sleep efficiency [$F(1, 156)$510.56, p50.001].	Little effect on fatigue - fatigue in both groups changed over time, with increases during the treatments and decreases after treatments ended [F(5, 192)562.46, $p < 0.001$]. The fatigue pattern was similar between the BT and HEC groups [$F(5, 192)$51.33, p50.253]
Chaoul et al.	2018	There were no group differences in total sleep disturbances or fatigue levels over time	Group main effect ($F = 1.86$, $P = 0.16$) and the group × time interaction ($F = 0.25$, $P = 0.96$) for the PSQI total score were not significant	Group main effect ($F = 0.12$, $p = 0.89$), contrast comparisons and the group × time interaction ($F = 0.49$, $p = 0.82$), were not significant
Cohen et al.	2004	Better sleep quality, duration and less disturbances; however, there were no significant differences in fatigue	Significantly lower sleep disturbance scores during follow-up compared with patients in the waitlist control group (5.8 vs. 8.1; $P < 0.004$). This included better subjective sleep quality ($P < 0.02$), faster sleep latency ($P < 0.01$), longer sleep duration ($P < 0.03$), and less use of sleep medications ($P < 0.02$).	BFI - TY group: Before 3.1 (2.4), follow up 3.1 (1.5). Control group: Before 2.8 (2.2), follow up 3.1 (1.5)
Dirksen and Epstein	2008	Patients scored lower on ISI and had significantly lower fatigue	ISI scores lower 23.91 (SD 4.27) to 14.38 (SD 5.31)	CBT-I group improved on fatigue (11.1 SD 6.7 to 5.7 SD 5.3). Statistically significant interaction effects were found for fatigue [$t(70) = 1.87$, $P = 0.07$]
Espie et al.	2008	Standardised relative effect sizes were large for complaints of difficulty initiating sleep, waking from sleep during the night and for sleep efficiency (percentage of time in bed spent asleep). Significant reduction in daytime fatigue	CBT was associated with median reduction in SOL of 16 min (95% CI, 10 to 22 min) and in WASO of 38 min (95% CI, 28 to 59 min). Effect sizes were moderate to large and were both statistically significant ($P < 0.001$). SE increased by 10% (95% CI, 9% to 12%), $p = <0.001$	FSI data: −1.20 to −0.42 $p = <0.001$
Garland et al.	2010	Improvement in sleep scores and reduction in fatigue scores with both CBT-I and acupuncture. CBT-I showed better improvement than acupuncture	CBT-I was more effective than acupuncture posttreatment ($P < 0.001$); however, both acupuncture and CBT-I produced reductions in insomnia severity. Acupuncture group reported an ISI score reduction of −8.31 (95% CI: −9.36 to −7.26) points compared with −10.91 (95% CI: −11.97 to −9.85) points in the CBT-I group. PSQI - acupucture: −4.39 (−5.10 to −3.67) CBT-I: −5.90 (−6.61 to −5.18)	MFSI - acupuncture: −10.82 (−13.94 to −7.70), CBT-I: −12.48 (−15.69 to −9.27)

(Continues)

TABLE 5 (Continued)

Author	Year	Summary of results	Effect on sleep	Effect on fatigue
Heckler et al.	2016	CBT-I improved fatigue as measured by two separate scales. Positive effect on ISI. Armodafinil had no effect	ISI score difference between pre and post CBT: −5.31 ($p = 0.002$)	BFI: $P = 0.002$, std. error = 0.32, effect size (ES) = 0.46; FACIT-fatigue: $P < 0.001$, std. error = 1.74, ES = 0.64
Irwin et al.	2017	CBT-I and TCC groups showed improvements in sleep quality, sleep diary measures, and related symptoms ($P < 0.01$). Improvement shown to fatigue scores however, this was not significant ($P > 0.5$)	PSQI - 11.2 (0.5) to 6.8 (0.4), $F = 1.21$, $p = 0.001$	MFSI - 17.6 (1.5) to 6.4 (1.6), $F = 0.55$, $p = >0.5$
Kröz et al.	2017	Sleep quality and fatigue significantly improved with MT. Changes in fatigue and sleep quality were not significant in the AT group. CT group showed significant improvement in sleep, but changes in fatigue were not significant	Difference in PSQI pre and post intervention at T2 - AT: −0.3 (2.8) $p = >0.05$ MT: −2.4 (4.0) $p < 0.05$ CT: 3.1 (3.2) $p = <0.05$	Difference in CFS-D pre-intervention and postintervention at T2 - AT: −3.4 (9.1) $p = >0.05$ MT: −9.1 (7.9) $p = < 0.01$ CT: −7.3 (10.2) p= > 0.05
Lin et al.	2019	YOCAS participants demonstrated significantly greater improvements in CRF compared with participants in standard survivorship care at postintervention ($P < 0.01$). YOCAS participants reported significantly better sleep quality and improvements in CRF	Improvements in overall sleep quality and reductions in daytime dysfunction (eg, excessive napping) resulting from yoga significantly mediated the effect of yoga on CRF (22% and 37%, respectively, both $P < 0.01$). PSQI = significantly greater improvements in overall sleep quality (−0.8 ± 0.3, $P < 0.01$), subjective sleep quality (−0.1 ± 0.1, $P = 0.05$) and daytime dysfunction (−0.2 ± 0.1, $P < 0.01$) at postintervention	MFS = significantly greater improvements in CRF (−6.8 ± 1.4, $P < 0.01$) at postintervention
McQuade et al.	2017	QGTC group reported longer sleep duration but this difference did not persist over time. There were no group differences in other domains of sleep or fatigue	Differences in sleep duration between treatment groups: (QGTC = 7.01 hours; LE = 6.42; WL = 6.50; $p = 0.05$). PSQI scores - QGTC pre:6.85 (0.76), mid: 5.63 (0.54), post: 5.16 (0.52). LE pre: 5.58 (0.78), mid: 5.74 (0.55), post: 5.33 (0.63). WLC pre: 6.58 (0.69), mid: 6.41 (0.48), post: 5.77 (0.50)	No differences in fatigue
Poier et al.	2018	Improvements shown for fatigue and insomnia at T1 and T2 in MT, CT and AT. Difference between AT and MT shown to be significant. Data uses EORTC scores but does not include PSQI or CFS-D scores	EORTC difference in insomnia at T2 - AT: −10.3 (21.1) MT:−33.3 (32.0) $p = 0.019$	EORTC difference in fatigue at T2 - AT: −0.9 (23.8) MT:−20.6 (22.1) $p = 0.012$
Ritterband et al.	2012	CBT group showed improvements in overall insomnia severity, sleep efficiency, sleep onset latency, soundness of sleep, restored feeling upon awakening, and general fatigue	Improvement in insomnia severity ($F1,26 = 22.8$; $P < 0.001$), sleep efficiency ($F1,24 = 11.45$; $P = 0.002$), sleep onset latency ($F1,24 = 5.18$; $P = 0.03$), soundness of sleep ($F1,24 = 9.34$; $P = 0.005$), restored feeling upon awakening ($F1,24 = 11.95$; $P = 0.002$). ISI score of 17.1 at pre-assessment to 8.2 at postassessment, ($t[13] = 10.15$, $p < 0.01$)	Improvement in general fatigue ($F1,26 = 13.88$; $P = 0.001$). Significantly improved fatigue scores from 22.86 to 9.50 ($t[13] = 3.63$, $p < 0.01$)
Savard et al.	2014	Sleep improved more with CBT than the control. PCBT showed decreased fatigue compared with VCBT and control	Change in ISS scores - PCBT-I: −8.2 (−1.84) $P < 0.0001$, VCBT-I −6.2 (−1.40) $P < 0.001$, CTL: −3.0 (−0.69) $P < 0.001$, $F = 20.17$	Change in MFI scores: PCBT-I:-0.49 (−0.80) $P < 0.0001$, VCBT-I: −0.21b (−0.34) $P < 0.001$, CTL: −0.17 (−0.28) $P < 0.01$ F = 7.95

TABLE 5 (Continued)

Author	Year	Summary of results	Effect on sleep	Effect on fatigue
Savard et al.	2005	Significant differences from pretreatment to posttreatment were observed for all sleep measures, except total sleep time. MFI scores decrease over time	Sleep efficiency (F1,62 = 9.92; $P < 0.05$), total wake time (F1,62 = 15.91; $P < 0.001$), sleep onset latency (F1,70 = 12.92; $P < 0.001$), wake after sleep onset (F1,61 = 6.37; $P < 0.05$)	Fatigue (F1,158 = 11.70; $P < 0.001$)
Vargas et al.	2014	Women in CBSM reported greater improvements in PSQI sleep quality scores than controls. Women in CBSM also reported greater reductions in fatigue-related daytime interference than controls, though there were no significant differences in changes in fatigue intensity	PSQI sleep quality - PE: T1 5.59 (0.20), T2 5.01 (0.23), T3 4.43 (0.36). CBSM: T1 5.38 (0.20), T2 4.44 (0.22), T3 3.51 (0.33). Difference between groups $P = > 0.03$	Fatigue intensity- PE: T1 4.46 (0.16), T2 4.15 (0.22), T3 4.09 (0.26). CBSM: T1 4.27 (0.16), 3.74 (0.22), 3.64 (0.26). Difference between groups $p > 0.030$. Daytime interference - PE: T1 3.53 (0.19), T2 3.01 (0.20), T3 2.82 (0.25). CBSM: T1 3.53 (0.19), T2 3.01 (0.20), T3 2.82 (0.25). Between group difference $p < 0.05$
Yeh and Chung	2016	After intervention, the average fatigue, worst fatigue, and overall sleep quality scores all improved in the Qigong group. This change compared with the control group was significant	Overall sleep quality control: 590.98 ± 72.70 Qigong 945.49 ± 119.50 $p = <0.001$	Average fatigue control: 5.53 ± 1.71, Qigong: 0.43 ± 1.42. Worst fatigue control: 4.61 ± 1.58, Qigong: 0.27 ± 1.31 $p = <0.001$
Zachariae et al.	2018	Large effect sizes were found for improvements in insomnia severity (ISI), sleep quality (PSQI) and sleep efficiency; medium effect sizes for increased total sleep time, less time in bed, and fewer EMAs; and small effect sizes for shorter SOL, fewer NAs, reductions in fatigue (FACIT-F) and less time spent awake after sleep onset (WASO)	ISI scores - intervention: 14.9 (4.8) to 7.1 (4.4), control: 14.7 (4.5) to 12.8 (5.3), $P < 0.001$. PSQI - intervention: 10.2 (3.6) to 6.5 (2.8), control: 10.2 (3.0) to 9.3 (3.4), $P < 0.001$	FACIT-F scores - intervention: 35.8 (9.4) to 40.8 (8.5), control 35.1 (9.6) to 36.8 (10.6), $p < 0.001$
Zengin and Aylaz	2019	Experimental group showed improvement in both PSQI scores and FSS scores. The difference between the mean scores of the groups was statistically significant ($p = 0.000$).	Mean - test score from the PSQI was 5.5 ± 2.1 for the experimental group and 13 ± 2.4 for the control group	The mean posttest score from the FSS was 22.6 ± 1.9 for the experimental group and 41.0 ± 4.2 for the control group

Abbreviations: AT, aerobic therapy; BT, behavioural therapy; CI, confidence interval; CT, combination therapy; EMA, early morning awakening; HEC, healthy eating control; LE, light Exercise; MT, multimodal therapy; NA, nocturnal awakening; PE, physical exercise; QGTC, Qigong/Tai Chi; SE, sleep efficiency; SOL, sleep onset latency, Std., standard; TY, Tibetan yoga; WASO, wake after sleep onset; WLC, waitlist control; YOCAS, yoga for cancer survivors.

relatively small sample sizes with a mean sample size of 149 patients. Due to the nature of the interventions, blinding of the patients is not possible; however, some papers made the effort to blind the staff involved. This was not the case for all the papers, six of which did not mention any blinding, meaning it is difficult to determine the influence of bias on the studies. This is something that should be looked at for future papers to achieve more transparency. Similarly, eight papers failed to discuss their method of allocation.

For future research, daily sleep and fatigue assessments should be investigated to explore how the relationship between sleep and fatigue changes from day to day (Komarzynski et al., 2019). This would allow us to see if the better night's sleep directly impacted the amount of fatigue experienced the next day and vice versa. Currently, it is difficult to draw the conclusion that the improvement in sleep is the cause of the improvement in fatigue without considering that the interventions may have improved the fatigue directly, resulting in better sleep. Looking at how sleep and fatigue change daily may provide more clarity. A way to standardise the form of measure, methods of blinding and the patient populations should also be explored to allow direct comparison of data and to provide more consistency between papers.

5 | CONCLUSION

To conclude, improving sleep appears to be an effective method of reducing the severity of CRF symptoms. Of the methods used, CBT appears to be the most effective nonpharmacological treatment

option and may have other positives for cancer patients such as helping to form support networks with other CRF sufferers. This relationship between sleep and fatigue needs more research to determine whether the improvement in sleep is directly responsible for the improvement in fatigue or if there are other factors at play.

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University of Warwick Medical School.

CONFLICT OF INTEREST

Not applicable.

ETHICS APPROVAL

Not applicable.

CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

CODE AVAILABILITY

Not applicable.

DATA AVAILABILITY STATEMENT

Data are taken from PubMed (https://pubmed.ncbi.nlm.nih.gov/), OVID (https://ovidsp.ovid.com/) and Cochrane (https://www.cochranelibrary.com/) which are openly available public repositories that issues datasets with DOIs.

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