

YOGA AS TREATMENT FOR INSOMNIA AMONG CANCER PATIENTS AND SURVIVORS: A SYSTEMATIC REVIEW

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ABSTRACT

Between 15-90% of cancer patients and survivors report some form of insomnia or sleep quality impairment during and post-treatment, such as excessive daytime napping, difficulty falling asleep, difficulty staying asleep, and waking up too early. Insomnia and sleep quality impairment are among the most prevalent and distressing problems reported by cancer patients and survivors, and can be severe enough to increase cancer mortality. Despite the ubiquity of insomnia and sleep quality impairment, they are under-diagnosed and under-treated in cancer patients and survivors. When sleep problems are present, providers and patients are often hesitant to prescribe or take pharmaceuticals for sleep problems due to polypharmacy concerns, and cognitive behavioural therapy for insomnia can be very difficult and impractical for patients to adhere to throughout the cancer experience. Research suggests yoga is a well-tolerated exercise intervention with promising evidence for its efficacy in improving insomnia and sleep quality impairment among survivors. This article provides a systematic review of existing clinical research on the effectiveness of yoga for treating insomnia and sleep quality impairment among cancer patients and survivors.

Keywords: Yoga, sleep, insomnia, cancer, survivorship, exercise.

INTRODUCTION

Between 15-90% of cancer patients and survivors report some form of sleep quality impairment both during and post-treatment, such as excessive daytime napping, difficulty falling asleep, difficulty staying asleep, and waking up too early.¹⁻¹⁰ These sleep quality impairments are also symptoms of insomnia, which is defined by one or more of these symptoms (e.g., difficulty falling asleep or difficulty staying asleep) in severe and persistent forms (3 or more days per week for one month or longer).¹¹ Insomnia and sleep quality impairment are among the most prevalent and distressing problems reported by cancer patients and survivors, and can increase the risk of cancer-related fatigue and depression, impair cancer-treatment adherence, physical function and quality of life, and, when severe, increase cancer mortality.^{1-10,12,13} Despite the ubiquity of insomnia

and sleep quality impairment, they are under-diagnosed and under-treated in cancer patients and survivors.^{1-10,12,14}

Treatment options for insomnia and sleep quality impairment include: 1) pharmaceuticals, which do not cure insomnia and can lead to toxicities, negative interactions with cancer therapeutics, dependency, and rebound impairment after discontinuation; 2) traditional exercise, which is recommended in treatment guidelines, but not widely implemented in survivorship care plans beyond the use of generalised statements, in which survivors are encouraged to be physically active and exercise; and 3) psychobehavioural interventions.^{1-10,13} Yoga is a well-tolerated exercise intervention with promising evidence for its efficacy in improving insomnia and sleep quality impairment among survivors.

A Holistic Mind-Body Mode of Exercise

Yoga is an increasingly popular mind-body practice and is also characterised as a mindfulness mode of exercise.¹⁵⁻¹⁸ There are many different styles and types of yoga. These are based on Eastern traditions from India (e.g. Classical, Advaita Vedanta, Tantra), Tibet (e.g. Tibetan), and China (e.g. Chi Kung, Tai Chi).^{15,19,20} The word yoga is derived from its Sanskrit root 'yuj' which literally means 'to yoke' or join together. In this case, yoga refers to joining the mind and the body.^{15,19,20} The earliest forms of yoga were firmly rooted in physical and mindful (breathing and meditative) practices and led to what is known today as classical yoga which forms the basis for most of the yoga currently taught today.¹⁹ Hatha yoga, the foundation of all yoga styles and the most popular form, includes both Gentle Hatha and Restorative yoga, and is growing in acceptance for therapeutic use in traditional Western medicine.^{13,15-18,21-24} Gentle Hatha yoga focuses on physical aspects and is part of many styles of yoga, including Iyengar, Anusara, and others.^{15-18,21} Restorative yoga focuses on full relaxation and is part of the Iyengar style.^{25,26} The combination of Gentle Hatha and Restorative yoga may provide an effective approach for improving sleep because it utilises a holistic sequence of meditative, breathing, and physical alignment exercises, requiring both the active and passive engagement of skeletal muscles.^{15,16,21,22,25,26} Existing scientific evidence suggests that yoga is effective for improving insomnia and sleep quality impairment in cancer patients and survivors.^{13,20,27-36}

EXISTING SCIENTIFIC EVIDENCE

Yoga for the Treatment of Insomnia and Sleep Quality Impairment

Research suggests that yoga is helpful in treating depression, anxiety, fatigue and other conditions associated with sleep disorders among healthy individuals and those with cancer.³⁷⁻³⁹ Herein, we review the extant literature on yoga and its use in the treatment of sleep problems among cancer patients (Table 1).

Yoga Programme Evaluations

Four evaluations of community yoga programmes for cancer patients and survivors suggest that yoga

may improve insomnia and sleep quality impairment.⁴⁰⁻⁴³ For example, Joseph et al.⁴⁰ conducted an early study comparing yoga, support therapy, and meditation interventions among cancer survivors undergoing radiation therapy where participants in the yoga group reported improvements in sleep, treatment tolerance, mood, appetite, and quality of life. These yoga programmes were based in cancer centres or community-based yoga studios, and offered yoga classes specifically for cancer patients receiving treatment and survivors who had completed at least primary treatments. The yoga classes included a wide variety of postures and mindfulness exercises from different styles and types, and they were offered 1-2 times a week for 60-90 minutes. Participants in two of these programmes also attributed improvements in strength, physical function, and physical fitness to their yoga practice.^{42,43} However, these reports utilised convenience samples and did not use rigorous research methods designed to answer specific scientific questions about the effects of yoga on sleep quality impairment. These programmes also did not use standardised yoga interventions that can be accurately and consistently replicated for dissemination and explicitly prescribed for the treatment of insomnia or sleep quality impairment. Finally, all of these studies used only patient-reports of insomnia or sleep quality impairment, some of which have not undergone rigorous validation, and no objective assessments of sleep such as polysomnography or actigraphy.

Phase I and II Pilot Clinical Trials

Although limitations exist (see Limitations of Existing Scientific Data on Yoga and Sleep section to follow), one Phase I and seven Phase II studies provide preliminary support for the safety, feasibility and efficacy of yoga for improving insomnia and sleep quality impairment among cancer patients and survivors.^{20,25,27-30,34-36} Cohen et al.²⁰ published the first study investigating yoga and sleep using a validated measure of sleep quality impairment with defined clinical cut-offs (i.e., Pittsburg Sleep Quality Index) among survivors' post-adjuvant treatment. These studies assessed a range of yoga doses from 1-5 sessions/week with classes lasting 50-120 minutes using a variety of different styles and types of yoga over 4-26 weeks. The interventions included a variety of postures and mindfulness exercises.

Table 1. Published Phase I-III clinical research trials investigating the efficacy of yoga for treating insomnia and sleep quality impairment.

Phase I	Trial Design	Sample	Treatment Status	Type of Yoga	Dose Information	Outcomes
Ulger O et al., 2010 ²⁹	1-arm	Breast Cancer (N=20)	Post-adjuvant treatment	Classical	Frequency: 2x/week Duration: 60 min/session 4 weeks Intensity: low to moderate	Sleep * Measure(s): Turkish version of Nottingham Health Profile
Phase II	Trial Design	Sample	Treatment Status	Type of Yoga	Dose Information	Outcomes
Cohen L et al., 2004 ²⁰	2-arm RCT w/ SC waitlist	Lymphoma (N=39)	Mixed receiving active treatment and within 12 months post-adjuvant treatment	Tibetan	Frequency: 1x/week Duration: NA min/session 7 weeks Intensity: low	Sleep * Sleep meds* Measure(s): Pittsburgh Sleep Quality Index
Danhauer SC et al., 2009 ²⁵	2-arm RCT w/ SC waitlist	Breast Cancer (N=44)	Mixed receiving active treatment and within 2 to 24 months post-adjuvant treatment	Integral (restorative yoga postures)	Frequency: 1x/week Duration: 75 min/session 10 weeks Intensity: low	Sleep * Measure(s): Pittsburgh Sleep Quality Index
Carson JW et al., 2009 ²⁸	2-arm RCT w/ SC waitlist	Breast Cancer (N=37)	Post-adjuvant treatment	Yoga of awareness	Frequency: 1x/week Duration: 120 min/session 8 weeks Intensity: low to moderate	Sleep * Measure(s): Daily diary sleep rating
Vadira SH et al., 2009 ³⁰	2-arm RCT w/ SC + support therapy	Breast Cancer (N=88)	During adjuvant radiotherapy	Integrated	Frequency: 3x/week Duration: 50 min/session 6 weeks Intensity: low to moderate	Sleep * Measure(s): European Organisation for Research in the Treatment of Cancer QOL C30

Phase I	Trial Design	Sample	Treatment Status	Type of Yoga	Dose Information	Outcomes
Chandwani KD et al., 2010 ³⁴	2-arm RCT w/ SC waitlist	Breast Cancer (N=61)	During adjuvant radiotherapy	Patanjali from VYASA	Frequency: 2x/week Duration: 60 min/session 6 weeks Intensity: low to moderate	Sleep NC Measure(s): Pittsburgh Sleep Quality Index
Bower JE et al., 2012 ²⁷	2-arm RCT w/ SC + health education	Breast Cancer (N=31)	Survivors post-adjuvant treatment	Iyengar	Frequency: 2x/week Duration: 90 min/session 12 weeks Intensity: low to moderate	Sleep NC Measure(s): Pittsburgh Sleep Quality Index
Dhruva A et al., 2012 ³⁶	2-arm RCT w/ SC waitlist	Mixed types of Cancer (N=23)	Receiving intravenous chemotherapy	Pranayama	Frequency: 1x/week Duration: 60 min/session 12 months Intensity: low	Sleep *  Measure(s): General Sleep Disturbance Scale
Cadmus-Bertram L et al., 2013 ³⁵	2-arm BRCT w/ SC waitlist	Breast Cancer (N=32)	Post-adjuvant treatment	Viniyoga	Frequency: 5x/week Duration: 75 min/session 6 months Intensity: low to moderate	Sleep NC Measure(s): Pittsburgh Sleep Quality Index
Phase III	Trial Design	Sample	Treatment Status	Type of Yoga	Dose Information	Outcomes
Mustian KM et al., 2010 ³²	2-arm RCT w/ SC waitlist	Mixed Cancer Survivors (N=410)	Survivors post-adjuvant treatment	YOCAS®	Frequency: 2x/week Duration: 75 min/session 4 weeks Intensity: low to moderate	Sleep *  Sleep meds*  Measure(s): Pittsburgh Sleep Quality Index & Actigraphy

RCT: randomised, controlled trial; BRCT: block-randomised, controlled trial; NC: no change; SC: standard care; HE: health education; NA: not available in published article.

The interventions were deemed safe and feasible for cancer patients receiving treatment and for survivors. Participants enjoyed the yoga interventions and in five studies reported improvements in insomnia and sleep quality impairment; three studies showed no changes in insomnia or sleep quality impairment.^{27,34,35} Bower et al.²⁷ published the first study testing the efficacy of yoga for treating sleep problems that both blinded participants to the study hypotheses and used a rigorous time and attention control condition. Six of the Phase II randomised controlled trials (RCTs) compared yoga to a waitlist control, one to a support therapy control condition and one to a health education control condition.^{27,30} The latter two studies suggest that yoga may be more effective for improving insomnia and sleep quality impairment than counselling, health education, time and attention.

Phase III Randomised Controlled Clinical Trials

Recently, Mustian et al.¹³ published the first and only multicentre, Phase III, RCT trial examining the effects of yoga on insomnia and sleep quality impairment, assessed both via validated patient-report measures and objective actigraphy measures. This clinical trial is the most definitive trial to date, and demonstrates that yoga is effective for improving insomnia and sleep quality impairment when compared to a usual care waitlist control condition.¹³ The trial compared a standardised yoga intervention (YOCAS[®]: 4 weeks, two times a week, 75 minutes/session; Gentle Hatha and Restorative Yoga) to a usual care waitlist control condition among 410 cancer survivors from 12 community oncology practices throughout the United States. Participants in the yoga condition demonstrated significant moderate-to-large improvements in patient-reported outcomes of insomnia and sleep quality impairment as well as significant improvements on objective actigraphy assessments of sleep outcomes, including wake after sleep onset and sleep efficiency. Yoga participants also significantly decreased their sleep medication use by 21%, while control participants increased their sleep medication use by 5%. Adherence to YOCAS[®] was good at 80%, and there were no study-related adverse events. All (100%) participants found the YOCAS[®] programme useful and would recommend it to other cancer survivors experiencing sleep problems.¹³ Although positive,

results are not generalisable to all types of yoga (e.g. yoga in a heated room, vigorous aerobic yoga), the majority of participants were women, white, and well-educated, and there were no long-term follow-ups to determine if the benefits of yoga on sleep lasted beyond the immediate post-intervention period.

LIMITATIONS OF EXISTING SCIENTIFIC DATA

While very promising, this body of scientific literature needs to be interpreted with caution due to design limitations. None of the Phase I-II studies were a definitive Phase III RCT that was planned and powered a priori to test the effects of yoga on insomnia or sleep quality impairment as a primary outcome. Many studies did not use validated patient reports of insomnia or sleep quality impairment, or objective assessments of sleep problems. The sample sizes were small, ranging from 20-88. They did not screen for or require a specific level of insomnia or sleep quality impairment as part of participant eligibility. The studies did not blind participants with the exception of the Bower study.²⁷ Yoga interventions were not standardised and were highly variable in content, type, intensity and duration of yoga, making it impossible to determine the actual dose of yoga needed to improve insomnia or sleep quality impairment. The yoga interventions were not described in great detail, making repeatability and standardised dissemination impossible. While general comments suggested the interventions were safe and that participants enjoyed them, no specific details were provided on the rate of adverse events. Information on participant attendance, compliance and attrition, details of the prescribed yoga dose versus the actual dose achieved (e.g. mode, frequency, intensity, duration), and information on sustainability of improvements in sleep quality impairment stemming from yoga were limited.

The Phase III clinical trial addressed many of the limitations of the Phase I-II clinical trials. For example, the Phase III trial was appropriately a priori designed and powered to test sleep as the primary outcome with a sample of 410 survivors, screened for a pre-defined baseline level of sleep quality impairment, used validated patient report and objective measures of sleep, rigorously standardised the yoga intervention, and checked for intervention quality, fidelity and

drift. The yoga prescription in the intervention was fully detailed in the publication along with accurate reporting of adverse events, attendance, compliance, and attrition, as well as the achieved dose of yoga versus the prescribed dose of yoga. To date, we could find no studies that have compared yoga to a gold-standard treatment for insomnia or sleep quality impairment, such as pharmaceuticals or cognitive behavioral therapy for insomnia – a required next step in clinical research if yoga is to be considered as such a treatment. In addition, no studies examined the individual components of yoga (i.e. physical postures, breathing and mindfulness activities) to determine which single component, if any, is primarily responsible for the positive effects stemming from yoga or any possible biological mechanisms (e.g. circadian, muscular, cardiovascular, pulmonary, neurological, immunological or neuroendocrine). Yoga may improve insomnia or sleep quality impairment, but an important body of knowledge needs to be developed in order to better tailor yoga prescriptions to improve sleep problems, and meet the unique needs of individual cancer patients and survivors. Finally, these studies include primarily Caucasian, well-educated, middle to upper-middle class women; they have very little racial, economic, social, cultural, gender or age diversity in the sample populations limiting external validity. Importantly, this limits the ability to determine which patient profile may be best suited for and have the best response to yoga therapy. For example, what about the impact of being male, having a cancer diagnosis other than breast cancer, or being non-white, socially isolated, or unemployed.

CLINICAL IMPLICATIONS

While yoga is increasingly popular throughout the world, and there are many books and DVDs as well as cancer centre and community programmes marketed toward cancer survivors (e.g. 'Gentle Yoga for Cancer Patients,' 'Yoga for Breast Cancer Patients and Survivors,' and 'Healing Yoga'), there is little, if any, scientific evidence as to the efficacy of these programmes for improving insomnia or sleep quality impairment among cancer survivors. These yoga programmes are not professionally regulated with respect to instructor qualifications and licensure, or adherence to best practice, standard of care or evidence-based therapeutic guidelines, resulting in significant

variability as to what is offered to cancer patients and survivors. For example, some yoga programmes focus on very gentle, low-intensity, meditative practices (e.g. Restorative, Integral, Svaroopa), while others focus on vigorous practices (e.g. Power, Ashtanga), and yet others focus on both (e.g. Hatha, Iyengar, Kundalini).⁴⁴ Some programmes modify the yoga environment by using heaters and humidifiers (e.g. Bikram) or props such as straps, blocks, ropes and chairs (e.g. Iyengar).⁴⁴ Class structure varies considerably with some classes focusing only on physical postures and no mindfulness exercises, while others only include mindfulness exercises and no physical postures. The small number of studies examining the safety and effectiveness of only limited styles and types of yoga for improving insomnia and sleep quality impairment among survivors, coupled with the lack of regulation and wide variability of yoga offerings, substantially increases the chance that patients and survivors may spend a sizeable amount of time, energy and money participating in yoga programmes that may not be safe or effective. For example, yoga in a room heated to over 100 degrees Fahrenheit may be contraindicated for some survivors, and vigorous yoga may result in excessive muscle soreness and joint pain, increasing insomnia or sleep quality impairment. With this in mind, oncology practitioners can play an important role in helping cancer patients and survivors safely and effectively participate in yoga.

Despite their limitations, these Phase I-III studies collectively suggest that: 1) cancer patients and survivors can safely participate in yoga during and after cancer treatments; 2) yoga interventions are feasible in a variety of cancer centres and community-based yoga studios; 3) cancer patients and survivors participating in these yoga programmes enjoy them and find them beneficial; 4) participation in low-to-moderate intensity yoga that incorporates Gentle Hatha and Restorative postures, breathing and meditation exercises ranging from one-five sessions/week for 50-120 minutes per session over a period of 4-26 weeks may lead to improvements in insomnia and sleep quality impairment; and 5) participation in standardised yoga programmes designed explicitly for cancer patients and survivors experiencing sleep problems, such as YOCAS[®], will reduce the insomnia and sleep quality impairment they experience.

Clinicians can provide important information to help cancer patients and survivors understand how they can safely begin or continue an exercise programme – in this specific case, yoga – during and after treatments.⁴⁵ Patients and survivors can benefit from knowing potential contraindications (e.g. orthopaedic, cardiopulmonary and oncologic) that might affect their exercise safety and tolerance.⁴⁶ Contraindications do not necessarily mean that a cancer patient or survivor cannot participate in yoga at all; in fact, this is rarely the case. In most instances, contraindications simply require specific modifications to the yoga regimen so that the individual can safely and effectively participate and achieve physical and mental health benefits. The American College of Sports Medicine (ACSM) Exercise Guidelines for Cancer Patients and Survivors – the only guidelines currently based on scientific evidence – provide an excellent resource regarding recommendations for screening and evaluation of cancer patients and survivors prior to participation in yoga (Tables 2 and 3).⁴⁶

In addition, referral resources can help patients and survivors connect with the most qualified and competent yoga instructors in their community, particularly those who have special training and experience working with cancer patients and survivors, or individuals with other medical conditions. Patients and survivors with interest in yoga may also benefit from understanding that the styles and types of yoga that have been tested and been shown safe and effective for improving sleep among cancer patients and survivors include primarily, Gentle Hatha or Restorative postures combined with breathing and meditation exercises, and they are of low-to-moderate intensity. When screening patients and survivors for sleep problems and making clinical recommendations about the use of yoga for managing sleep problems, research suggests yoga is effective for individuals who reported mild-to-moderate sleep quality impairment as well as clinical insomnia, continue to report sleep problems after trying pharmaceutical treatments, demonstrate greater than 1 hour of wakefulness in the middle of the night, and have very poor sleep efficiency (60% or lower), or some combination

Table 2. Exercise guidelines for cancer patients and survivors adapted from the American College of Sports Medicine.^{45,46}

Mode of Exercise	Recommendation
<u>Aerobic Exercise</u>	Achieve a weekly volume of 150 minutes of moderate intensity exercise or 75 minutes of vigorous intensity exercise, or some combination of the two.
<u>Resistance Exercise</u>	Perform strength training exercises 2-3 times per week. Include exercises that target all of the major muscle groups.
<u>Flexibility Exercise</u>	Include stretching exercises for all of the major muscle groups on all the days that other exercises are performed.
Additional Information	Return to normal activity as soon as possible during and following cancer treatment. Some exercise is better than none. Start slowly and progressively increase. Strive to achieve the recommended levels of exercise. See a medical professional if any questions or concerns arise. See an exercise oncology professional for assistance with exercise testing, prescription, and monitoring.

Table 3. Examples of exercise contraindications among cancer patients and survivors adapted from the American College of Sports Medicine.^{45,46}

Examples of Cancer-Specific Concerns	Examples of Recommendations
Extreme fatigue, anaemia, and ataxia	Refer to medical specialist and exercise oncology professional to determine if exercise is safe. If determined to be safe, exercise at a low intensity, as tolerated, preferably under the supervision of an exercise oncology professional.
Surgery	Allow sufficient time to heal after surgery before commencing exercise.
Pain at surgery site	Refer to surgeon and/or physical therapist for clearance prior to exercise. Use exercises that do not involve that area of the body until pain is appropriately managed.
Limited mobility at surgery site	Refer to surgeon and/or physical therapist for clearance prior to exercise. Consider physical activity that does not involve that area of the body.
Risk of hernia due to ostomy	Avoid contact sports and exercises that increase intra-abdominal pressures.
Swelling and lymphoedema	Refer to oncologist and physical therapist for clearance prior to exercise. Monitor limb circumference and stop exercise and seek medical evaluation if circumference changes in patients/survivors. Patients at increased risk can wear a compression garment when exercising.
Peripheral neuropathy	Refer to neurologist, physical therapist and exercise oncology professional. Monitor closely for balance impairments. Include exercises that improve balance.
Cardiovascular toxicities	Refer to cardiologist and exercise oncology professional to determine if exercise is safe.
Compromised immune function	Refer to exercise oncology professional. Prescribe exercise at a low-to-moderate intensity. Ensure facility is clean to reduce infection risk.
Increased fracture risk	Avoid exercise that puts excessive stress on bones, including high impact activities.

of these characteristics. Patients and survivors with these characteristics were shown to derive the greatest benefits from participation in yoga – specifically, improved sleep with reduced medication use.

SUMMARY AND FUTURE RESEARCH DIRECTIONS

Although a definitive Phase III RCT has been published and positive results were noted from

this study and the other smaller Phase I-II studies preceding it, the variability across studies and methodological limitations in the published literature continue to limit the extent to which yoga can be considered effective for treating insomnia or sleep quality impairment among cancer patients and survivors. Further research is needed to determine whether yoga is equivalent or superior to existing gold standard pharmaceutical and cognitive behavioral treatments for insomnia and sleep quality impairment. Studies need to employ validated gold-standard patient reported outcomes of insomnia and sleep quality impairment along with objective measures of insomnia and sleep quality impairment. Studies also need to conduct long-term follow-up assessments (e.g., 3, 6, 9, 12 months post intervention) to determine the duration and magnitude of any sleep benefits derived from yoga. In addition, a wider variety of yoga types and intensities need to be examined for their safety and efficacy in treating sleep problems among cancer patients and survivors. Dismantling trials are needed to determine which component of yoga (e.g. postures, breathing or meditation) is primarily responsible for its effectiveness, along with mechanistic studies to determine the biopsychosocial pathways

through which yoga exerts a positive influence on sleep and other toxicities related to cancer and its treatments, such as fatigue, functional decline, cognitive impairment, and deregulated immune function, among others. Trials are needed to elucidate effective ways to increase yoga participation among racially, economically, socially and culturally diverse patients and survivors, as well as older and male cancer patients and survivors. Trials are needed to determine which patients and survivors are most likely to benefit from yoga as a treatment for sleep problems. Trials are also needed to compare the efficacy of yoga to other modes of exercise, such as walking and resistance training, for improving sleep. Finally, trials are needed that extend yoga to the cancer patients' and survivors' care partners (e.g. sister, brother, mother, father, child, spouse, or friend), who provide unpaid care and support to the patient at significant expense to their own health throughout the cancer experience, and without whom effective treatment, support and recovery would not be possible for these patients – these trials may show yoga to be a low-cost and effective therapeutic intervention for both patient and care partner in dyads – with even greater benefits to the patient or survivor than when interventions are directed solely at the individual.

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