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Psychological Interventions to Reduce Stress, Anxiety, and Depression in Cancer Patients: A Systematic Review

Intervenciones Psicológicas para Reducir el Estrés, la Ansiedad y la Depresión en Pacientes con Cáncer: Una Revisión Sistemática

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SUMMARY

Introduction: *Cancer imposes not only a physical but also a substantial psychological burden, manifesting as anxiety, stress, and depression that may disrupt the hypothalamic–pituitary–adrenal (HPA) axis and compromise immune function. This study aimed to evaluate the effectiveness of psychological interventions in alleviating these symptoms among patients with cancer.*
Methods: *This systematic review followed JBI, CRD, and PRISMA guidelines to assess the efficacy of psychological therapies in reducing stress, anxiety, and depression among cancer patients. Eligible studies were English-language randomized controlled trials (RCTs) published from 2020 to 2025, identified through Web of Science, ProQuest, ScienceDirect, and Scopus using MeSH terms and related keywords. Study selection was conducted independently by two reviewers using the PICOS criteria and comprised the identification, screening, and inclusion stages. Data were extracted using a standardized, pilot-tested form that covered study characteristics, intervention details, and outcomes, with all data cross-checked for accuracy and consistency.*
Results: *Twenty-two RCTs involving adult cancer patients met the inclusion criteria. Interventions examined included mindfulness-based programs, cognitive behavioral therapy (CBT), yoga, music therapy, virtual reality (VR), light therapy, digital-based approaches, and multimodal interventions. Overall, most interventions significantly reduced psychological distress. Mindfulness and CBT consistently improved stress, anxiety, and depression, while yoga and music therapy enhanced emotional well-being. Technology-based and VR interventions showed promising results in increasing accessibility to mental health care. Some studies also reported positive effects on cortisol regulation. However, variations in study populations, intervention duration, and outcome measures limited comparability.*
Conclusion: *Psychological interventions were effective in alleviating stress, anxiety, and depression among cancer patients and may contribute to improved biological stress regulation. Integrating these non-pharmacological therapies into routine cancer care is recommended, and further long-term, culturally sensitive studies are needed to strengthen evidence-based practice.*

Keywords: *Cancer, psychological interventions, stress, anxiety, depression.*

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RESUMEN

Introducción: *El cáncer impone no solo una carga física, sino también una carga psicológica sustancial, que se manifiesta como ansiedad, estrés y depresión, y puede alterar el eje hipotálamo-hipófiso-adrenal (HHA) y comprometer la función inmunológica. Este estudio tuvo como objetivo evaluar la efectividad de las intervenciones psicológicas para aliviar estos síntomas en pacientes con cáncer.*

Métodos: *Esta revisión sistemática siguió las directrices de JBI, CRD y PRISMA para evaluar la eficacia de las terapias psicológicas en la reducción del estrés, la ansiedad y la depresión en pacientes con cáncer. Los estudios elegibles fueron ensayos clínicos aleatorizados en inglés publicados entre 2020 y 2025, identificados en Web of Science, ProQuest, ScienceDirect y Scopus mediante términos MeSH y palabras clave relacionadas. La selección de estudios siguió los criterios PICOS y fue realizada de manera independiente por dos revisores en las etapas de identificación, selección e inclusión. Los datos se extrajeron mediante un formulario estandarizado y probado en piloto que cubría las características del estudio, los detalles de la intervención y los resultados. Todos los datos fueron verificados para asegurar su precisión y consistencia.*

Resultados: *Veintidós ensayos clínicos aleatorios (ECA) que involucraron a pacientes adultos con cáncer cumplieron con los criterios de inclusión. Las intervenciones examinadas incluyeron programas basados en mindfulness, terapia cognitivo-conductual (TCC), yoga, musicoterapia, realidad virtual (RV), terapia de luz, enfoques digitales y intervenciones multimodales. En general, la mayoría de las intervenciones redujeron significativamente el malestar psicológico. La atención plena y la TCC mejoraron de manera consistente el estrés, la ansiedad y la depresión, mientras que el yoga y la musicoterapia mejoraron el bienestar emocional. Las intervenciones basadas en tecnología y en realidad virtual mostraron resultados prometedores en el aumento de la accesibilidad a la atención de salud mental. Algunos estudios también reportaron efectos positivos en la regulación del cortisol. Sin embargo, las variaciones en las poblaciones de estudio, la duración de las intervenciones y las medidas de resultado limitaron la comparabilidad.*

Conclusión: *Las intervenciones psicológicas fueron efectivas para aliviar el estrés, la ansiedad y la depresión en pacientes con cáncer y pueden contribuir a una mejor regulación biológica del estrés. Se recomienda integrar estas terapias no farmacológicas en el cuidado rutinario del cáncer, mientras que se necesitan más estudios a largo plazo y culturalmente sensibles para fortalecer la práctica basada en la evidencia.*

Palabras clave: *Cáncer, intervenciones psicológicas, estrés, ansiedad, depresión.*

INTRODUCTION

Cancer is a chronic illness that affects individuals across multiple dimensions, both physical and psychological (1). In 2020, an estimated 19.3 million new cancer cases and 10 million deaths were reported worldwide, underscoring its substantial global health burden (2). In Indonesia, the prevalence of cancer continues to rise, influencing not only clinical outcomes but also the psychological well-being and overall quality of life of patients (3).

In addition to discomfort and the negative consequences of therapies like chemotherapy and radiation, cancer patients typically deal with severe mental stress. Cancer patients have incredibly high rates of stress, anxiety, and depression. According to meta-analysis research, between 30 and 40 percent of cancer patients suffer from psychological conditions such as anxiety and depression (4-7). Etikasari et al. (2021) (8) and Gayatri et al. (2021) (9) emphasizes the significance of managing psychological aspects in palliative care, particularly in light of the existence of exhaustion, future uncertainty, shifting social roles, and a lack of family support.

Dysregulation of the neuroendocrine system, specifically the hypothalamic-pituitary-adrenal (HPA) axis, which regulates cortisol levels, is recognized as a consequence of these detrimental psychological circumstances (10). Cortisol is the stress hormone that contributes to the body's response to psychological stress. On the other hand, persistently elevated cortisol levels might impair immunity, worsen the prognosis for cancer, and potentially lessen the efficacy of treatment (11-14). As a result, managing psychological stress becomes an essential part of cancer patients' overall treatment (15).

According to recent research, this treatment has been shown to reduce stress, anxiety, and depression, and may also decrease cortisol levels, a biological marker of chronic stress (14,16). However, comprehensive scientific evidence regarding the direct relationship between the reduction of psychological symptoms and changes

in cortisol levels remains limited, particularly among cancer patients from diverse cultural backgrounds. This study was thus carried out as a systematic review to assess the effectiveness of various psychological interventions in reducing levels of stress, anxiety, and depression in cancer patients.

METHODS

The framework of this review was based on the criteria of the Joanna Briggs Institute (JBI) and the Center for Reviews and Dissemination (CRD), as well as the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (17,18). The literature search was conducted systematically in four electronic databases: Web of Science, ProQuest, ScienceDirect, and Scopus. The search covered studies published between January 2020 and March 2025. To ensure comprehensiveness, both Medical Subject Headings (MeSH) (for PubMed-indexed content accessible via ProQuest) and free-text keywords were used. Boolean operators (AND, OR) and truncation were applied to broaden the scope. The main keywords included: "cancer," "stress," "anxiety," "depression," and "randomized controlled trial (RCT)".

The inclusion and exclusion criteria were determined using the PICOS framework (Population, Intervention, Comparison, Outcome, and Study design). This review applied PICOS-based eligibility criteria. It was included studies enrolling adults with a confirmed cancer diagnosis, irrespective of cancer type or stage (Population), that evaluated psychological interventions designed to reduce stress, anxiety, or depression (Intervention). Studies were required to include a comparison condition—such as standard care, placebo, or an alternative intervention (Comparison)—and to report primary outcomes on psychological distress (stress, anxiety, and/or depression); secondary outcomes could include biological markers (e.g., cortisol) when available (Outcome). Only randomized controlled trials published in peer-reviewed journals (Study design) were considered. The search was limited to articles published from January 2020 through March 2025 and written in English. Studies excluded were those which did not involve adults with cancer, did not test a psychological intervention, lacked a control group, were not RCTs, were not peer-reviewed, were published outside the specified period, or were not in English. Studies were excluded if they were qualitative investigations, non-randomized controlled trials (RCTs) (e.g., observational, quasi-experimental, case series), review articles, theoretical papers, expert opinions, conference abstracts, dissertations, or publications in languages other than English.

The study selection process consisted of three stages: identification, screening, and final inclusion. A total of 548 articles were initially identified across four databases. After removing duplicates, 523 records were screened based on titles and abstracts. Of these, 32 full-text articles were assessed for eligibility, and finally, 22 randomized controlled trials (RCTs) met all inclusion criteria. Screening and selection were performed independently by two reviewers using predefined eligibility criteria. Any discrepancies in study inclusion were discussed and resolved through consensus. If disagreement persisted, a third reviewer was consulted for final adjudication. For data extraction, a standardized form was piloted across three randomly selected studies to ensure clarity and consistency before full implementation. Extracted variables included: type of psychological intervention, author(s), year of publication, country, study population (sample size, age, type of cancer), intervention characteristics (duration, delivery format), and primary outcomes (stress, anxiety, depression). Data extraction was performed independently by two reviewers and cross-checked to minimize errors.

The risk of bias in each RCT study was evaluated using the Cochrane Collaboration's Risk of Bias Tool, as adapted by Sterne et al. (19). The assessment was conducted across various domains, including randomization methods, completeness of outcome data, and selective reporting. The primary outcomes reviewed in this study were the effects of the intervention on stress, anxiety, and depression levels in cancer patients.

RESULTS

Study characteristics

From the systematic search in four databases (Scopus, ScienceDirect, ProQuest, and Web of Science), a total of 548 articles were initially retrieved. After applying inclusion and exclusion criteria, 22 randomized controlled trials (RCTs) were included in the final review. All studies evaluated the effectiveness of psychological interventions on stress, anxiety, and depression in cancer patients. Participants ranged from adolescents and adults (14–80 years) (Figure 1).

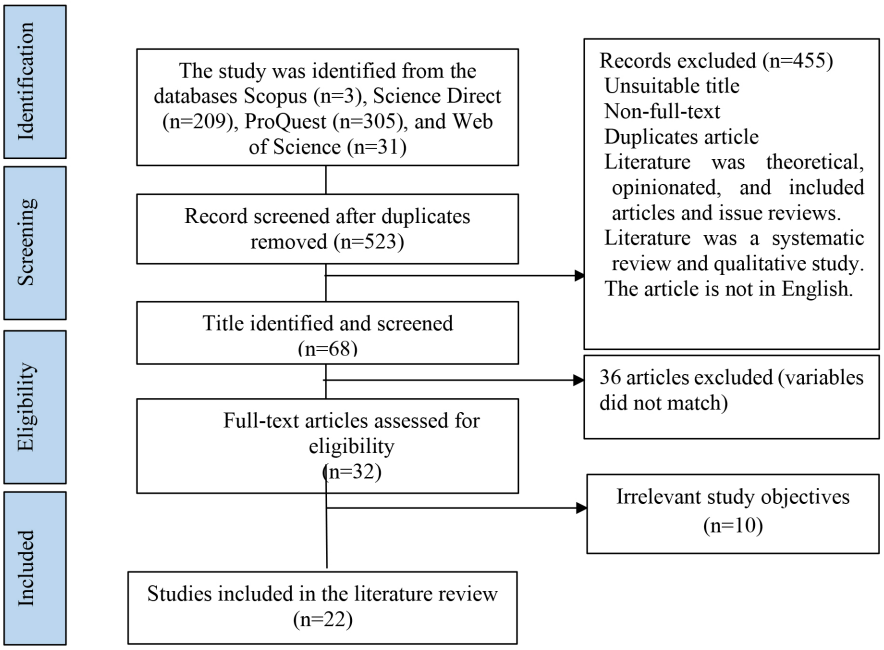

Figure 1. PRISMA flow diagram of included studies.

The interventions included mindfulness-based programs, cognitive-behavioral therapy (CBT), yoga, music therapy, the Pythagorean Self-Awareness Intervention (PSAI), technology-based approaches (such as virtual reality and web-based CBT), multimodal interventions, and light therapy. Across studies, most interventions reduced psychological distress, with mindfulness and CBT consistently demonstrating significant improvements, while other modalities showed promising but more variable outcomes (Table 1).

Given the heterogeneity in intervention types, duration, delivery formats, outcome measures, and study populations, a meta-analysis was not performed. Instead, a narrative synthesis approach was used. Effect measures reported across studies varied, including standardized mean differences (SMDs), relative risks (RRs), confidence intervals (CIs), and p-values; however, inconsistent reporting and outcome scales precluded quantitative pooling.

Table 1. Characteristics of Included Studies

Type of Intervention	Study (Author, Year)	Country	Sample and Age (years)	Type of Cancer
Mindfulness-Based Interventions	Pereira et al., 2022 (20)	Portugal	18–65	Breast, prostate, colorectal
	Světlák et al., 2023 (21)	Czech Republic	≥18	Breast
	Lengacher et al., 2019 (22)	USA	Mean: 56.6	Breast
	Oliveira et al. 2024	USA	Mean: 50	Colorectal
Music Therapy	Tollabzadeh, Rezvani and Behzadipour, 2023 (30)	Iran	20–63	Not specified
	Sun et al., 2023 (33)	China	18–74	Not specified
Cognitive Behavioral Therapy	Penedo et al., 2021 (27)	USA	Mean: 50	Prostate
	Laidsaar-Powell et al., 2025 (88)	Australia	Not reported	Not specified
Somatic Yoga & Meditation	Galantino et al. 2019 (39)	USA	47–81	Not reported
Pythagorean Self-Awareness	Charalampopoulou et al. 2020 (43)	Greece	Mean: 52.8	Breast
Technology-Based Interventions	Mizrach et al., 2022 (48)	USA	14–29	Not reported
	Fan et al., 2021 (49)	China	25–62	Breast
	Li et al., 2022 (50)	China	15–39	Not reported
Multimodal Therapy & Physical Activity	Kröz et al., 2023 (54)	Germany	56,5–59,9	Breast
	Vikmoen et al., (2022) (55)	Norway	>18	Breast
	Djurhuus et al., 2022 (56)	Denmark	>18	Prostate
Light Therapy	Johnson et al., 2020 (66)	Canada	Mean: 58.1	Not reported
Virtual Reality (VR)	Burrai et al., 2023 (74)	Italy	>18	Not reported
	Buche et al., 2023 (75)	France	55.4	Breast
	Torres García et al., 2024 (76)	Spain	30-80	Breast
	Uslu and Arslan, 2023 (77)	Turkey	18-65	Breast
	Zhang et al., 2024 (78)	China	≥18	Leukemia

DISCUSSION

Mindfulness-Based Stress Reduction in Cancer Patients

Several studies demonstrate that mindfulness-based interventions (MBIs) effectively reduce stress, anxiety, and cortisol levels among cancer patients (20-23). For example, both salivary and hair cortisol significantly decreased after MBSR or MBCT. Mindfulness is thought to reduce stress reactivity by increasing awareness of emotions and bodily sensations, and by activating parasympathetic pathways that downregulate the HPA axis (24-26). This mechanism not only improves psychological well-being but also has potential biological benefits, including enhanced immune regulation. Because mindfulness is relatively low-cost, easy to administer, and empowers patients with self-management skills, it is highly feasible to integrate into nursing practice.

While mindfulness emphasizes acceptance and awareness, cognitive behavioral therapy (CBT) focuses on restructuring maladaptive thoughts and behaviors. Both interventions are effective, but their benefits may vary depending on patient characteristics. Mindfulness tends to be more beneficial for patients with generalized stress, uncertainty about prognosis, or high spiritual needs. At the same time, CBT shows more potent effects in patients with clinically significant anxiety and depression, particularly when cognitive distortions dominate their coping patterns (27,28). CBT also requires structured sessions and trained therapists, whereas mindfulness can be delivered more flexibly, including in group or digital formats. Thus, when choosing between mindfulness and CBT, consideration should be given to the patient's psychological profile, the availability of trained professionals, and cultural acceptance.

Despite their effectiveness, psychological interventions face challenges. Costs for structured CBT or VR-based interventions may be prohibitive, particularly in low- and middle-income countries. Accessibility remains a concern, especially in rural or remote areas with limited mental health resources. Moreover, professional training is crucial to ensure safe and effective delivery, as improper implementation may reduce treatment fidelity. Health systems need to invest in workforce development, especially nurses and psychologists, to integrate these therapies into routine oncology care (29).

Most evidence in this review originates from Europe and North America, with limited data from Southeast Asia. The cultural context is highly relevant, as family support, spiritual values, and community-based coping strategies are central in Indonesia and its neighboring countries (9). This cultural emphasis on collective resilience suggests that group-based or family-integrated psychological interventions may be more acceptable and effective. Local adaptation is therefore essential before large-scale implementation.

Psychological interventions not only alleviate distress but may also influence biological processes. By modulating cortisol levels and reducing systemic inflammation, these interventions could theoretically improve treatment adherence, immune recovery, and even survival outcomes (14,16). However, direct evidence linking psychological therapies to hard endpoints such as survival rates or long-term adherence to chemotherapy remains scarce. More longitudinal studies are needed to clarify whether improvements in psychological well-being translate into better oncological outcomes.

The effects of music therapy

Music therapy has consistently demonstrated effectiveness in reducing anxiety and regulating cortisol levels among cancer patients in both inpatient and outpatient settings (30-33). Its mechanism is believed to involve stimulation of the limbic system and enhancement of neurotransmitters such as dopamine and serotonin, which contribute to relaxation and emotional regulation (34). Unlike cognitive-behavioral interventions that require active patient participation, music therapy can be more suitable for patients with limited verbal communication, severe fatigue, or advanced disease stages, where concentration and cognitive effort are difficult.

When compared with mindfulness and CBT, music therapy generally produces more modest improvements in depression but is highly effective in acute anxiety reduction and short-term

relaxation. It is beneficial in procedural contexts, such as chemotherapy infusion or radiotherapy sessions, where immediate stress relief is needed. In contrast, mindfulness and CBT provide longer-term benefits by reshaping coping styles and thought patterns. This suggests that music therapy may serve best as a complementary intervention, addressing acute distress while other modalities target long-term psychological adjustment. Despite its advantages, non-invasiveness, safety, and adaptability, music therapy faces several limitations. Access to trained music therapists is limited, especially in low- and middle-income countries, and the cost of structured programs may be prohibitive in under-resourced health systems. In Indonesia and other Southeast Asian settings, where hospital music therapy programs are still uncommon, implementation would require capacity building, integration into nursing roles, and culturally adapted approaches (e.g., incorporating traditional or religious music familiar to patients) (35).

Beyond psychological outcomes, some studies suggest that music therapy may have indirect benefits, including improvements in biological and clinical endpoints. By lowering cortisol and promoting relaxation, it could enhance immune function, support adherence to cancer therapy, and improve tolerance to treatment. However, evidence on survival outcomes remains limited and inconclusive, underscoring the need for long-term studies that assess whether improvements in psychological and biological stress markers translate into tangible benefits in survival rates or disease progression (36).

Cognitive Behavioral Therapy (CBT)

Web-based cognitive behavioral therapy (CBT) has been shown to significantly reduce anxiety and depression in cancer patients, particularly in men with prostate cancer (37). The underlying principle of CBT is that maladaptive thoughts influence emotions and behaviors; by restructuring these thought patterns, patients can reduce psychological distress and modulate physiological stress responses, including cortisol regulation (27,28). When compared with other psychological interventions, CBT demonstrates a consistently strong effect across different cancer types and severity levels, especially in patients with clinically significant depressive or anxiety symptoms. Unlike mindfulness-based programs, which are more preventive and beneficial for general stress reduction, CBT is particularly effective for patients already experiencing moderate to severe psychological disorders. This makes CBT a preferable choice in oncology settings where psychiatric comorbidities are prevalent. However, for patients with fatigue or limited cognitive capacity due to chemotherapy, less cognitively demanding interventions such as music therapy or relaxation-based approaches may be more practical.

Despite its effectiveness, CBT has limitations regarding cost, accessibility, and the need for trained professionals. Delivering CBT requires psychologists or other mental health professionals, who may not be available in resource-limited settings across Indonesia and Southeast Asia. Web-based or hybrid CBT models can expand access, yet digital literacy, internet infrastructure, and financial barriers remain challenges that must be addressed before large-scale implementation (37).

Beyond psychological outcomes, emerging evidence suggests that CBT may also influence biological processes. Several studies report reductions in stress-related hormones and improvements in immune regulation among CBT participants, suggesting potential effects on adherence to cancer therapy and possibly on survival outcomes. However, robust evidence linking CBT directly to long-term endpoints, such as disease progression or overall survival, remains limited. In the Indonesian context, where family involvement is central to patient care, CBT protocols may need to be adapted to incorporate family support components. This cultural adaptation could enhance patient engagement, reduce stigma, and improve the sustainability of psychological interventions in oncology care (38).

Yoga and Meditation

Evidence suggests that yoga and meditation can provide meaningful benefits for cancer patients by reducing psychological distress and improving biological regulation. Galantino et al.

(2019) reported that somatic yoga and meditation lowered cortisol levels, enhanced quality of life, and reduced the risk of falls associated with chemotherapy-induced neuropathy (39). These practices stimulate the parasympathetic nervous system, restore autonomic balance, and improve attention and mental calmness, thereby helping regulate stress hormones (28,40).

Compared with other interventions, yoga and meditation appear particularly effective in enhancing physical stability, sleep quality, and emotion regulation. In contrast, mindfulness-based interventions and CBT more consistently reduce anxiety and depressive symptoms across diverse cancer populations. Thus, yoga may be most beneficial for patients experiencing physical side effects of chemotherapy (e.g., fatigue, neuropathy), while CBT and mindfulness are better suited for patients with marked psychological symptoms. The complementary use of these approaches could yield greater benefits.

Despite their promise, several limitations must be acknowledged. The effectiveness of yoga and meditation depends on the availability of qualified instructors with oncology experience, which may not be readily accessible in many clinical settings (41). Additional challenges include the cost of structured yoga programs, variation in patient physical ability, and the lack of standardized protocols. Moreover, the successful implementation of such interventions requires professional training for healthcare providers to ensure patient safety and adherence to best practices.

In Southeast Asia, including Indonesia, yoga and meditation are culturally acceptable because they align with spiritual and holistic health practices. However, their adoption in cancer care remains limited, partly due to a lack of institutional support, uneven distribution of trained practitioners, and the prioritization of biomedical over psychosocial care. Tailoring interventions to local cultural norms, integrating family involvement, and leveraging community-based programs could enhance feasibility in these settings (42).

Notably, yoga and meditation not only reduce stress and anxiety but may also affect biological pathways, including cortisol regulation and immune function. This psychobiological effect raises the possibility of improving hard outcomes, including better adherence to cancer therapy, reduced treatment complications, and potentially improved survival, although current evidence remains inconclusive. Longitudinal studies with biological endpoints and survival analysis are necessary to determine whether psychological interventions yield durable clinical benefits.

Pythagorean Self-Awareness Intervention (PSAI)

Charalampopoulou et al. (2020) (43-45) demonstrated that PSAI, which integrates self-monitoring and daily contemplation on moral principles, significantly improved sleep quality, reduced psychological distress, and lowered hair cortisol levels over eight weeks. Unlike more structured approaches such as cognitive-behavioral therapy (CBT), PSAI relies on introspection and self-discipline and aligns closely with cognitive-metacognitive principles, in which patients actively evaluate their daily thoughts and behaviors (46). This reflective practice may regulate HPA axis activity and promote emotional stability (47).

Comparatively, CBT and mindfulness-based interventions have more substantial evidence for reducing anxiety and depression across diverse cancer populations, particularly in patients with moderate to severe distress or those undergoing intensive treatment. PSAI, while promising, may be more effective in cultural contexts that emphasize spirituality, moral values, and community-based coping, which are standard in Southeast Asia, including Indonesia. Thus, PSAI could complement established interventions, such as CBT, by offering a culturally congruent alternative for patients who are less receptive to Western psychological frameworks.

However, implementing PSAI and similar interventions presents challenges. Unlike technology-based approaches or group CBT sessions, PSAI requires patient motivation and consistency, which may limit uptake. Moreover, accessibility remains an issue: while PSAI is low-cost and does not require specialized equipment, interventions such as CBT or VR may be costly, require professional facilitators, or necessitate infrastructure that is not widely available in

low- and middle-income countries. Therefore, training healthcare providers, particularly nurses and counselors, in low-cost, culturally sensitive interventions such as PSAI, yoga, or music therapy could increase accessibility in resource-limited settings.

In terms of biological outcomes, interventions such as PSAI, mindfulness, and yoga demonstrate measurable effects on cortisol regulation, a key biomarker of chronic stress. While these findings are promising, there remains limited evidence linking psychological interventions directly to hard outcomes, such as survival rates, treatment adherence, or recurrence rates. In the Indonesian context, where family support and religious coping are deeply embedded, integrating value-based interventions like PSAI into nursing and palliative care may enhance psychological resilience, improve adherence to cancer therapy, and indirectly contribute to better long-term outcomes.

Technology-Based Psychological Interventions

Technology-based psychological interventions, such as mobile health applications, wearable devices, and teleconsultation platforms, have shown promising results in reducing anxiety and improving psychological well-being in cancer patients (48–50). Compared with traditional face-to-face interventions, such as cognitive-behavioral therapy (CBT) or mindfulness, digital approaches offer unique advantages in accessibility and the immediacy of support. While CBT and mindfulness remain the most consistently effective interventions across diverse cancer populations, technology-based programs may be particularly beneficial for younger patients, those living in rural areas, and individuals with limited mobility, as they allow remote monitoring and flexible engagement (51).

However, several challenges limit the broader implementation of these approaches. First, technology-based interventions often require reliable internet access, compatible devices, and digital literacy, which may not be evenly distributed across patient populations. Cost considerations, both for healthcare providers in implementing digital platforms and for patients in accessing devices or data plans, pose further barriers. In addition, effective delivery requires trained healthcare professionals, such as oncology nurses and psychologists, who are familiar with digital mental health tools. Without adequate training and support, the effectiveness of these interventions may be reduced (52).

In Indonesia and other Southeast Asian countries, technology-based interventions hold significant potential given the geographical disparities in cancer care. Many patients face long travel distances and limited access to oncology centers, making digital tools an attractive option to complement conventional psychosocial services. Nevertheless, unequal distribution of internet infrastructure and varying levels of health literacy must be carefully considered in program design to avoid widening disparities. Culturally tailored content, such as incorporating family involvement, spirituality, and local language, may also improve acceptance and effectiveness in this region (53).

Beyond psychological outcomes, some studies have begun to explore biological and clinical implications. Reductions in cortisol levels have been observed following digital interventions, suggesting improved neuroendocrine stress regulation (50,51). While evidence directly linking these interventions to hard outcomes such as treatment adherence, quality of life improvement, or survival rates remains limited, psychological stability is known to influence adherence to chemotherapy, radiotherapy, and hormonal therapy. Thus, digital psychological interventions may indirectly improve long-term health outcomes, although further longitudinal studies are required to confirm this relationship.

Multimodal Therapy and Physical Activity

Multimodal interventions, which combine physical activity with supportive therapies such as art therapy, sleep optimization, and psychoeducation, have been increasingly recognized for their potential to improve outcomes in cancer patients. Kröz et al. (54) and Vikmoen et al. (55) demonstrated that these interventions can synergistically reduce stress hormone levels, particularly cortisol, and enhance patient vitality (56). The bio-psycho-social components of the multimodal

approach reinforce one another: physical exercise promotes the release of endorphins, which in turn modulate the stress response and reduce systemic inflammation. At the same time, psychoeducational and creative therapies support coping and emotional regulation (57,58).

Compared with single-modality interventions, such as exercise-only or psychoeducation-only programs, multimodal therapy tends to yield more comprehensive benefits (59). Exercise alone can improve physical function and reduce inflammation, but may not be sufficient to address psychological distress. Conversely, psychoeducational or creative therapies primarily target emotional well-being but have a limited impact on physiological stress markers. Patients with moderate functional capacity and mild-to-moderate psychological distress appear to gain the most from multimodal programs, as they can actively engage in physical activity while also benefiting from cognitive and emotional support (60). In contrast, patients with severe fatigue or advanced disease may require tailored adaptations, as the intensity of physical components may be challenging.

The integration of physical and psychosocial interventions can influence both psychological and biological processes. By lowering cortisol and systemic inflammation, multimodal therapy may enhance immune function and improve physiological resilience (61). Moreover, improved mood, reduced anxiety, and better sleep can support adherence to cancer therapy regimens, potentially impacting survival rates indirectly. Although current evidence demonstrates strong effects on biomarkers and quality of life, studies assessing direct outcomes, such as long-term survival or recurrence, remain limited, highlighting a gap in future research (62).

Several limitations must be acknowledged. Multimodal interventions often require substantial resources, including trained personnel, access to rehabilitation facilities, and patient adherence over several weeks, which can restrict scalability (63). Accessibility may be particularly challenging in low-resource settings, such as many regions in Indonesia and Southeast Asia, where oncology rehabilitation services are limited. Cost-effectiveness analyses are sparse, and professional training for therapists in combined modalities remains a significant barrier (64). Adapting to the local context, considering cultural preferences for therapy types, the availability of exercise facilities, and patient socioeconomic status, is essential to ensure feasibility and adherence.

Although much of the evidence originates from Europe and the Americas, preliminary experiences in Southeast Asia suggest that culturally adapted multimodal programs can be effective. For example, incorporating local forms of physical activity (e.g., light traditional dance or tai chi) and culturally acceptable art or relaxation practices may increase patient engagement (65). Developing scalable, cost-conscious interventions that leverage community- or home-based resources may facilitate broader implementation in Indonesia by addressing barriers related to accessibility and cost.

Overall, multimodal therapy combining physical activity with psychosocial support represents a promising approach to enhancing both mental and physical outcomes in cancer patients. Its benefits extend beyond improvements in quality of life, potentially influencing adherence and resilience through the interplay of psychological and biological mechanisms. Nevertheless, careful consideration of patient conditions, resource availability, and cultural context is critical for successful implementation, particularly in Southeast Asia.

Light Therapy

After four weeks of bright-light treatment for cancer patients experiencing fatigue, Johnson et al. (2020) reported improvements in sleep quality and a more regular cortisol rhythm (66–68). Light therapy works by stimulating the suprachiasmatic nucleus (SCN), the brain's central circadian clock. Balanced circadian rhythms play a crucial role in regulating melatonin and cortisol, two hormones that are frequently disrupted in cancer patients and are associated with fatigue, mood changes, and insomnia (69). Neurobiological evidence further suggests that exposure to bright light may enhance mood, immune function, and daily cortisol profiles (70).

Compared with other non-pharmacological interventions such as cognitive-behavioral therapy for insomnia (CBT-I) or physical activity

programs, light therapy appears particularly effective for patients with primary circadian rhythm disturbances, including disrupted sleep-wake cycles and morning fatigue (70). Meanwhile, CBT-I may provide broader benefits for patients with complex psychological comorbidities such as anxiety and depression. At the same time, exercise interventions are more effective in addressing muscle weakness and overall physical fatigue (71). Thus, the choice of intervention should be tailored to patient characteristics: light therapy is preferable for those with predominant circadian and hormonal dysregulation. At the same time, multimodal approaches may be necessary for patients with overlapping physical and psychological symptoms.

Despite its promise, several limitations of light therapy must be highlighted. First, cost and accessibility vary significantly. At the same time, light boxes are relatively affordable in high-income countries; they may still pose a financial barrier in low- and middle-income settings such as Indonesia. Second, patient adherence is crucial, as the therapy requires regular, timed exposure to achieve benefits. Third, professional guidance and training are often necessary to ensure the correct application, particularly regarding the timing and intensity of light, which may not always be feasible in resource-limited healthcare systems (72).

Relating these findings to the local context, cancer patients in Indonesia and Southeast Asia often face additional challenges, including limited access to supportive care services, lower health literacy, and sociocultural barriers that influence acceptance of non-pharmacological interventions. Implementing light therapy in this region requires integrating it into existing hospital-based oncology care and developing simplified, culturally adapted guidelines for home use. Local research is also necessary to determine whether the efficacy observed in Western populations generalizes to Asian patients, given potential genetic, environmental, and lifestyle differences that may affect circadian regulation (73).

Ultimately, beyond providing symptomatic relief, the psychological and biological mechanisms of light therapy may hold broader clinical significance. By stabilizing circadian rhythms and improving cortisol regulation, light therapy could enhance immune function, reduce systemic inflammation, and potentially improve adherence to chemotherapy or radiotherapy schedules (66). Although current evidence remains limited, future studies should investigate whether these physiological benefits translate into tangible outcomes, such as improved survival, reduced recurrence rates, or enhanced long-term quality of life. Integrating light therapy into multimodal supportive care thus represents a promising pathway to improve not only subjective well-being but also biological resilience in cancer patients.

Virtual Reality (VR) Intervention

Burrai et al. (74), Buche et al. (75), Torres García et al. (76), Uslu and Arslan (77), and B. Zhang et al. (78) demonstrated that guided imagery and virtual reality (VR) relaxation interventions are effective in lowering cortisol hormone levels and reducing anxiety, stress, and depression in cancer patients. By creating immersive experiences, VR helps patients disengage from unpleasant or stressful conditions often associated with cancer therapy. Physiologically, VR stimulates the limbic system and reduces hypothalamic-pituitary-adrenal (HPA) axis activity, thereby lowering cortisol secretion. When combined with guided imagery or visual relaxation, these interventions leverage neuroplasticity and distraction-based mechanisms to reframe patients' psychological responses (79). Anxiety levels have been consistently shown to be lower among patients using VR-supported guided imagery compared to conventional relaxation methods (80-82).

Findings across studies suggest that VR-based relaxation may be more effective than guided imagery alone, particularly in patients undergoing invasive procedures or intensive treatments where anticipatory anxiety is high. For patients with advanced disease or those experiencing severe treatment-related distress, the immersive, multisensory nature of VR provides greater benefits for distraction and emotional regulation. In contrast, guided imagery without VR remains beneficial for patients with mild-to-moderate anxiety or in contexts where cost and infrastructure limit VR implementation. Thus,

patient condition, disease stage, and available resources are key determinants in choosing the appropriate intervention (83).

The reduction in anxiety and stress through VR-guided interventions is not only psychologically relevant but also biologically significant. Decreased cortisol levels indicate modulation of the stress response, which may, in turn, indirectly influence immune function, chemotherapy adherence, and recovery trajectories. While current studies primarily focus on psychological outcomes, emerging evidence suggests that enhanced emotional regulation may support treatment adherence and, in turn, influence long-term survival rates. However, definitive links to hard outcomes such as survival require further longitudinal studies (84).

Despite its promise, VR implementation is constrained by several limitations. High device costs, limited availability in healthcare facilities, and the need for professional training to deliver interventions effectively are barriers to broad adoption (85). Accessibility issues are particularly evident in low- and middle-income countries (LMICs), where health infrastructure remains limited. Additionally, motion sickness and user discomfort may reduce the feasibility for certain patients, especially older adults. These factors must be considered when integrating VR into routine cancer care.

In Indonesia and other Southeast Asian countries, where disparities in healthcare access and technology adoption persist, implementing VR-guided interventions presents both opportunities and challenges. On the one hand, the growing digital health movement, increased smartphone penetration, and government interest in telemedicine create fertile ground for the introduction of VR-based psychological support (86). In addition, the high cost of VR hardware, the unequal distribution of healthcare resources between urban and rural areas, and the limited training of healthcare professionals remain critical barriers. Adaptation strategies, such as utilizing affordable VR devices, integrating interventions into community health programs, and training nurses in digital health, are essential to ensure feasibility and sustainability in this region (87).

Overall, VR-assisted guided imagery represents a promising adjunct to traditional psychological interventions in oncology care. Its comparative advantage lies in addressing severe anxiety and stress, while guided imagery alone remains a practical option in resource-limited settings. To maximize its impact, future research should focus on cost-effectiveness, implementation models suited to LMICs, and long-term evaluation of hard outcomes such as adherence, immune function, and survival.

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CONCLUSION

This systematic review finds that various psychological interventions, including mindfulness, CBT, yoga, music therapy, technology-based approaches (e.g., VR), multimodal approaches, and light therapy, effectively reduce stress, anxiety, and depression in cancer patients. These therapies affect patients' psychological states and biological markers, such as cortisol levels, which are involved in immune function and stress management. The holistic component of cancer care, often overlooked, is significantly strengthened by this non-pharmacological approach.

The implications of these findings are significant for nursing practice and healthcare services in general. Healthcare professionals, particularly nurses and psychologists, should integrate psychological interventions into cancer care standards across hospitals and the community. The use of technology such as digital applications and virtual reality can expand the reach of interventions, especially for patients in remote areas or those with physical limitations. In the future, the development of professional training, the provision of supporting facilities, and further research on the long-term effectiveness of these interventions are essential to sustain and adapt them across diverse cultural contexts.

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