

## Effectiveness of non-pharmacological interventions on quality of sleep of breast cancer patients undergoing chemotherapy: a systematic review and meta-analysis

Intan Rismatul Azizah<sup>a</sup>, Tintin Sukartini<sup>b</sup>, Ira Suarilah<sup>b,\*</sup>, Iwan Ardian<sup>a</sup>, Nutrisia Nu'im Haiya<sup>a</sup> & Niken Tri Winarti<sup>a</sup>

<sup>a</sup>Faculty of Nursing, Universitas Islam Sultan Agung, Semarang, Indonesia, 50183

<sup>b</sup>Faculty of Nursing, Surabaya, Universitas Airlangga, Indonesia, 60115

\*E-mail: ira.suarilah@fkip.unair.ac.id

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Insomnia is a frequent sleep problem experienced by patients undergoing chemotherapy. Various non-pharmacological approaches are applied to manage this condition; however, their influence on sleep quality in patients with breast cancer remains unclear. This study examines the effectiveness of these approaches in reducing insomnia through a systematic review and meta-analysis of randomized controlled trials. Relevant studies are retrieved from CINAHL, Web of Science, PubMed, and Scopus, covering publications from inception to February 2024. The Joanna Briggs Institute (JBI) assesses the methodological quality of the included trials. Data analysis is conducted using STATA 17.0, applying a random-effects model to estimate pooled effect sizes. Thirteen trials (n=13) involving 942 patients with breast cancer receiving chemotherapy are included. Most participants are in stage II, with a mean age of 55.8 years, and the majority are married. The interventions consist of acupuncture, acupressure, electroacupuncture, tai chi, aromatherapy, and massage. The overall analysis shows that non-pharmacological interventions significantly improve sleep quality, with a standardized mean difference (SMD) of -0.91 (95% CI: -1.51 to -0.30,  $p = 0.00$ ,  $I^2 = 94.82\%$ ;  $\tau^2 = 1.15$ ;  $Q = 58.18$ ;  $df = 12$ ). Outcomes are measured using the Pittsburgh Sleep Quality Index (PSQI) and the Insomnia Severity Index (ISI). The findings indicate that these interventions effectively reduce insomnia and enhance sleep quality in patients with breast cancer undergoing chemotherapy. Despite these positive results, broader generalization of the findings still requires further confirmation due to the variability of the non-pharmacological methods applied.

**Keywords:** Breast cancer, Chemotherapy, Insomnia, Non pharmacological, Quality of sleep

**IPC Code:** Int Cl.<sup>26</sup>: NA

Breast cancer remains the leading type of cancer affecting women and occupies the top position among newly diagnosed cancer cases across the globe<sup>1,2</sup>. In 2020, the World Health Organization (WHO) reported 2.26 million women suffering from breast cancer world-wide<sup>3</sup>. According to the WHO, in Indonesia, breast cancer accounts for 18.6% of non-communicable disease (NCDs)-related premature deaths. One of the main causes of the highest number of deaths among women with breast cancer is the delay in medical treatment<sup>4-6</sup>.

Breast cancer management is complex and can be difficult to follow, and chemotherapy is the most recommended treatment<sup>7</sup>. A total of 83% of women with breast cancer living in developed and developing countries were treated with chemotherapy<sup>8</sup>. Nevertheless, sleep disorders are major problems in patients undergoing chemotherapy<sup>9,10</sup>, resulting in

poor quantity and quality of sleep<sup>11</sup>.

The rate of insomnia among patients with breast cancer receiving chemotherapy ranges from 19% to 75%<sup>12</sup>, which is approximately two to three times higher than the prevalence observed in the general population<sup>13</sup>. Due to insomnia, the number of patients withdrawn from chemotherapy increased<sup>14</sup>. For decades, pharmacological interventions, such as benzodiazepines and non-benzodiazepine hypnotics, have been used to help patients with cancer insomnia<sup>12</sup>. Later, the following non-pharmacological interventions are highly preferred: acupuncture, massage, aromatherapy, acupressure, Tai-Ji<sup>15-17</sup>, and massage and aroma therapy is going to be highly preferred<sup>18</sup>.

Previous reviews have reported non-pharmacological interventions, documenting the importance of interventions in reducing the negative effects of chemotherapy. However, it was limited to narratively exploring the effect of non-pharmacological

\*Corresponding author

management on insomnia in the general population<sup>19</sup>, and patients with mixed cancers<sup>15,20</sup>. An up-to-date systematic review and meta-analysis is needed to evaluate the effectiveness and practicality of non-pharmacological interventions in reducing insomnia among patients with breast cancer who are undergoing chemotherapy. It emphasizes the global and rapid development of the potential benefits of non-pharmacological interventions among patients with breast cancer undergoing chemotherapy.

## Methods

This study was recorded in the PROSPERO international prospective register of systematic reviews (registration number CRD42024562510) and was carried out in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines<sup>21</sup>.

### Search strategy

A systematic review was conducted using studies published from database inception to February 2024, drawing data from CINAHL, Web of Science, PubMed, and Scopus. The search strategy was developed based on Medical Subject Headings (MeSH) terms and included the following keywords: "Non-pharmacological therapy" OR "Acupuncture" OR "acupuncture therapy" OR "acupuncture treatment" OR "acupuncture points" OR "acupoint therapy" and acupressure OR "acupoint pressure" OR Music OR "Music Therapy" OR "Tai chi" OR "Tai Ji" OR "Massage therapy" OR "Massage" OR "Aromatherapy" OR "Aroma Therapy" OR "Aroma Therapies" OR Yoga AND "breast cancer " OR "Breast Neoplasms" AND "sleep initiation and maintenance disorders" OR "Insomnia". The initial search strategy was developed for one database and subsequently adapted to suit the search requirements of the remaining databases, as detailed in Appendix 1.

### Eligibility criteria and study selection

The population, intervention or issue of interest, comparison, outcome, and study design (PICOS) framework was applied to define the inclusion criteria. Study eligibility was determined based on the following requirements: a) research involving women with breast cancer who were receiving chemotherapy; b) studies implementing non-pharmacological interventions, including mindfulness, tai chi, acupuncture, acupressure, and hypnotherapy; and c) randomized controlled trial designs. Articles that did

not meet the PICOS criteria, failed to report the number of cases for each outcome, or did not provide full-text access were excluded from the review.

Six independent reviewers screened all potentially relevant titles and abstracts. In cases of disagreement, a third reviewer facilitated discussion until agreement was achieved. The selection process was carried out in two stages: the first stage involved screening based on titles and abstracts, while the second stage consisted of full-text evaluation of the eligible studies.

### Data extraction

Key data from the selected studies was independently collected by two reviewers. The extracted information included the authors' names, year of publication, country of origin, study design, research variables, sample size, measurement instruments, analytical methods, type of intervention, intervention frequency, duration, intensity, as well as participants' age, marital status, and stage of breast cancer. Any differences identified during the extraction process were resolved through discussion until both reviewers reached a shared agreement.

### Study risk of bias assessment

The methodological quality of the included studies was evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal tool for randomized controlled trials. This instrument consists of a series of questions with response options of "Yes," "No," "Unclear," and "Not Available"<sup>22</sup>. Articles were considered high quality when they achieved a score of 75% or higher<sup>23</sup>. The appraisal process was carried out independently by two researchers, and any differences in judgment were discussed and resolved through mutual agreement.

### Statistical analysis

The combined prevalence of poor sleep quality among patients with breast cancer receiving chemotherapy was estimated using a random-effects model<sup>24,25</sup>. Standardized mean differences (SMDs) and 95% confidence intervals (CIs) were calculated to synthesize results from studies that applied different measurement scales by analyzing changes in the mean and standard deviation (SD) of outcomes between pre- and post-intervention assessments. Mean differences and SDs were computed, and SMDs comparing the intervention and control groups were used to determine the magnitude of the effect size based on Cohen's *d*.

Forest plots and funnel plots were produced to support the analytical process in this study. In

addition, variability among the included studies was examined by assessing heterogeneity using the  $I^2$  statistic under a random-effects model; values of 25%, 50%, and 75% represented low, moderate, and high heterogeneity, respectively<sup>26,27</sup>. Statistical significance was defined at a threshold of  $p < 0.05$ . All meta-analyses were performed using the Metaprop command in STATA version 17.

## Results

### Study selection

The initial database search identified 405 articles obtained from Scopus ( $n = 44$ ), PubMed ( $n = 31$ ), Web of Science ( $n = 148$ ), Science Direct ( $n = 319$ ), and CINAHL ( $n = 182$ ). From these records, 341 articles were automatically excluded using Mendeley's screening system and were therefore not included in further analysis. After duplicate records were removed, the titles and abstracts of the remaining 383 studies were reviewed, leading to the exclusion of 261 articles. Subsequently, the full texts of 122 studies were assessed for eligibility, resulting in the removal of 93 papers because they did not address the target population ( $n = 76$ ), did not apply the intervention of interest ( $n = 17$ ), or did not employ the appropriate study design ( $n = 11$ ). In total, 18 studies were identified as eligible (Fig. 1). Among these, four studies were excluded due to irrelevant applications, leaving 13 studies that fulfilled all selection criteria and were included in the meta-analysis.

### Meta-analysis of effectiveness of non-pharmacological interventions among patients with breast cancer undergoing chemotherapy

A total of 13 studies were included to measure the overall effect of non-pharmacological interventions on sleep disorders among patients with breast cancer undergoing chemotherapy. The two instruments used to measure effectiveness were the Pittsburgh Sleep Quality Index (PSQI) ( $n=10$ ) and Insomnia Severity Index (ISI) ( $n=3$ ). The test results in (Fig. 2) forest plot show that the Standardized mean differences (SMDs) are -0.91 (95% CI: -1.51 to -0.30,  $p=0.00$ ,  $I^2 94.82\%$ ;  $\tau^2 1.15$ ;  $Q=159.67$ ;  $df=12$ ), indicating a significant difference in improving sleep quality between the intervention and control groups after the intervention (Fig. 2).

### Quality assessment

The 13 questions from the JBI tool for randomized control studies were used to assess the quality of the 13 included studies. All research scores showed a low risk of bias. The high criteria set to determine the

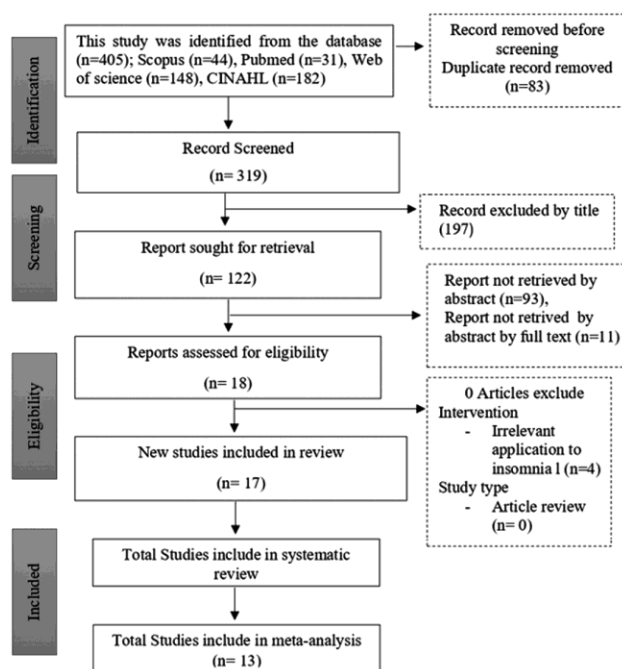


Fig. 1 — Preferred reporting items for systematic reviews and meta-analysis (PRISMA) from Page *et al.*, 2021, <http://www.prisma-statement.org/>

eligibility of participants to be included in the study is an effort to eliminate confounding factors, as well as strategies to deal with confounding factors, resulting in higher scores resulting from the JBI being of good quality. The results of the funnel plot and Egger's regression test showed significant results ( $p = 0.440$  and  $t = 0.77$ , respectively) for the overall effect of non-pharmacological therapy on sleep (Fig. 3).

### Study characteristics

All 13 included studies were RCTs. Two studies for each were conducted in the United States of America (the USA)<sup>17,28</sup>, China<sup>16,29</sup>, Hong Kong<sup>30</sup>, and Iran<sup>31,32</sup>. Another one study was taken in Korea<sup>33</sup>, Turkey<sup>34</sup>, Sweden<sup>35</sup>, and Brazil<sup>36</sup> respectively in (Table 1).

A total of 942 breast cancer participants in (Table 1), with details of 469 participants in the intervention group and 473 participants in the control group with the average age of the intervention group being 54.82 years and the average age of the control group participants being 55.8 years<sup>16,17,28–30,32–35,37</sup>. The marital status were reported in 8 studies<sup>17,29–31,34,36,37</sup>, 75.4% of those in the intervention group were married while 74% in the control group. The breast cancer stages of participants both the intervention and control groups were in stage II, in the intervention group there were 35.4%, and in the control group 37.4% were in stage II<sup>16,29,30,34,35,37</sup>.

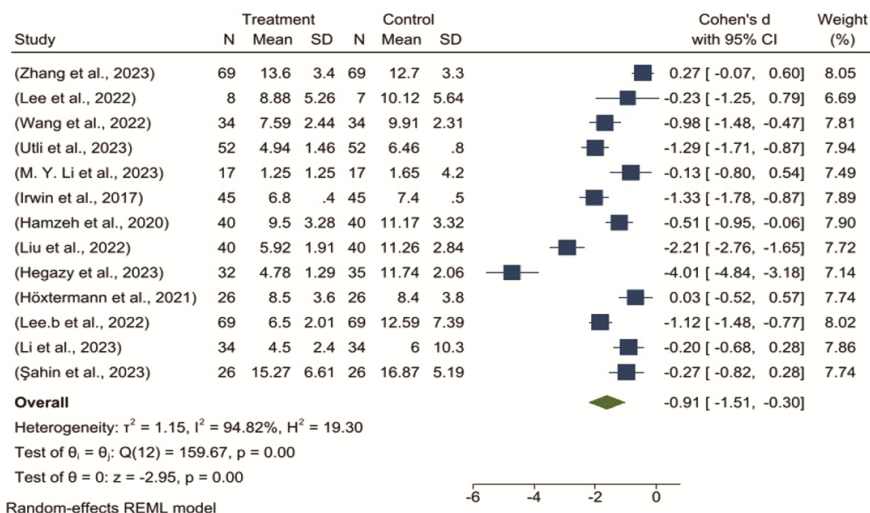


Fig. 2 — Effect of non-pharmacological interventions on quality of sleep of chemotherapy patients with breast cancer after the intervention

Table 1 — Summary of included studies

No	Author/Year	Country	Study Design	Sample Size		Mean Age		Marital Status		Stage			
				Experimental (E)	Controls (C)	Experimental (E)	Controls (C)	Experimental (E)	Controls (C)	I	II	III	IV
1.	Zhang <i>et al.</i> , 2023 <sup>30</sup>	Hong Kong	RCT	69	69	51.7	52.7	M :48 S/D/W: 21	M: 45 S/D/W: 24	E :13 C: 13	E: 29 C: 29	E :15 C :15	E :10 C :10
2.	Lee <i>et al.</i> , 2022 <sup>33</sup>	Korea	RCT	8	7	57.63	63.32	NA	NA	NA	NA	NA	NA
3.	YY Wang <i>et al.</i> , 2022 <sup>29</sup>	China	RCT	34	34	53.43	52.32	M: 31 S/D/W: 3	M: 30 S/D/W: 4	E :10 C :8	E :16 C :20	E :7 C :3	E :1 C :3
4.	Li <i>et al.</i> , 2023 <sup>28</sup>	United States of America	RCT	55	54	60.42	60.70	NA	NA	NA	NA	NA	NA
5.	Utli <i>et al.</i> , 2023 <sup>34</sup>	Türkiye	RCT	52	52	51.9	51.9	M: 43 S/D/W: 9	M: 47 S/D/W: 5	NA	NA	E :31 C :39	E :21 C :13
6.	MY Li <i>et al.</i> , 2023 <sup>16</sup>	China	RCT	17	17	50	53.5	NA	NA	E :7 C :7	E :5 C :5	E :4 C :4	NA
7.	Irwin <i>et al.</i> , 2017 <sup>17</sup>	America	RCT	45	45	59.6	60	M :19 S/D/W: 26	M: 28 S/D/W : 12	NA	NA	NA	NA
8.	Şahin <i>et al.</i> , 2023 <sup>36</sup>	Türkiye	RCT	15	15	NA	NA	M: 14 S/D/W: 1	M: 12 S/D/W: 13	NA	NA	NA	NA
9.	Hamzeh <i>et al.</i> , 2020 <sup>31</sup>	Iran	RCT	40	40	NA	NA	M: 33 S/D/W: 7	M: 30 S/D/W: 10	NA	NA	NA	NA
10.	Liu <i>et al.</i> , 2022 <sup>38</sup>	China	RCT	49	49	NA	NA	M: 39 S/D/W : 10	M: 37 S/D/W : 12	NA	NA	NA	NA
11.	Kashani & Kashani, 2014 <sup>32</sup>	Iran	RCT	27	30	43.23	43.92	NA	NA	NA	NA	NA	NA
12.	Hegazy <i>et al.</i> , 2023 <sup>35</sup>	Sweden	RCT	32	35	64.69	64.91	NA	NA	E :0 C :3	E :20 C :23	E :12 C :9	NA
13.	Höxtermann <i>et al.</i> , 2021 <sup>37</sup>	German	RCT	26	26	55.68	54.8	M :19 S/D/W: 7	M: 19 S/D/W: 7	E :11 C :13	E: 10 C :9	E :4 C :4	NA
Total (Σ)				469	473	548.28	558.07	M =246 S/D/W=84 ΣE = 330	M =248 S/D/W=87 ΣC=335	E :41 C :44 ΣE=226	E :80 C :86 ΣC=230	E :73 C :74	E :32 C :36
Average= Σ ÷ n						54.82	55.8	-	-	-	-	-	-
Percentage (%)						-	-	M = 75.54% S/D/W=25.4%	M = 74.0% S/D/W=25.9%	E :18.1% C :19.1%	E :35.4% C :37.4%	E :32.3% C :32.1%	E :14.2% C :11.3%

Notes: NA= Not Available, RCT: Randomized Controlled Trials, M=Marry, S/D/W=Single/Divorced/Widow/Widower, Σ: Total, n=number of articles

**Non-pharmacological interventions**

The details of the non-pharmacological interventions to increase the quality of sleep

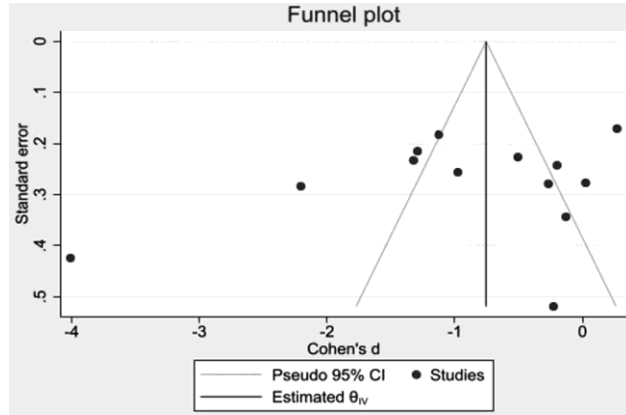


Fig. — 3 Funnel plot for assessed quality of sleep of chemotherapy patients with breast cancer after the intervention

among patients with breast cancer undergoing chemotherapy in this study are depicted in (Table 2). The diverse non-pharmacological interventions used to reduce stress included acupressure (n=4)<sup>16,29,34,38</sup>, acupuncture (n=3)<sup>28,30,37</sup>, aromatherapy (n=2)<sup>31,36</sup>, massage (n=2)<sup>32,35</sup>, and one study applied electroacupuncture<sup>33</sup>.

This study also highlights the benefits of mixed non-pharmacological interventions in improving the quality of sleep in patients with breast cancer undergoing chemotherapy in (Table 2). The following combinations were used: acupuncture with cognitive behavioral therapy (CBT)<sup>28</sup>, acupressure combined with mindfulness-based stress reduction (MBSR)<sup>38</sup>, Tai-Ji therapy combined with CBT<sup>17</sup>, aromatherapy of foot soak and lavender oil inhalation therapy<sup>36</sup>, and mixed aromatherapy combining lavender and peppermint essential oils<sup>31</sup>.

Table 2 — Summary of interventions including studies

No Author/ Year	Participants	Nonpharmacological Interventions		Intervention area or point	Time of Interventions			Outcomes measurements and instrument	
		Name	Type		Duration of intervention	Frequency of intervention	Intervention Leg	Outcomes	Instrument
1. Zhang <i>et al.</i> , 2023 <sup>30</sup>	Breast cancer patients with chemotherapy-associated insomnia	Acupuncture	Single	1. EX-HN1 2. GV20 3. GV24 4. PC6 5. KI3 6. SP6	18 weeks	Daily for the first 6 weeks and 4 times a week for weeks 7 to 18	NA	Insomnia	1. Insomnia severity index (ISI)
2. Lee <i>et al.</i> , 2022 <sup>33</sup>	Breast cancer related insomnia for at least 3 months, meeting the criteria for insomnia disorder of the Diagnostic and Statistical Manual of Mental Disorders	Electroacupuncture	Single	1. GV20 2. EX-HN3 3. Bilateral HT7 4. PC6 5. BL63 6. KI4	4 weeks	3 times a week	30 min	Insomnia	1. Insomnia Severity Index (ISI)
3. Wang <i>et al.</i> , 2022 <sup>29</sup>	Breast cancer patients with chemotherapy associated insomnia	Adaptive Auricular Point Acupressure	Single	1. Shenmen (TF4), 2. Xin 3. Pizhixia	3 Weeks	4 times a day	30 min every morning, afternoon, evening and evening	Quality of sleep	1. Pittsburgh Sleep Quality Index (PSQI)
4. Li <i>et al.</i> , 2023 <sup>28</sup>	Breast cancer patients with chemotherapy who reported insomnia and moderate or worse fatigue	Acupuncture and cognitive behavioral therapy	Combination	1. HT 7 2. SP 6 3. GV 20 4. GV 24 5. Shenmen	8 Weeks	2 times per week for the first 2 weeks, and 1 time per week from week 3 to week 8	Weeks 1-2: 60 min Weeks 3-8: 30 min	Insomnia and fatigue	1. Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF) Questionnaire
5. Utli <i>et al.</i> , 2023 <sup>34</sup>	Breast cancer patients with chemotherapy who reported pain and fatigue of stage III and IV cancer patients receiving palliative care	acupressure	Single	NA	4 Weeks	1 time a day	20 min	Pain Insomnia Fatigue	1. Numeric Pain Rating Scale Questionnaire 2. Brief Fatigue Inventory Questionnaire 3. AFF Questionnaire

... Contd.

Table 2 — Summary of interventions including studies (Contd.)

No Author/ Year	Participants	Nonpharmacological Interventions		Intervention area or point	Time of Interventions			Outcomes measurements and instrument	
		Name	Type		Duration of intervention	Frequency intervention	Intervention Leg	Outcomes	Instrument
6. Li <i>et al.</i> , 2023 <sup>16</sup>	Breast cancer patients with chemotherapy who reported fatigue-sleep disturbance-depression symptom cluster (FSDSC)	acupressure	Single	NA	7 Weeks	1 time a day	36 min	Insomnia Anxiety Quality of life	1. Pittsburgh Sleep Quality Index (PSQI) 2. Hospital Anxiety and Depression Scale (HADS) 3. Functional Assessment of Cancer Therapy-Breast Cancer (FACT-B)
7. Irwin <i>et al.</i> , 2017 <sup>17</sup>	Breast cancer patients with chemotherapy who reported insomnia	Tai Chi Chi (TCC) and Cognitive behavioral therapy (CBT)	Combination	NA	3 months	1 time a week	2 h	Quality of sleep	1. Pittsburgh Sleep Quality Index (PSQI)
8. Şahin <i>et al.</i> , 2023 <sup>36</sup>	Breast cancer patients with chemotherapy who reported insomnia	Aromatherapy (foot soak and lavender oil inhalation therapy)	Combination	NA	2 Weeks	1 time a day (At night)	Soak your feet for 20 min at a temperature of 38-40 <sup>0</sup> combined with inhalation therapy for 5 min	Insomnia	1. Insomnia Severity Index (ISI)
9. Hamzeh <i>et al.</i> , 2020 <sup>31</sup>	Breast cancer patients with chemotherapy who reported insomnia	Aromatherapy (Aromatherapy with Lavender and Peppermint Essential Oils)	Single	NA	1 Week	1 time a day (At night)	20 min	Quality of sleep	1. Pittsburgh Sleep Quality Index (PSQI)
10. Liu <i>et al.</i> , 2022 <sup>38</sup>	Breast cancer patients with chemotherapy who reported sleep disorders, as well as the potential effects of these interventions on relieving fatigue, anxiety, and depression	Acupressure (Mindfulness-based stress reduction with acupressure)	Combination	1. Yin-tang, 2. Shenmen, 3. Neiguan, 4. Baihui, 5. Anmian	1 week	MBSR at 10.00 am then continued with 30 minutes of acupressure only Acupressure at 15.00 30 minutes (each point 6 minutes)	One time MBSR and 2 times a day Acupressure	Quality of sleep	1. Pittsburgh Sleep Quality Index (PSQI)
11. Kashani & Kashani, 2014 <sup>32</sup>	Breast cancer patients with chemotherapy who reported insomnia	Massage	Single	back, spine, shoulders and neck	4 Weeks	3 times a week	20 min at night	Quality of sleep	1. Pittsburgh Sleep Quality Index (PSQI)
12. Hegazy <i>et al.</i> , 2023 <sup>35</sup>	Breast cancer patients with chemotherapy who reported insomnia	Massage	Single	back, spine, shoulders and neck	6 Weeks	2 times a week	30 min	Quality of sleep	1. Pittsburgh Sleep Quality Index (PSQI)
13. Höxtermann <i>et al.</i> , 2021 <sup>37</sup>	Breast cancer patients with chemotherapy who reported insomnia	Auricular acupuncture	Single	ears	5 Weeks	2 times a week	20 min	Quality of sleep Anxiety Quality of sleep	1. Pittsburgh Sleep Quality Index (PSQI) 2. Hospital Anxiety and Depression Scale (HADS) 3. Functional Assessment of Cancer Therapy-Breast Cancer (FACT-B)

### **Length of intervention**

Nine studies (n=9) in (Table 2) reported an intervention length of 1 to 4 weeks<sup>29,31-34,36-39</sup>. Three studies (n=3) were 7 to 8 weeks<sup>16,28,35</sup>, and two studies (n=2) were 13 to 20 weeks<sup>17,30</sup>.

Acupuncture was applied for 4-18 weeks, with a frequency of 1-3 times per day, each therapy lasting 20-30 min<sup>28,30</sup>, electro acupuncture delivered for 4 to 6 weeks, 3 times per day, lasting 26-30 min<sup>33</sup>, acupressure was applied for 3 - 7 weeks, 1 to 4 times per day, each therapy lasting 30 min<sup>16,29,34</sup>. Tai-Ji therapy was delivered for 3 months, 2 h weekly<sup>17</sup>. Aromatherapy was delivered 1 to 2 weeks, 1 time a day at night, 20 min per intervention<sup>31,36</sup>, massage was given for 4 to 6 weeks, every 2 days, 20 - 30 min per intervention<sup>32,35</sup>.

### **Discussion**

This meta-analysis was conducted to evaluate how effective non-pharmacological interventions are in improving sleep quality among patients with breast cancer who are receiving chemotherapy. Analyses revealed that non-pharmacological implementation effectively increased quality of sleep-in among people living with breast cancer undergoing chemotherapy. The following variety of interventions were specifically described and tested to the outcomes; acupressure<sup>16,29,34,38</sup>, conventional acupuncture<sup>28,30,37</sup>, electroacupuncture therapy<sup>33</sup>, Tai-Ji<sup>17</sup>, aromatherapy intervention<sup>31,36</sup>, and massage<sup>32,35</sup>.

In the present analysis, among the various intervention programs aimed at improving sleep quality, acupressure is identified as the most frequently used strategy. This intervention is commonly implemented over a period of 3-7 weeks, delivered one to four times daily, with each session lasting approximately 30 min<sup>16,29,34</sup>. Meanwhile, the most effective therapy considering the shortest duration of time is aromatherapy with length of intervention was 1 to 2 weeks, 1 time a day at night, for a total 20 minutes per intervention<sup>31,36</sup>.

Concerning the diversity of non-pharmacological interventions, this study highlights acupressure as the most chosen non-pharmacological intervention and widely applied to reduce sleep disorders<sup>16,29,34,38</sup>. Acupressure is well-known as a therapeutic modality originating from China. It has working principle to restore balance by stimulating different acupuncture points<sup>40</sup>. Acupressure works by delivering sensory input to the trigeminal sensory nuclear complex

(TSNC), which then projects signals to brain areas responsible for regulating neurobehavioral interaction with the surrounding environment<sup>41</sup>. The neuromodulatory activity of the TSNC and its functional connections with the ascending reticular activating system influence serotonin- and noradrenaline-producing neurons in the brainstem reticular formation, thereby contributing to the regulation of excessive sympathetic nervous system activity<sup>42</sup>. The result is in line with previous study that noted interventions involving variety of acu-punctures are beneficial to reduce sleep disorders such as insomnia in cancer patients<sup>43</sup>.

A various type of acu-punctures has developed from traditional needles to electroacupuncture, laser acupuncture, transcutaneous electrical acupuncture stimulation, and acupressure<sup>44</sup>. Types of electroacupuncture<sup>33</sup>, and auricular acupuncture were used in this study<sup>37</sup>. Electroacupuncture (EA) combines traditional acupuncture techniques with electrical stimulation. This therapy is grounded in the theory of meridians and collaterals within traditional Chinese medicine, in which specific points are stimulated to produce therapeutic effects. Insomnia is recognized as a condition resulting from dysregulation of the brain's nervous system. Electroacupuncture modulates this system by influencing neural activity and regulating inflammatory markers such as IL-1 $\beta$  as well as brain-derived neurotrophic factors<sup>45</sup>. Further, EA stimulates the vagus nerve and the parasympathetic nervous system, as well as other neurotransmitters that act on the sleep center, including melatonin. Melatonin plays an active role in regulating sleep by reducing sleep latency and extending the duration of slow-wave sleep<sup>46</sup>. Those activities result secretion of melatonin and end-up with deep sleep.

Concerning frequency, duration, and length of intervention, this study shows aromatherapy was the fastest targeted effects<sup>31,36</sup>. Aromatherapy with main ingredients linalool and linalool acetate effectively improve quality of sleep by relaxing the nervous system and the muscles. For example; aroma of Lavender was mostly chosen to relax and stimulate the frequency of alpha brainwaves. Pleasant scent or aroma is known to have sedative and anti-neuro-depressive effects that helped breast cancer patients minimize sleep disorders caused by chemotherapy<sup>47</sup>.

Another non-pharmacological intervention was massage<sup>32,35</sup>. Those studies presented massage

therapy in various forms, including stroking, kneading, applying friction, and other physical manipulations of muscles and connective tissue. The basic principle of massage therapy is to modulate body functions through careful manipulation of the muscles of the body to produce certain physiological effects on the musculoskeletal system, nerves, and blood vessels, thereby relieving tension, and improving sleep quality<sup>48</sup>. Massage was found as the most popular non-pharmacological interventions applied in people with palliative care<sup>49</sup>. In line with past meta-analysis, the current study considers massage as safe, low cost, has minimal risks, and no adverse effects intervention that effectively reduce sleep disorders among breast cancer patients undergoing chemotherapy.

A significant change in quality of sleep was also demonstrating in a single group of those treated by combination two non-pharmacological interventions. Mixed interventions combining acupuncture with CBT found decreasing insomnia through focusing on changing thought patterns and sleep behavior<sup>28</sup>. Acupuncture provides a physical approach that can provide direct relief for physical symptoms that disturb sleep, such as pain and muscle tension while CBT helps patients with cancer identify and change unhealthy sleep patterns and manage stress and anxiety<sup>50</sup>. It has been studied single CBT as non-pharmacological intervention might not directly reduce discomfort experienced by cancer patients undergoing chemotherapy<sup>51</sup>. This study strengthened the evidence on a combination of acupuncture and CBT was more represent holistic, comprehensive, and effective for treating insomnia of breast cancer patients undergoing chemotherapy.

Accordingly CBT also was applied in combination with Tai-Ji and effectively increase quality of sleep of breast cancer patients undergoing chemotherapy<sup>17</sup>. Light and gentle movements of Tai-Ji exercise regulates the physiological functions of organs, tissues and cells throughout the body, carried out through muscle activation through regular movements to suppress the level of arousal, and shorten the awakening cycle<sup>52</sup>. However, the disadvantages of Tai-Ji include a steep learning curve, where patients may need time to master proper movements to gain maximum benefit. Additionally, Tai-Ji's practice requires time commitment and consistency in regular practice to gain significant results<sup>52</sup>. This mixed non-pharmacological interventions help patient to relieve

tension in the body and mind, while identify and change thought patterns that may disrupt sleep<sup>53</sup>.

The combination of acupressure with MBSR are another potential non-pharmacological interventions to addresses the psychological factors underlying insomnia<sup>38</sup>. MBSR teaches meditation, yoga, and self-awareness techniques to reduce stress, improve sleep quality, and provide patients with tools to manage anxiety or tension, which can worsen insomnia<sup>54</sup>. By combining acupressure, which reduces physical symptoms, with MBSR, which manages stress and improves psychological well-being, chemotherapy patients can obtain a comprehensive approach that helps them sleep better<sup>55</sup>. Additionally, acupressure has the advantage of non-invasively reducing physical symptoms, such as pain and nausea, in patients undergoing chemotherapy. However, the drawback of acupressure lies in repeated sessions of long-term effects<sup>56</sup>. In addition, its effectiveness depends on the skill of the practitioner.

A mixed intervention of acupressure with mindfulness-based stress reduction (MBSR) is another potential solution because it provides a holistic approach. MBSR activities covers meditation, yoga, and self-awareness techniques to reduce stress, improve sleep quality, and provide patients with tools to manage anxiety or tension, which can worsen insomnia<sup>54</sup>. A combination of acupressure and MBSR effectively reduces physical symptoms, reduce stress and improves psychological well-being resulted sleep better<sup>55</sup>. Another form of mixed non-pharmacological intervention was Tai-Ji and mindfulness-based stress reduction (MBSR). However, Tai-Ji required series of practices to gain sufficient effects. Therefore, the effectiveness depends on the skill of the practitioner.

Concerning instrument to measure targeted outcomes in this meta-analysis, the PSQI and the ISI were used the effectiveness of the given interventions. The two instruments have been widely applied and recognized for its psychometrics testing<sup>57,58</sup>. Based on the available evidence, both single and combined non-pharmacological interventions among patients with breast cancer undergoing chemotherapy appear to be promising. However, further investigation is still required to clarify whether individual interventions or combinations of interventions provide greater benefits compared to the effects of a single approach alone. Therefore, additional studies that examine which combinations and sequences of treatments yield the most optimal outcomes are considered necessary.

**Limitations**

Despite the considerable effectiveness of non-pharmacological interventions in reducing sleep disturbances among patients with breast cancer undergoing chemotherapy, several limitations remain in the analysis of these interventions. First, different levels of risk of bias are identified across the included studies, indicating the need for more rigorously designed trials in future research. Secondly<sup>17,28,31-33,36,38</sup>, several of the thirteen studies do not report the stage of breast cancer, which may limit the representativeness of the findings for the broader breast cancer population. Third, substantial heterogeneity is observed in the pooled outcome analysis. This variation among studies is likely related to multiple factors, including the wide range of non-pharmacological programs implemented, differences in intervention duration, and variability in follow-up periods. Together, these factors contribute to the high level of heterogeneity noted, highlighting the complexity of evaluating intervention effectiveness in addressing sleep disorders. Fourth, some of the randomized controlled trials included present insufficiently detailed methodological descriptions, which may have a significant impact on the potential risk of bias in the pooled estimates. This bias may result from deviations from the intended intervention protocols, such as the absence of participant or provider blinding. In addition, several outcomes associated with other effects of chemotherapy, including pain, hot flashes, nausea, vomiting, and fatigue, are not examined. These limitations emphasize the importance of conducting more comprehensive and methodologically sound studies to better evaluate targeted non-pharmacological interventions for patients with breast cancer undergoing chemotherapy.

**Conclusion**

The current meta-analysis indicated that non-pharmacological interventions effectively reduce insomnia and improve quality of sleep of breast cancer patients undergoing chemotherapy as well. This meta-analysis emphasized the effectiveness of acupuncture, electroacupuncture, acupressure, massage, aromatherapy, CBT, MBSR, and Tai-ji. Aromatherapy delivered for 20 min per night, in a minimum of one week effectively reduced insomnia. This highlights the potential of single and mixed non-pharmacological interventions as a valuable treatment

option for addressing sleep disorders among breast cancer patient undergoing chemotherapy. The application of a regular non-pharmacological intervention might preserve the quality of sleep of patients which is crucial in palliative care. Therefore, it is essential to tailor single or mixed interventions non-pharmacological interventions that fit the patient's needs. Each intervention can be set in different durations, and intensities to enable patients to respond appropriately to any sleep disorder.

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**Conflict of Interest**

None declared

**Declaration of use of AI in scientific writing**

Nothing to disclose.

**Author Contributions**

IRA: contributed to the study design, data collection, and data analysis, participated in manuscript preparation and critical revision, and approved the final version. TS: contributed to the research design, data acquisition, and interpretation, assisted in drafting and revising the manuscript, and approved the final version. IS: contributed to the study framework, data collection, and interpretation, supported manuscript writing and revision, and approved the final version. IA: contributed to research planning, data acquisition, and analysis, participated in manuscript drafting and critical review, and approved the final version. NNH: contributed to study conceptualization, data collection, and analysis, assisted in manuscript preparation and revision, and approved the final version. NTW: contributed to research design, data collection, and interpretation, participated in manuscript drafting and revision, and approved the final version.

**Data Availability**

The data produced and or examined in this study can be obtained from the corresponding author upon a reasonable request.

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