



## Effect of aromatherapy on cancer complications: A systematic review

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### ABSTRACT

**Purpose:** The aim of this study was to determine the effect of aromatherapy on cancer complications.

**Methods:** In this systematic review, international (PubMed, Web of Science, Scopus, EMBASE and CENTRAL) and national databases (SID and Magiran) were searched from inception of the databases to April 31, 2019. JBI and Jadad scales were used to assess the quality of the studies included.

**Results:** of 43 Studies conducted on 3239 cancer patients in 13 countries from 1995 to 2019, entered the final stage. The results showed that the aromatherapy improves the various physical and psychological complications, although few studies have shown that aromatherapy had no effect on skin reactions.

**Conclusion:** Considering the various complications and costs in cancer patients, it seems that the aromatherapy can be used as a proper supplemental treatment to improve complications, although further studies are needed to determine the protocol and the standard dosage.

### 1. Background

Cancer is one of the most important health challenges in the world today, with 1,762,450 new cancer cases and 606,880 deaths occurring in the United States only in 2018, the most fatal of which is the lung cancer and the most common type was the breast cancer.<sup>1</sup> Cancer patients suffer from various physical complications (hair loss, nausea, vomiting, pain, fatigue, loss of appetite, malnutrition, and weakness) and psychological complications (depression, stress, and anxiety), which can reduce their quality of life.<sup>2,3</sup> Today, despite the many advances in cancer treatment and the use of various therapies such as surgery, chemotherapy, hormone therapy, radiotherapy, and immunotherapy or biological therapy, patients are still suffering from the above complications due to the absence of the definitive treatment.<sup>4</sup> Today, the use of soothing treatments, such as complementary and alternative medicine, become more commonly used to relieve the cancer symptoms considering their organic nature, low risk, fewer complications, and lower costs.

Aromatherapy has been used widely as a popular method of

complementary medicine in treating various complications in various patients.<sup>5,6</sup> Aromatherapy is used in the form of massage, bathing, and inhalation through essential oils obtained from aromatic herbs. In the inhalation aromatherapy, the aromatic essence stimulates the olfactory receptor cells and then transmits them to the limbic system and causes a positive effect.<sup>7</sup> In Aromatherapy massage, plant aromatic and volatile oils are gradually absorbed through the skin barrier within 10 to 40 min and exert their physiological and physical effects.<sup>8</sup> Different individual studies have shown that the aromatherapy of cancer patients has been used to improve the complications of fatigue, depression, pain, sleep disorders, stress, anxiety, nausea and vomiting, and increase their quality of life.<sup>9–12</sup> Individual studies have shown that cancer patients use a wide range of different types of inhalation aromatherapy and aromatherapy massage through inhalation of odors and massage of the skin with pure odors or diluted with other scents.<sup>13–18</sup> Aromatherapy is applied either topically or through inhalation. Topical use includes the aromatherapy massage in which the aroma is absorbed through the skin. In the inhalation method, the odors are spread in the air through a diffuser or spray; then, the scent molecules are absorbed through the

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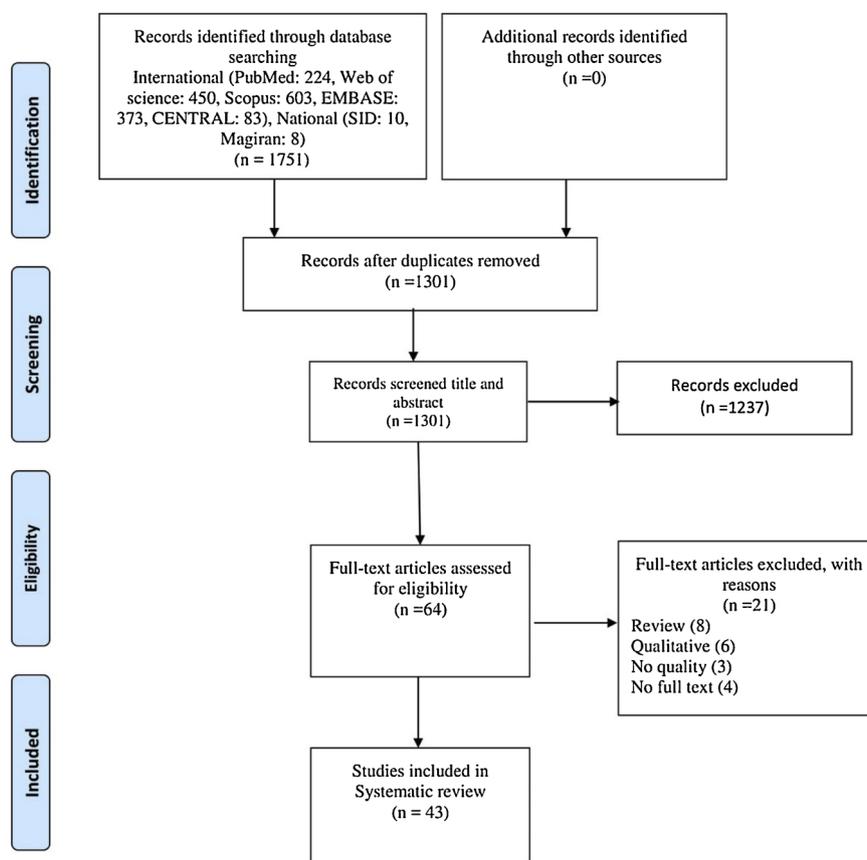


Fig. 1. Study selection process.

nasal membrane, stimulate the olfactory nerve, and produce nerve impulses. This impulse passes via the nervous system, reaches the limbic system of the brain, and exerts its relaxation and physiological effects.<sup>19,20</sup>

Previous relevant review studies usually reviewed only one source until 2010.<sup>14</sup> As well as another recent studies were carried out as literature review.<sup>21</sup> Despite existing review and individual studies, due to the variety of aromas, doses used, and the duration of aromatherapy courses, there is still no comprehensive study providing the same guide used by health care providers, nurses, and patients. Therefore, this study investigates the effects of aromatherapy on cancer complications in cancer patients based a systematic review approach in order to more accurately and comprehensively measure the effects of different aromas used in cancer patients.

## 2. Methods

### 2.1. Design and eligibility criteria

This systematic review study was conducted using Cochran's book and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used to report the present systematic review.<sup>22</sup> All clinical trial studies (with or without control group), quasi-experimental studies that examined the effects of any aroma in the form of inhalation, massage, bath, and drinks were included. To comprehensively examine the aromas used and complications in cancer patients, there is no limitation on the aromas used and outcomes. The target population included cancer patients. Review and qualitative, and poor quality studies, and non-full text articles were excluded. All articles were included without applying any language and time restrictions.

### 2.2. Search strategy

The electronic databases were searched from the inception of databases to April 31, 2019 and included international (PubMed, Scopus, Web of Science, EMBASE, and Cochrane CENTRAL) and national databases (SID and Magiran). The MEDLINE search strategy was first finalized, then adapted for search in other databases. PROSPERO was also searched for ongoing or recently completed systematic reviews. The search was conducted by two researchers independently. The search strategy was prepared using the MESH terms, Emtree vocabulary and free words from related articles. Keywords used included: Aromatherapy, inhalation aromatherapy, massage aromatherapy and cancer.

### 2.3. Selection of studies and data extraction

According the protocol, two researchers conducted the search, screening, quality assessment, and extraction of data. Extracted items included the (id, author, study characteristics (Country, Design, and number of Participants), Participant's characteristics (Age (mean or range), Gender, Type of Cancer, and Risk of bias), outcomes Intervention (Treatment group(s), Type, dose, frequency of Aromatherapy and Administration method, Duration per session/Total number of sessions/Total Duration of intervention) and results were also collected.

### 2.4. Quality assessment

The quality assessment of the RCT included studies were assessed using the Jadad scale whose rating criteria take into account randomization, double blinding, and withdrawals or dropouts.<sup>23</sup> The scoring

**Table 1**  
Description of the study characteristics, outcome, measurement, interventions and results.

ID	Author	Study Characteristics 1. Country 2.Design 3.Participants	Participant's characteristics 1. Age (mean or range) 2.Gender (male/female) 3.Type of Cancer 4.Risk of bias	Outcomes 1.Variables 2.tools	Intervention 1. Treatment group(s) 2.Type, dose, frequency of Aromatherapy and Administration method 3.Duration per session/Total number of sessions/Total Duration of intervention	Results
1	Ardakani, Maria Tavakoli (2016) <sup>25</sup>	1.Iran 2.RCT 3.60	1.36 2.31/29 3.Multiple type 4.5	1. Oral mucositis 2. NCI-CTC	1. Herbal aromatherapy using <i>Matricaria recutita</i> and <i>Mentha piperita</i> herbal mouthwash. 2. Herbal aromatherapy, three times a day 3.30 S, 21, one week.	Positive effect on oral mucositis
2	Ayik, C. (2018) <sup>26</sup>	1.Turkey 2.RCT 3.80	1.61 2.44/36 3. Colorectal Cancer 4.2	1. Anxiety, sleep quality 2. SAI, RCSI.	1. Massage aromatherapy using lavender. 2. Massage aromatherapy, 5 ml, twice times a day. 3.10 min, two, one day.	Positive effect on anxiety, sleep quality
3	BabashahKohanestani, F (2013) <sup>9</sup>	1.Iran 2.Quasi-experimental 3.70	1.ND 2.ND 3.AML 4.Included	1. Pain 2.VAS	1. Inhalation aromatherapy using lavender. 2. Inhalation aromatherapy, 2 drops on a gaz, once time a day. 3.9 hours, three, three days.	Positive effect on pain
4	Barclay, Janet (2006) <sup>27</sup>	1.United Kingdom 2.RCT 3.81	1.61 2.77/4 3.Lymphedema 4.3	1. Symptom relief, wellbeing 2. MYMOP2	1. Massage aromatherapy using wheatgerm oil with fennel, sage, geranium, black pepper and juniper essential oils. 2. Massage aromatherapy, 5 ml, and daily. 3. Unknown, 180, six month.	Positive effect on a symptom relief, and wellbeing
5	Blackburn, L. (2017) <sup>13</sup>	1.USA 2.RCT 3.50	1.19-72 2.28/22 3.AML 4.	1.Insomnia, Symptom burden 2.PSQI, ESASR	1. Inhalation aromatherapy using wheatgerm with lavender, peppermint, or chamomile. 2. Inhalation aromatherapy, one drop of each aromas, daily. 3. Night, 14, three weeks.	Positive effect on insomnia, Symptom burden
6	Chang, S. Y. (2008) <sup>28</sup>	1.South Korea 2.Quasi-experimental 3.58	1.62.4 2.44/14 3.Multiple type 4.	1. Pain, Depression, Anxiety 2. BPI-K, SDS, SAT.	1. Massage aromatherapy using Bergamot, Lavender, and Frankincense. 2. Massage aromatherapy, 50 ml, and daily. 3.5 min, 7, one week.	Positive effect on pain and depression No effect on Anxiety
7	Corner, J. (1995) <sup>29</sup>	1.United Kingdom 2.Quasi-experimental 3.52	1.47.8 2.5/47 3.Multiple type 4.included	1. Anxiety 2. HADS	1. Massage aromatherapy using a lavender, rosewood, lemon, rose & valerian blend. 2. Massage aromatherapy, %2, weekly. 3. 30 M in. 8, eight weeks.	Positive effect on anxiety
8	Dyer, J (2013) <sup>30</sup>	1.United Kingdom 2.RCT 3.115	1.53.7 2.16/99 3.Multiple type 4. 3	1.Wellbeing 2.MYCaW	1. Massage aromatherapy using a volatile. 2. Massage aromatherapy, Unknown. 3. Unknown, 4, Unknown.	Positive effect on wellbeing
9	Eghballi, M. (2018) <sup>31</sup>	1.Iran 2.RCT 3.100	1.46 2.0-100 3.Breast cancer 4.3	1. Nausea and Vomiting 2. RINVR	1. Inhalation aromatherapy using the Peppermint. 2. Inhalation aromatherapy, 2 drops, three times daily. 3.20 min, three, one day.	Positive effect on nausea and vomiting
10	Evans, A. (2018) <sup>32</sup>	1.USA 2.RCT 3.49	1.8 to 21 2.30/19 3.Multiple type 4.4	1. Nausea and Vomiting 2. PeNAT	1. Inhalation aromatherapy using essential oil of ginger. 2. Inhalation aromatherapy, 4 drops, Unknown. 3. Unknown, three, Unknown.	No effect on nausea and vomiting
11	Goepfert, M. (2017) <sup>15</sup>	1.Germany 2.RCT 3.20	1. ND 2.10-10 3.Multiple type 4. 3	1. Vital Signs 2.Physical exam	1. Inhalation aromatherapy using essential oil of lemon and Lavender. 2. Inhalation aromatherapy, 3-4 drops by surgical mask. 3.10 min, four, 40.	Improved the vital signs
12	Graham, P.H (2003) <sup>33</sup>	1.Australia 2.RCT 3.313	1.65 2.162/151 3.Multiple type 4.3	1. Anxiety and depression 2. HADS, SPHERE	1. Inhalation aromatherapy using essential oil of Lavender and bergamot. 2. Inhalation aromatherapy, 3 drops by gas during radiotherapy 3.15-20 min, Unknown, 1.5.h.	no effect on depression, Positive effect on anxiety
13	Gravett, Peter (2001) <sup>34</sup>	1.United Kingdom 2.Case series 3.32	1.ND 2.0/30 3.Breast cancer 4.ND	1. Skin disorders. 2.WHO criteria	1. Massage aromatherapy using calendula and chamomile. 2. Massage aromatherapy, Unknown. 3. Unknown, Unknown, 14 Days.	no effect on skin rashes

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Table 1 (continued)

ID	Author	Study Characteristics	Participant's characteristics	Outcomes	Variables	Intervention	Results
14	Halm, M. A. (2014) <sup>35</sup>	1. USA 2. RCT 3. 24	1. ND 2.0/24 3. Breast cancer 3.3	1. Skin reaction, pain intensity, and QOL 2. RTOG, P-VAS, QLI	1. Skin reaction, pain intensity, and QOL 2.,	1. Massage aromatherapy using Helichrysum; Frankincense; Lavender, and Geranium. 2. Massage aromatherapy, three times a day. 3. Unknown, 90, 1 month.	no effect on skin reaction, pain intensity, and QOL
15	Heydarirad, G (2019) <sup>10</sup>	1. Iran 2. RCT 3. 45	1.50 2.17/28 3. Multiple type 4.4	1. Sleep quality 2. PSQI	1. Sleep quality 2. PSQI	1. Inhalation aromatherapy using Rosa damascene. 2. Inhalation aromatherapy, 5 drops, every night. 3. Unknown, 14, two weeks.	Positive effect on Sleep quality
16	İlter, S. M. (2019) <sup>36</sup>	1. Turkey 2. Quasi-experimental 3. 60	1.20-60y 2.29/31 3. Multiple type 4. Included	1. pain, vital sign 2. VAS	1. pain, vital sign 2. VAS	1. Inhalation aromatherapy using orange, chamomile, and lavender. 2. Inhalation aromatherapy, three drops, every night.	Positive effect on pain. No effect on vital signs.
17	Imanishi, J (2009) <sup>37</sup>	1. Japan 2. RCT 3. 12	1.40-59 2.0/12 3. Breast cancer 4.2	1. Anxiety, Immune system markers 2. HADS, FITC, CD16, PE-CD8, FITCCD4 antibodies, CFS-CXCR3 and PE-CCR4	1. Anxiety, Immune system markers 2. HADS, FITC, CD16, PE-CD8, FITCCD4 antibodies, CFS-CXCR3 and PE-CCR4	1. Massage aromatherapy using Sandalwood, Lavender and orange. 2. Massage aromatherapy, Unknown, twice a week. 3. 30 min, 8, 4 weeks.	Positive effect on anxiety, No effect on mood status, and Immune Measurements
18	Izgu, N (2019) <sup>38</sup>	1. Turkey 2. RCT 3. 46	1.56 2.27/19 3. Gastrointestinal cancer 4.3	1. Painful paresthesia, Neuropathic Pain and Fatigue 2. NPRS, PFS	1. Painful paresthesia, Neuropathic Pain and Fatigue 2. NPRS, PFS	1. Massage aromatherapy using peppermint, chamomile, and rosemary. 2. Massage aromatherapy, 50 ml, three times in week. 3. 40 min, 18, 6 weeks.	Positive effect on pain and fatigue
19	Khalili, Z (2014) <sup>17</sup>	1. Iran 2. RCT 3. 66	1.44.6 2.38/28 3. Multiple type 4.4	1. Nausea and Vomiting 2. VAS	1. Nausea and Vomiting 2. VAS	1. Inhalation aromatherapy using Cardamom oil. 2. Inhalation aromatherapy, two drops, two times one day. 3. 5 min, 2, 1 day.	Positive effect on nausea and vomiting
20	Khiewkhem, S. (2013) <sup>18</sup>	1. Thailand 2. RCT 3. 66	1.59 2.41/25 3. Colorectal Cancer 4.3	1. Immune system markers, severity of the symptoms (pain, fatigue, stress or anxiety, nausea, and depression) 2. severity scale, Blood sample	1. Immune system markers, severity of the symptoms (pain, fatigue, stress or anxiety, nausea, and depression) 2. severity scale, Blood sample	1. Massage aromatherapy using coconut and ginger oil. 2. Massage aromatherapy, Unknown, three times. 3.45 min, 3, one week.	Positive effect on fatigue, presenting symptom, pain and stress and Immune system profile
21	Kite et al. (1998) <sup>39</sup>	1. United Kingdom 2. Quasi-experimental 3. 58	1.58 2.11/47 3. Multiple type 4. Included	1. anxiety 2. HADS	1. anxiety 2. HADS	1. Massage aromatherapy using Lavender, chamomile, geranium, juniper, bergamot, jasmine and rose. 2. Massage aromatherapy, two days each week. 3.45 min, 12, six weeks.	positive effect of Anxiety
22	Kohara, H (2004) <sup>40</sup>	1. Japan 2. Quasi-experimental 3. 20	1.64 2.11/9 3. Multiple type 4. Included	1. Fatigue 2. CFS	1. Fatigue 2. CFS	1. Bath aromatherapy using Lavender. 2. Bath aromatherapy, 1%, two drops in warm water. 3. three min, 1, one day.	Positive effect on fatigue
23	Lai, T. K. (2011) <sup>41</sup>	1. China 2. RCT 3. 32	1.31-90 2.24/8 3. Multiple type 4.3	1. Constipation, Quality of life 2. CAS, MQOL-HK.	1. Constipation, Quality of life 2. CAS, MQOL-HK.	1. Massage aromatherapy using orange, pepper, rosemary, marjoram and olive oils. 2. Massage aromatherapy, Unknown, once time daily. 3.15-20 min, 5, five days.	Positive effect on constipation and quality of life
24	Louis, M. (2002) <sup>11</sup>	1. USA 2. Quasi-experimental 3. 17	1.61 2.9/8 3. Multiple type	1. Vital sign, pain, anxiety, & depression 2. BP machine, verbal 11-point scale	1. Vital sign, pain, anxiety, & depression 2. BP machine, verbal 11-point scale	1. Massage aromatherapy using lavender. 2. Massage aromatherapy, 3 drops, once time. 3.60 min, 1, one days.	Positive effect on Vital sign, pain, anxiety, and depression
25	Lua, P. I. (2015) <sup>12</sup>	1. Malaysia 2. RCT 3. 60	1.47.6 2.0-60 3. Breast cancer 4.3	1. Nausea and Vomiting, and quality of life 2. VAS, EORTCCQLQ-C30 scores	1. Nausea and Vomiting, and quality of life 2. VAS, EORTCCQLQ-C30 scores	1. Inhalation aromatherapy using ginger oils. 2. Inhalation aromatherapy, 2 drops, three times daily. 3.2 min, 15, 5 days.	No significant effect on nausea and vomiting Positive effect on quality of life.
26	Maddocks-Jennings, W (2009) <sup>42</sup>	1. Australia 2. RCT 3. 19	1.45-75 2.15/5 3. head and neck cancer 4.3	1. Oral mucositis, Pain, nutrition status 2. VAS, VAS, Unknown	1. Oral mucositis, Pain, nutrition status 2. VAS, VAS, Unknown	1. Gargle using manuka, kanuka oils. 2. Gargle, 2 drops in 15 ml warm water, 3-5 times daily. 3.15 S, 24-40, 8 days.	Positive effect on oral mucositis, Pain, nutrition status
27	Nakayama, M. (2016) <sup>43</sup>	1. Japan 2. RCT 3. 71	1.60 2.16/55 3. Thyroid Cancer 4.4	1. Salivary Gland Damage 2. Scintigraphy	1. Salivary Gland Damage 2. Scintigraphy	1. Inhalation aromatherapy using Citrus lemon, Zingiber. 2. Inhalation aromatherapy, 0.5-1 ml, three times daily. 3.10 min, Unknown, two weeks.	Positive effect on Salivary Gland Damage

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Table 1 (continued)

ID	Author	Study Characteristics 1. Country 2. Design 3. Participants	Participant's characteristics 1. Age (mean or range) 2. Gender (male/female) 3. Type of Cancer 4. Risk of bias	Outcomes 1. Variables 2. Tools	Intervention 1. Treatment group(s) 2. Type, dose, frequency of Aromatherapy and Administration method 3. Duration per session/Total number of sessions/Total Duration of intervention	Results
28	Ndao, D. H. (2012) <sup>44</sup>	1. USA 2. RCT 3.37	1.12 2.27/10 3. Multiple cancer 4.	1. Anxiety, nausea, and pain. 2. STAIC, VAS	1. Inhalation aromatherapy using Bergamot. 2. Inhalation aromatherapy, four drops, once. 3. Unknown, Unknown, once.	No effect on Anxiety, nausea, and pain.
29	Nekuzad, N. (2012) <sup>45</sup>	1. Iran 2. RCT 3.60	1.30-70 2. ND 3. Gastrointestinal cancer 4.3	1. Chemotherapy-Induced Phlebitis 2. Phlebitis scale	1. Massage aromatherapy using Sesame Oil. 2. Massage aromatherapy, 10 drops, and twice a day. 3.35 min, 14, two weeks.	Positive effect on phlebitis
30	Ovayolu, O. (2014) <sup>46</sup>	1. Turkey 2. RCT 3.280	1.20-50 2.0-280 3. Breast cancer 4.3	1. Physical and psychological symptoms, Quality of life 2. Rotterdam symptom checklist, Quality of life scale	1. Massage/Inhalation aromatherapy using lavender, mint, chamomile, jasmine, violet, rosemary and eucalyptus Oil. 2. Massage aromatherapy, Inhalation, 2-4 ml, 90 ml inhalation, three times a week. 3. Massage aromatherapy: 35 min, Inhalation aromatherapy: 5 min, 12, one month.	Positive effect on Physical and psychological symptoms and quality of life
31	Özkaraman, A. (2018) <sup>47</sup>	1. Turkey 2. RCT 3.70	1.58-22 2.11/59 3. Multiple type 4.3	1. Anxiety, sleep quality 2. STAI, PSQI	1. Inhalation aromatherapy using lavender oil group, tea tree Oil. 2. Inhalation aromatherapy, 3 drops, every night. 3.5 min, 30, one month.	Positive effect on sleep quality and anxiety
32	Salihah, N. (2016) <sup>48</sup>	1. Malaysia 2. RCT 3.60	1.47-3 2.0-60 3. Breast cancer 4.4	1. Nutritional status 2. WHO criteria	1. Inhalation aromatherapy using ginger Oil. 2. Inhalation aromatherapy, 2 drops, three times a day. 3.2 min, 42, two weeks.	Positive effect on Nutritional status.
33	Santosh, D. (2011) <sup>49</sup>	1. India 2. Quasi-experimental 3.60	1.28 2.22/38 3. Multiple type 4. Included	1. Anxiety 2. BAI	1. Massage and Inhalation aromatherapy using lavender Oil. 2. Massage and Inhalation aromatherapy, 6 drops, every hour. 3.10 min, Unknown, Unknown.	Positive effect on anxiety
34	Soden, K. (2004) <sup>50</sup>	1. United Kingdom 2. RCT 3.42	1.73 2.10/32 3. Multiple type 3.3	1. Pain, anxiety or quality of life. 2. VAS, VSH, and HADS	1. Massage aromatherapy using lavender. 2. Massage aromatherapy, 1%, every week. 3.30 min, 4, four weeks.	no effect on pain, anxiety or quality of life.
35	Sriningsih, I. (2017) <sup>51</sup>	1. Indonesia 2. Quasi-experimental 3.60	1. ND 2. ND 3. Cervical cancer 4. Included	1. Nausea and vomiting. 2. MASCC-Antiemesis Tool	1. Inhalation aromatherapy using ginger. 2. Inhalation aromatherapy, 5 drops, once time. 3.10 min, 1, 1 days.	Positive effect on nausea and vomiting.
36	Stringer, J. (2008) <sup>52</sup>	1. United Kingdom 2. RCT 3.39	1.51 2.16/23 3. Haematological cancer 4.3	1. Cortisol and prolactin. Quality of life 2. taking blood, EORTC QLQ-C30	1. Massage aromatherapy using not specific aroma. 2. Massage aromatherapy, follow-up 0.5 hourly for 2 h and at 24 h. 3.20 min, four, Unknown.	Positive effect on cortisol, prolactin, and Quality of life.
37	Tamaki, K. (2017) <sup>53</sup>	1. Japan 2. RCT 3.153	1.52 2.0/153 3. Breast cancer 4.3	1. Vital signs. Quality of life 2. Physical examination, EORTC QLQ-C30	1. Inhalation aromatherapy using ylang-ylang, orange, and lavender. 2. Inhalation aromatherapy, 1 day. 3.19 hours, 1, 1 day.	No effect on QOL, and vital sign
38	Wilcock, A. (2004) <sup>54</sup>	1. United Kingdom 2. RCT 3.29	1.71 2.20/19 3. Multiple type 4.3	1. Mood, physical symptoms and quality of life 2. MYMOP, POMS	1. Massage aromatherapy using lavender and chamomile oils. 2. Massage aromatherapy, weekly. 3.39 min, 4, four weeks.	effect on Mood, physical symptoms and quality of life
39	Wilkinson, S.M. (1999) <sup>55</sup>	1. United Kingdom 2. RCT 3.87	1.52 1.2/9/78 3. Multiple type 4.5	1. Anxiety, Depression, Pain, Fatigue, Nausea/Vomiting and Quality of life 2. SAI, CES-D, EORTC pain, fatigue, nausea/vomiting, EORTC-QOL scale	1. Massage aromatherapy using Roman chamomile oils. 2. Massage aromatherapy, weekly. 3.1 hour, 4, four weeks.	Positive effect on clinical anxiety, depression, pain, fatigue, nausea and vomiting, and quality of life
40	Wilkinson, S.M. (2007) <sup>56</sup>	1. United Kingdom 2. RCT 3.288	1.51 1.5/2.38-250 3. Multiple type 4.4	1. anxiety and/or depression 2. CES-D, EORTC	1. Massage aromatherapy using two oils. 2. Massage aromatherapy, weekly. 3.1 hour, 4, 4 weeks.	effect on clinical anxiety, depression.
41	Xiao, Y. (2018) <sup>57</sup>	1. China 2. RCT 3.100	1. ND 2.0-100 3. Breast cancer 4.4	1. Anxiety, Pain 2. VAS, NNRS	1. Inhalation aromatherapy using Bergamot, Geranium, lavender. 2. Inhalation aromatherapy, 3 drops, 15 min. 3.15 min, 1, 1 day.	effect on anxiety

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Table 1 (continued)

ID	Author	Study Characteristics	Participant's characteristics	Outcomes	Variables	Intervention	Results
42	Yayla, E. M. (2019) <sup>58</sup>	1. Turkey 2. Quasi-experimental 3. Participants	1. Age (mean or range) 2. Gender (male/female) 3. Type of Cancer 4. Risk of bias	1. Pain and Anxiety 2. VAS, STAI	1. Pain and Anxiety	1. Inhalation aromatherapy using Lavender and eucalyptus. 2. Inhalation aromatherapy, 3 drops, once. 3. three min, one, one.	Only Lavender have effect on pain. No effect on anxiety.
43	Zorba, Phnar (2018) <sup>59</sup>	3. 123 1. Turkey 2. Quasi-experimental 3.75	1. Included 1. 44.96 2.0/75 3. Breast cancer	1. Nausea and Vomiting 2. CINV	1. Nausea and Vomiting	1. Inhalation/Massage aromatherapy using peppermint, bergamot, and cardamom. 2. Inhalation/Massage aromatherapy, 2 ml for inhalation, once. Every 21 days. 3. Three min (inhalation), 20 Min (massage), Unknown	Effect on Nausea and Vomiting

NCI-CTC: National Cancer Institute Common Toxicity Criteria, SAI: State Anxiety Inventory, RCSIQ: Richard-Campbell Sleep Questionnaire, MYMOP2: Measure Yourself Medical Outcome Profile 2, ESASr: Edmonton Symptom Assessment Scale-Revised, BPI-K: Brief Pain Inventory- Korean version, SDS: Zung Self-Rating Depression Scale, HADS: Hospital Anxiety and Depression Scale, MYCaW: Measure Yourself Concerns and Wellbeing, RINVR: Rhodes index of nausea, vomiting and retching, PeNAT: The Pediatric Nausea Assessment Tool, SPHERE: Somatic and Psychological Health Report, RTOG: Radiation Therapy Oncology Group Acute Skin Toxicity Grades, P-VAS: Pain Visual Analog Scale, QLI: Quality of Life Index, PSQI: Pittsburgh Sleep Quality Index, NPRS: Numerical Pain Rating Scale, PFS: Piper Fatigue Scale, CFS: Cancer Fatigue Scale, CAS: Constipation Assessment Scale, MQOL-HK: McGill quality of life for Hong Kong Chinese, BA: Beck Anxiety Inventory, VSH: Verran and Snyder-Halpern Sleep Scale, MASCC-Antiemesis Tool: Multinational Association for Supportive Care in Cancer- Antiemesis Tool, MYMOP: Measure Yourself Medical Outcome Profile, POMS: Profile of Mood State, S: second, Min: minutes, ND: non-determined.

range in the Jadad scale goes from 0 to 5 in which a higher score represents higher quality of the study. Also, the quality of quasi-experimental studies was assessed by JBI quasi-experimental appraisal tool.<sup>24</sup> The JBI tool contains 10 items and evaluates the entered studies in terms of cause and effect, the control group, the same intervention in the intervention and control groups, the presence of the control group, the number of variables examined before and after the intervention, the exact description of the follow-up process, the same measurement method of variables in the two groups, the constant measurement method of variables in the two groups, using appropriate statistical tests, and overall evaluation.<sup>24</sup>

### 3. Results

#### 3.1. Study selection

A total of 1751 articles were retrieved from the initial search. Of the 1301 non-duplicated studies in the title and abstract screening process, 1237 were excluded because they had unrelated titles. Of the remaining 64 studies, 43 met the eligibility criteria. Of the 21 excluded studies, eight were review articles, six were qualitative, four did not have the full text, and three did not meet quality requirements for inclusion (Fig. 1).

#### 3.2. Study characteristics

A total of 43 studies conducted on 3239 cancer patients in 13 countries between 1995 and 2019 entered the final stage. Majority of studies (n = 31) were clinical trials (RCTs). The sample size was between 12 and 313 individuals. The age range of the participants was between 28 and 72 years old. The participants' gender was reported in 41 studies. Of 3109 individuals, the majority were female participants (N = 2249, 72.3%). Patients with multiple types of cancer were investigated in majority of studies (N = 22) (Table 1). Out of 43 enrolled studies, 31 were RCTs, whose quality was evaluated through the Jadad tool. The range of scores of the studies was 3–5. Nine studies were quasi-experimental, 9 items of which were evaluated with the JBI tool. According to the studied items, all studies were included. A study was a case series whose quality was not evaluated due to lack of a suitable tool.

#### 3.3. Interventions characteristics

##### 3.3.1. Types of interventions, selection of aromas, and administration method

Out of 43 studies included, inhalation aromatherapy, massage aromatherapy, and other forms of aromatherapy were used in 21, 22, and 3 studies, respectively. Inhalation aromatherapy and aromatherapy massage were used simultaneously in three studies. The aromas were used purely or in combination of aromas with the help of an aromatherapist. More than 32 types of aromas were used in the included studies. The most commonly used aromas included: lavender (n = 18), chamomile (n = 6), and ginger (n = 5).

##### 3.3.2. Inhalation aromatherapy

Of the 43 studies, inhalation aromatherapy was used in 21 studies (48.8%). A total aroma dose of 1–6 drops were used in 17 studies. Inhalation aromatherapy was carried out in most studies using two drops (N = 5). Moreover, an aroma dose of 0.5–4 ml aroma was used in two studies. Also, the aroma dose was unknown in one study. In the remaining 15 studies, the duration of each aromatherapy period was very varied ranging from 2 min to 19 h. The most common duration was between 2 min and 20 min in most studies (n = 12). The most common duration of the aromatherapy course was 10 min (n = 4). The duration of each aromatherapy course was not known in three studies. The aromatherapy was repeated was from every hour to three times a week.

Aromatherapy was repeated on a daily basis in most studies (n = 5). The frequency of each aromatherapy course was not mentioned in the four studies. The total number of aromatherapy courses was not mentioned in the three studies. Overall, patients experienced 1 to 42 aromatherapy courses in the remaining 18 studies. In most studies, patients experienced a total of 3 aromatherapy courses. The duration of the whole intervention was not known in three four. The duration of the intervention varied from 1.5 h to 1 month in the remaining 17 studies.

### 3.3.3. Aromatherapy massage

Of the 43 studies, the inhalation aromatherapy was used in 22 studies (51.1%). The exact aroma dose was unknown in more than half of the studies (n = 12). The above dose varied between 2 and 50 ml and 3 to 10 drops in 10 remaining studies. The aromatherapy massage was repeated in 20 studies and varied from once an hour to once a week. The duration of each aromatherapy massage course was mentioned in 19 studies, varying from five minutes to one hour. The most commonly used aromatherapy massage duration was 30 min (n = 3). The total number of massage therapies was mentioned in 16 studies and varied between 1 and 180 courses. In most studies, patients experienced a total of four massage therapies. The duration of the whole intervention was mentioned in 20 studies. The overall intervention duration varied from one day to six months in different studies. Interventions were performed in most studies (n = 8) over a one-month period.

## 3.4. The effect of the aromatherapy on cancer complications

The studied complications were Anxiety (n = 16), Pain (n = 13), Quality of life (n = 9), Nausea and Vomiting (n = 9), Depression (n = 6), Physical and psychological symptoms relief (n = 4), Sleep quality (n = 4), Fatigue (n = 4), Vital sign (n = 4), oral mucositis (n = 2), Skin disorders (n = 2), Wellbeing (n = 2), Nutrition status (n = 2), Immune Measurements (n = 2), Mood (n = 1), Constipation (n = 1), Salivary Gland Damage (n = 1), Chemotherapy-Induced Phlebitis (n = 1), and Cortisol and prolactin (n = 1). In all interventions, standard instruments were used to assess the effect of the aromatherapy on cancer complications. Considering the incidence of various complications, various instruments were used to investigate them. The most commonly used tools were VAS (n = 8) and HADS (n = 5).

### 3.4.1. Psychological complications

**3.4.1.1. Anxiety.** The present study examined the effect of the aromatherapy on anxiety (n = 16). Massage aromatherapy and inhalation aromatherapy were used in 12 and 4 studies, respectively. Aromatherapy massage improved anxiety symptoms in 9 studies. The aromatherapy massage did not improve anxiety symptoms in 2 studies. The most effective anti-anxiety aromas included lavender (n = 8), chamomile (n = 3), and bergamot (n = 3). The aromatherapy massage did not have a significant effect on anxiety in two studies. In the 4 studies, the inhalation aromatherapy also reduced the anxiety level. Lavender was also the most commonly used aroma used during the inhalation aromatherapy.

**3.4.1.2. Depression.** A total of 6 studies had investigated the effect of aromatherapy massage (n = 5) and inhalation aromatherapy (n = 1) on depression. Results showed that inhalation aromatherapy does not have a significant effect on depression. The results showed that aromatherapy massage method reduced depression in cancer patients in all of the studies. Lavender was also the most commonly used aroma.

**3.4.1.3. Quality of life.** A total of 9 studies have examined the effect of the aromatherapy on the quality of life in cancer patients. Five studies showed a significant effect of aromatherapy massage on improving quality of life. The most commonly used aroma was lavender. The aromatherapy had no significant effect on quality of life in 4 studies.

Inhalation aromatherapy was used in two studies and it had significant effect on improving the quality of life only in one study where ginger was used.

**3.4.1.4. Other psychological complications.** Two studies have examined the effect of aromatherapy massage on wellbeing. Both studies showed that aromatherapy massage had boosted the wellbeing status. One study also showed that aromatherapy massages improved the mood status in cancer patients.

### 3.4.1.5. Physical complications

**3.4.1.5.1. Pain.** A total of 13 studies have examined the effect of the aromatherapy on pain. Most studies (n = 8) were performed using massage aromatherapy intervention. Five studies also showed pain relief after the inhalation aromatherapy. One study was also carried out using gargle and the results showed a significant effect on pain relief. The most commonly used aroma was lavender. Among the studies reviewed, three studies showed that aromatherapy did not have a significant effect on the pain.

**3.4.1.5.2. Nausea and vomiting.** A total of 9 studies have examined the effect of aromatherapy on nausea and vomiting. The inhalation aromatherapy method was used in seven studies, and the aromatherapy massage method was also used in three studies. The effective aromas in the studies that were performed using the inhalation aromatherapy included peppermint, cardamom, and ginger. The results of two studies where ginger aroma was used, showed that the inhalation aromatherapy had no significant effect on nausea and vomiting. The aromatherapy massage, which was used in two remaining studies, have improved nausea and vomiting symptoms.

**3.4.1.5.3. Immune system.** Two studies have examined the effect of aromatherapy massage on the function of immune system. One study showed improvement in immune indexes in patients. The effective aromas on the immune indexes included coconut and ginger. One study also showed that aromatherapy massage does not have a significant effect on immune indexes.

**3.4.1.5.4. Sleep quality.** Four studies have investigated the effect of aromatherapy on the sleep quality in cancer patients. Inhalation aromatherapy was used in the three studies, which indicated improved sleep quality after the inhalation aromatherapy. One study that was conducted through aromatherapy massage showed that aromatherapy massage with lavender essential oil improves the quality of sleep. Lavender was the most common aroma used in the two methods.

**3.4.1.5.5. Fatigue.** A total of 4 studies have investigated the effect of aromatherapy massage (n = 3) and aromatherapy bath (n = 1) on fatigue. All of the studies showed improvement in fatigue after the aromatherapy. The most commonly used aroma was chamomile.

**3.4.1.5.6. Vital signs.** Four studies investigated the effect of the aromatherapy on the vital signs. Aromatherapy massage and the inhalation aromatherapy led to an improvement the vital signs (N = 2 studies) and did not have a significant effect on vital signs in two study.

**3.4.1.5.7. Physical and psychological symptoms relief.** Studies have investigated the effect of aromatherapy massage (n = 3) and inhalation aromatherapy on physical and psychological symptoms relief. All studies showed a significant effect of the aromatherapy on the improvement of physical and psychological symptoms relief. The most commonly used aromas were lavender, chamomile.

**3.4.1.5.8. Other complications.** Studies have shown that the aromatherapy has had a significant and beneficial effect on nutritional status (N = 1), salivary gland damage (N = 1), chemotherapy-induced phlebitis (N = 1), cortisol and prolactin (N = 1), constipation (n = 1), oral mucositis (n = 2). The results also showed that the aromatherapy has no significant effect on the healing of skin disorders

#### 4. Discussion

Due to the high costs imposed to the health system, the treatment of various cancer complications through complementary and alternative therapies can be one of the priorities for cancer care, this systematic review study was conducted to determine the effect of the aromatherapy on cancer complications. A total of 43 studies, which were carried out on 3239 cancer patients in 13 countries during 1995 and 2019 entered the final stage. The inhalation aromatherapy, aromatherapy massage aromatherapy bath, and gargle were used in the present study. The most common studied complications included anxiety, pain and quality of life. The most common aromatherapy method was the aromatherapy massage. The most commonly used aroma was lavender. The results of the current study showed that the aromatherapy relieved a various range of cancer related symptoms including: Anxiety, Pain, Quality of life, Nausea and Vomiting, Depression, Physical and psychological symptoms relief, Sleep quality, Fatigue, Vital sign, oral mucositis, Skin disorders, Wellbeing, Nutrition status, Immune Measurements, Mood, Constipation, Salivary Gland Damage, Chemotherapy-Induced Phlebitis, and Cortisol and prolactin. With regard to anxiety, the results showed that inhalation aromatherapy and aromatherapy massage with lavender improved symptoms of anxiety in most studies, which is consistent with studies carried out on hemodialysis patients,<sup>60-62</sup> patients undergoing cholecystectomy,<sup>63</sup> first stage of labor,<sup>64</sup> and elderly.<sup>65</sup> The aromatherapy massage improved depression symptoms, but the inhalation aromatherapy didn't yield such positive results. The results on quality of life are contradictory are almost the same, which are consistent with studies carried out on hemodialysis patients,<sup>60,62</sup> and elderly,<sup>65</sup> as only half of the studies show a positive effect on the quality of life. Such discrepancy can be due to the type of variable being studied because quality of life is essentially a multidimensional variable, and most of the aromatherapy studies have been performed in a limited time period; while, apart from the different dimensions, for an intervention to effectively enhance the quality of life, time is also a very important variable.

Such contradiction can be also due to various tools used to measure quality of life in two studies. Also, the results of few previous studies on mood indicate the beneficial effects of the aromatherapy on the mood status. Regarding physical dimensions, the most commonly complication reported was pain. All studies show pain relief through inhalation aromatherapy and massage, which is consistent with individual studies that show the effect of the aromatherapy on the pain relief in other populations, including elderly,<sup>65</sup> cesarean section,<sup>66</sup> postoperative knee pain,<sup>67</sup> labor pain,<sup>68</sup> and back pain.<sup>69</sup> Systematic review studies have also shown that the aromatherapy in different doses can relieve pain in patients with chronic pain<sup>70</sup> and also dysmenorrhea.<sup>20</sup> Results also indicated that aromatherapy had a significant effect on the reduction of nausea and vomiting. Some studies have also shown that aromatherapy has no significant effect on nausea and vomiting, which is consistent with the previous systematic review studies carried out by Cochran and showed that aromatherapy does not have a significant effect on the reduction of nausea and vomiting.<sup>71,72</sup> Another systematic review study also indicates the effect of the aromatherapy on reducing nausea and vomiting in various patients.<sup>73</sup> Consistent with the present study, the results have been contradictory in other review studies, and methodological problems, the different procedure, and most importantly the quality of studies seem to have had a serious impact on the results. On the other hand, it seems there is no standard protocol for using aromatherapy to relieve nausea and vomiting. The results also revealed that the aromatherapy improve the sleep quality of cancer patients. The aromatherapy also improves sleep quality in other populations, including nurses,<sup>74,75</sup> ICU patients,<sup>76</sup> and patients during the recovery process.<sup>77</sup> The results of the present study on the fatigue are also consistent with other studies on other populations, such as postpartum women,<sup>78,79</sup> rheumatoid arthritis,<sup>80</sup> indicating an improvement in

fatigue after aromatherapy. Few studies have also shown that the aromatherapy will improve immune markers and vital signs, which is inconsistent with Lytle, J.S.'s study that showed aromatherapy does not improve the vital signs.<sup>77</sup> Considering the limited number of studies and the simple size, investigating the effect of aromatherapy on vital signs requires further studies. In spite of the beneficial effects of various aromatherapy techniques on the various cancer complications, it seems that caution must be taken while generalizing the results because there are few clinical studies on different physical and psychological dimensions in cancer patients. Another challenge faces the use of aromatherapy is to determine the exact dosage, the frequency of using aromas used. According to the related literature, various studies indicate different doses of different frequencies and further studies are thus needed, especially clinical trials, with a much larger sample size, to judge the effects of the aromatherapy more confidently. Another major challenge for the aromatherapy is the duration of the studies, most of which lasted from a few days to one month, while achieving better treatment outcomes for consequences, such as the quality of life, requires the use of aromatherapy for at least several months.

**Limitations:** The most important limitation of the inability to perform meta-analysis due to the great difference in the instruments used, dosage, aromas, and the different durations of aromatherapy courses in different studies. Also, necessary information was not reported in some studies and attempts were thus made to contact with the authors.

**Strengths:** According to researchers' best knowledge, this is the first relevant study with high degree of comprehensiveness in terms of the period during which the articles were searched, the number of studies entered, and the number of databases examined. Also, articles entered without language restrictions. The most important strength of the study was its comprehensiveness in terms of the number of consequences examined, as well as the number of aromas examined, with more than 20 consequences and complications and 30 aromas being investigated.

#### 5. Conclusion

The results of the present study showed that the aromatherapy improves the common complications of cancer patients. Therefore, the aromatherapy treatment must be used with caution as an alternative and rapid treatment by patients and health personnel after consulting with aromatherapists. In order to better utilize the findings of this study, it is suggested to help patients to use the most effective properties of odors, including the relaxing effect of aromas like lavender, through creation of appropriate structures, such as large odor spreaders, in the chemotherapy departments and performing aromatherapy with proper scents in appropriate periods of time in patients who are not sensitive to the used odors. In addition, periodic training of nurses and patients on the importance of aromatherapy as a useful low cost treatment is recommended along with other therapies to reduce the complications of cancer. As the first review study that comprehensively enrolled all relevant studies, its results can be an appropriate guide which provides useful information about the most commonly used methods and dosages. The study also provides a suitable basis for healthcare providers, nurses, and patients to choose the type of commonly used odors among cancer patients and to select the appropriate scent tailored to the complications developed. Considering different treatment courses and aromas used, as well as the small sample size of studies that restrict its generalization to the clinical community, and the important challenge, this is the creation of standard aromatherapy protocols, it is recommended to carry out systematic clinical trials with a large sample size.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ctim.2019.08.003>.

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