The Anxiolytic Effects of Aromatherapy on Preprocedural Anxiety: An Integrated Review

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Abstract

Anxiety before procedures can negatively impact patients by increasing cortisol levels which delays wound healing and increases infection risk, increasing pain and sedation medication needs, and increasing hospitalization time. This review was conducted to find how inhaled essential oils affect pre-procedural anxiety of adults in acute care settings. Nine databases and some gray literature were searched within the past ten years, and documented using the PRISMA flow chart. Ten articles fitting the inclusion criteria were retrieved. Nine of the articles found a significant difference between the aromatherapy group and control group and pre- and post-intervention anxiety scores, and none reported adverse effects. Results align with other reviews with a majority favoring aromatherapy. Since results are mixed, further research is required.

The Anxiolytic Effects of Aromatherapy on Preprocedural Anxiety: An Integrated Review

Section One: Formulating the Review Question

Essential oils (EOs) have been used for centuries in healthcare, and in nursing since Florence Nightingale. Johnson, et al. (2017), Johnson (2019), and Smith and Kyle (2008) say that Nightingale used lavender EO on the forehead of wounded soldiers to relax them, and she believed that sensory variety such as different colors, light, and smells not only had psychological but physical effects also, so she used floral EOs to brighten the atmosphere to encourage healing. Johnson, et. al. (2017) note that the French and English consider aromatherapy a science and in Australia, England, France, and the United States it is considered an integrative and complementary practice. EOs are used in the hospital in many ways including for infection, insomnia, nausea and vomiting, pain and inflammation, stress and well-being, and for specific uses in some specialties.

In the 1930s, according to Smith and Kyle (2008), the French introduced aromatherapy to medical science. They used antiseptics in World War II and continued after the war. Blunt (2003) explains that hospitals in Europe now use essential oils with water to clean. Buckle (2015) expands that although not currently used in the hospital for infection, in the past, perfumers and glovemakers in Europe using EOs survived the Black Death. Lavender has been shown to reduce MRSA, rose can help the plague, and Rosa damascena has antibacterial properties. In the 1980s the Churchill Hospital and the Radcliffe Infirmary started using aromatherapy for insomnia with equal to better results than benzodiazepines and analgesics with great patient satisfaction, and they are currently used in the UK and Norway. Although not used in the hospital for pain, many EOs have been shown to have some analgesic effects and enhance analgesic medications. Finally, Buckle (2015) notes that countries throughout the world,

including Great Britain, India, Austria, and the U.S. have used EOs to reduce anxiety before procedures.

Searing (2020) states that 60% of Americans reported feelings of anxiety daily in March and April of 2020, which was an increase from previous years. Anxiety, a symptom of stress, commonly presents in hospitalized patients for many reasons including a sense of loss of control and helplessness, loss of identity, and the invasion of privacy. Many patients experience preprocedural anxiety. Shajimon (2013) found that patients in invasive cardiac procedures experience more state anxiety, an anxiety that is focused on the situation at hand, such as the procedure, than cardiac anxiety, a more chronic anxiety. Anxiety can be especially detrimental in cardiac patients due to the increased oxygen demand the sympathetic nervous system (SNS) response causes, the increased inflammatory response that occurs, and the risk for arrythmias. Gallager, et al. (2010) aids in explaining the inflammatory response can lead to coagulation and thrombus formation which, combined with an increased oxygen demand, can put patients at risk for ischemia, especially if the anxiety occurs over a long period of time while waiting for the procedure.

Gallager, et al. (2010) says that anxiety can interfere with normal functions and decrease patient cooperation during procedures. Several studies have shown a correlation between preprocedural anxiety and increased pain during the procedure, and one study even showed that parental anxiety can increase pain perception in children (Vitale, 2020, Vadalouka, 2009, Naik, 2018; Oommen, 2019). Puntillo, et al. (2014) says that in the ICU, pain is one of the main sources of psychological stress, and the most painful nonsurgical procedures identified were chest tube removal, wound drain removal, and arterial line insertion. In addition to anxiety increasing the need for pain medication, Ni, et al. (2013) notes that more sedating medications

may be needed during the procedure due to the arousing effects of the SNS. Schreiber, et. al. (2006) found that the strong correlation between anxiety and sedating effects in children may cause a strong desire for nonpharmacological techniques to lower anxiety before the procedure due to limits of drug type and amount in some emergency departments (EDs). Anxiety is prevalent in the U.S. and can cause increased pain sensitivity and decreased effect of sedation medications, which causes complications before procedures.

Johnson, et al. (2017) explains that inhalation of essential oils is thought to decrease stress by entering the limbic system and affecting the hypothalamus, endocrine system, and autonomic nervous system (ANS) to regulate heart rate, respiration rate, blood pressure and increasing peripheral perfusion, decreasing the stress response. Childers and Aleshire (2020) continues EOs either enter through olfactory receptors, immediately affecting the olfactory bulb, or enter the bloodstream through the alveoli. The olfactory bulb connects to the limbic system, which connects to the amygdala, regulating emotions. It also connects to the hippocampus, affecting memory; hypothalamus, regulating hormones; and the ANS and cingulate gyrus affecting BP, pulse, focus, and attention (Childers & Aleshire, 2020). Controlling the stress response through EOs affecting the brain by entering the olfactory receptors decreases anxiety of patients before procedures.

There are several ways to measure anxiety levels. Many studies use self-reported surveys due to their ease of use, but they are subjective. Gallager, et al. (2010) describes how the State Trait Anxiety Inventory (STAI) asks participants to rate their level of apprehension, tension, nervousness, worry, and activation of the autonomic nervous system (ANS), and it has been found to be valid and reliable in many populations. Julian (2011) says the Beck Anxiety Inventory (BAI) uses a 4-point Likert scale to measure nervousness, dizziness, inability to relax,

etc. Gallager, et al. (2010) also notes that vitals signs can be used to measure the ANS response because anxiety stimulates the sympathetic nervous system (SNS) which causes increased heart rate and blood pressure.

According to Nadendla (2015), cortisol, a hormone released by the adrenal cortex in times of stress, can also be used to assess anxiety, and was shown to be effective compared to Hamilton's anxiety scale. Polat (2018) says that salivary cortisol is superior to serum cortisol measurements because salivary cortisol is unbound. Salivary cortisol is also easier to obtain, less invasive, less stressful to obtain, and does not respond to changes in temperature, movement, or microorganism growth. Inder, et al. (2012) describes if using a sterile plastic urine jar or plastic tube, the patient spits/drools into it until about 3mL has been collected, which would take approximately 3 minutes. The Salivette systems contain a polyester or cotton inlay. The patient chews the swab inlay for 30 seconds to 3 minutes until 0.5 to 3mL of saliva is absorbed and puts it back into the tube. Swabs help filter cells and debris and allows for a non-viscous sample. Although many advantages exist in collecting salivary cortisol, smoking and oral injuries causing blood can elevate levels, skewing the results. Agatonovic-Kustrin, et al. (2020) distinguishes salivary cortisol measures chronic stress while the salivary biomarker chromogranin A (CgA) measures acute stress. Salivary cortisol and CgA provide useful measurements of anxiety.

Kang, et al. (2019) says that lavender essential oil (LEO), one of the most researched and used for decreasing anxiety, contains linalool which has been shown to inhibit the limbic system and transmission of the autonomic nervous system. It is also effects GABA-A (gamma-aminobutyric acid) receptors to reduce anxiety. Weaver, et al. (2020) affirms lavender has been shown to reduce stress and depression and improve moods. Ota, et. al. (2017) shows in a study that linalool caused significant reductions in cerebral blood flow to the right superior temporal

gyrus to insula, anterior cingulate cortex after inhalation, which would cause the sedative and anxiolytic effects. Tugut (2017 says the effect occurs 3-15 minutes after inhalation. Lavender seems to have the physiologic effect of decreasing stress soon after inhalation.

Although there is much research showing positive effects of EOs, Allard & Katseres (2016) suggests that essential oils may have more of a psychological effect from the perceived smell rather than a pharmacological effect. Babulka, et. al. (2017) found no difference between using rosemary and lavender essential oil and a placebo on cognitive performance, which may suggest that essential oils may increase alertness and attention due to a psychological effect like placebos. Agatonovic-Kustrin et. al. (2020) believes they have a pharmacological effect because they enter the bloodstream and have measurable effects. Whether a physiological or psychological effect, the research shows that they do decrease stress and anxiety.

Several reviews exist reviewing the literature for the anxiolytic effects of lavender, but not many have looked at other EOs for anxiety. A systematic review and meta-analysis with twenty-two articles found inhaled lavender to decrease anxiety, systolic blood pressure (SBP), heart rate, salivary cortisol, and CgA levels (Kang, et. al., 2019). In a systematic review, out of fifteen random controlled trials, Perry, et al. (2012) found seven to show positive effects of lavender on anxiety over the controls. Malcolm and Tallian (2018) did a review on patients with anxiety disorders using the oral preparation Silexan and found it to have a calming effect without sedation, dependence, tolerance, or withdrawal and a more rapid onset than first line anxiolytics, but even though there were no dangerous side effects in short term trials, the authors recommend using the oral preparation with caution. Three meta-analyses on the oral administration of lavender found it to be significantly effective in treating anxiety (Möller, et. al., 2017; Yap, et. al., 2019; Generoso, et. al., 2017).

In one review by Sahib, et al. (2012), on coriander, three articles were identified that showed the effects of coriander to be equal to those of diazepam in reducing anxiety. A majority of the 16 articles in Ghiasi's, et al. (2019) systematic review found aromatherapy to help anxiety during the first stage of labor. Dobetsberger & Buchbauer (2011) found in their review of 11 rigorous papers, that lavender *(Lavandula angustifolia),* neroli (*Citrus aurantium L.*), sweet orange (*Citrus sinensis L.*), shell flower leaves (*Alpinia zerumbet*), and black cumin seed (*Nigella sativa L.*) aromatherapy helps anxiety in many different settings, and aromatherapy massages had many beneficial effects. Sousa, et. al. (2015) and Agatonovic-Kustrin, et. al. (2020) found many different EOs to work in animal models for anxiety by using different mechanisms and different from the GABA/Benzodiazepine.

Defining Concepts and Variables

Variables are anything that change between studies that could cause a difference in outcome. Operational variables include levels of anxiety in individuals, the type of procedure, the EO used, and the mode of inhalation.

Rationale for Conducting the Review

Although there are many studies on the use of anxiolytic EOs in the hospital, there is no recent review looking at the different types of oils used and how they effect preprocedural anxiety in humans.

Purpose and Review Question

This review will explore the current research on anxiolytic EOs. The question is asked, "How do inhaled essential oils affect pre-procedural anxiety of adults in acute care settings?"

Formulate Inclusion and Exclusion Criteria

Research included in this review had to meet all the following inclusion criteria: an inhaled route, inpatients and outpatients that come into an acute care setting, intervention before the procedure, and articles in the past 10 years scoring level one or two of John Hopkins' quality evaluation. Oral and topical routes, outpatients in facilities outside the acute care setting such as primary care offices or dental offices, research that started the EO before coming into the acute care facility, aromatherapy combined with another method of reducing anxiety (music therapy, controlled breathing, massage), reviews that were not specifically preprocedural, and articles that were levels three, four, or five according to John Hopkins' quality evaluation were excluded.

Conceptual Framework

Whittemore and Knafl's (2005) "The integrative review: Updated methodology" was used as a framework. In the first stage of Whittemore and Knafl's framework, the literature search stage, computerized databases are searched with the same search terms and ancestry searching, journal hand searching, networking, and searching research registries are also recommended. The search process must be thoroughly documented including search terms, databases used, additional search strategies, and the inclusion and exclusion criteria. In the data evaluation stage, the researcher must decide whether to have broader criteria to include different designs and lose specificity or to do literature-specific quality evaluations and make analysis more complicated. When choosing sources that are similar, as this review has done, it is optimal to calculate quality scores and use those scores as part of the inclusion and exclusion criteria.

Whittemore and Knafl's data analysis stage uses the constant comparison method and contains five steps: data reduction, in which data is extracted and categorized; data display, in which matrices, charts, or graphs are made with similar data to aid in the next step; data comparison, in which patterns and themes are noted; conclusion drawing, in which it is moved

from the specifics to the general; and verification, in which the researcher returns to the sources to check the accuracy of his work. The results should be in a logical order, show the depth of the topic, and contribute to new understanding of the topic. Implications for further research and clinical practice should also be noted. Whittemore and Knafl's framework adds strength to integrative reviews and improves reporting of methods.

Section Two: Comprehensive and Systematic Search

A librarian helped choose the databases CINAHL, because of its specificity to nursing research; Proquest Nursing & Allied Health Database, because of its wide variety of journals in nursing and other health related disciplines; Cochrane library because it includes systematic reviews; PubMed, because of its comprehensiveness in medical sciences; Medline, due to its variety in medical sciences; and Clinical Key, because it may contain some helpful nursing articles. The databases KoreaMed, National Digital Science Library (NDSL), KMBase, Korean studies information service system, KISTI, EMBASE and PsychInfo (via OVID), AMED and CINAHL (via EBSCO), ISI Web of Knowledge, the ClinicalTrials.gov registry, the EMA Clinical Trials Register, and the ISRCTN, Scopus, SID, Iran Doc, and Google Scholar were found to be used in other reviews on the topic of EOs for anxiety (Kang, et. al., 2019; Perry, et. al., 2012; Moller, et. al., 2019; & Ghiasi, 2019). Based on the accessibility due to Liberty University's subscriptions, CINAHL, Nursing and Allied Health Database, Clinical Key, Cochrane Library, PubMed, MedLine, Springer, Scopus, PsychInfo, and OVID were searched along with ClinicalTrials.gov, EMA Clinical Trials Register, and Google Scholar. The librarian helped choose the search terms "("acute care" OR "intensive care" OR "critical care") AND ("Essential oils" OR "aromatherapy" OR "volatile oils" OR "plant oils") AND (anxiety OR anxiolytic)." The librarian did not include "aromatherapy" in her search terms which narrowed

the results a lot, so it was added. Because the librarian did not think there was enough information on the topic, a broader search was conducted still using inclusion criteria of inhaled route and acute setting and exclusion dental offices and aromatherapy combined with another method where the results of the aromatherapy alone could not be seen.

CINAHL was searched for articles within the last 10 years due to the limited articles found and yielded 16 articles. CINAHL was searched between June 1, 2021 and June 5, 2021. In each report that was retrieved, the "recommended articles," articles that "other readers read", or the "similar articles" were searched, until an article that had no articles that fit the criteria was reached. In "Complementary Health Approaches Used in the Intensive Care Unit" (Erdoğan & Atik, 2017), a systematic review, the included articles were searched, and one fit the criteria and was retrieved (Cho, et. al., 2013).

Nursing and Allied Health Database by ProQuest was searched between June 5, 2021 and June 12, 2021. There were 294 results within the last 10 years, so the search was narrowed down to the last 5 years which yielded 161 results. The limiter "full text articles" was applied. Next, PubMed was searched using the limiters "last 5 years" and "full text" with 15 results on June 13, 2021. On 6/15/21 Ovid used a little different search term: (acute care or intensive care or critical care) and (essential oils or aromatherapy or volatile oils or plant oils) and (anxiety or anxiolytic) within the last 5 years resulting in 58 articles. On 6/16/21 Clinical Key found no results for the original search terms with no modifiers, and Cochrane Library found 1 review and 17 trials between 1/1/2016 and 6/16/21. MEDLINE came up with 2 results on 7/1/21 with the limiters "full text", "scholarly (peer reviewed) journals", between 2016-2021. Scopus yielded 8 results since 2016 and PsychInfo 1 full text, peer reviewed result between 2016-2021 on July 2, 2021. Between 7/5/21 and 7/13/21, Springer was searched under the category "Medicine and Public

Health," "articles," in English between 2016-2021 with 199 results, most of which were conference proceedings.

Gray literature was then searched to increase the scope and reduce bias. On 7/14/21, the search on Google Scholar with limiters of "articles," English, 2016-2021, excluding patents and citations, found 2610 results. The librarian was able to help limit it down to 77 results using the terms ("acute care" OR "intensive care" OR "critical care") AND ("Essential oils" OR "aromatherapy" OR "volatile oils" OR "plant oils") AND ("anxiety" OR "anxiolytic") AND (preprocedural OR pre-op) NOT (pediatric OR peds OR children OR adolescents OR teens) between 2016-2021, including citations. ClinicalTrials.gov found 1 result using the original search terms on 7/19/21 with the recruitment: completed, expanded access: available, age group: adult and older adult, and first posted: 01/01/2016-07/19/2021 limiters applied. The EMA clinical trials registry did not come up with any results with the original search terms on 7/19/21. Using the same search terms, 585 results returned on a google search, and the first 100 were filtered through.

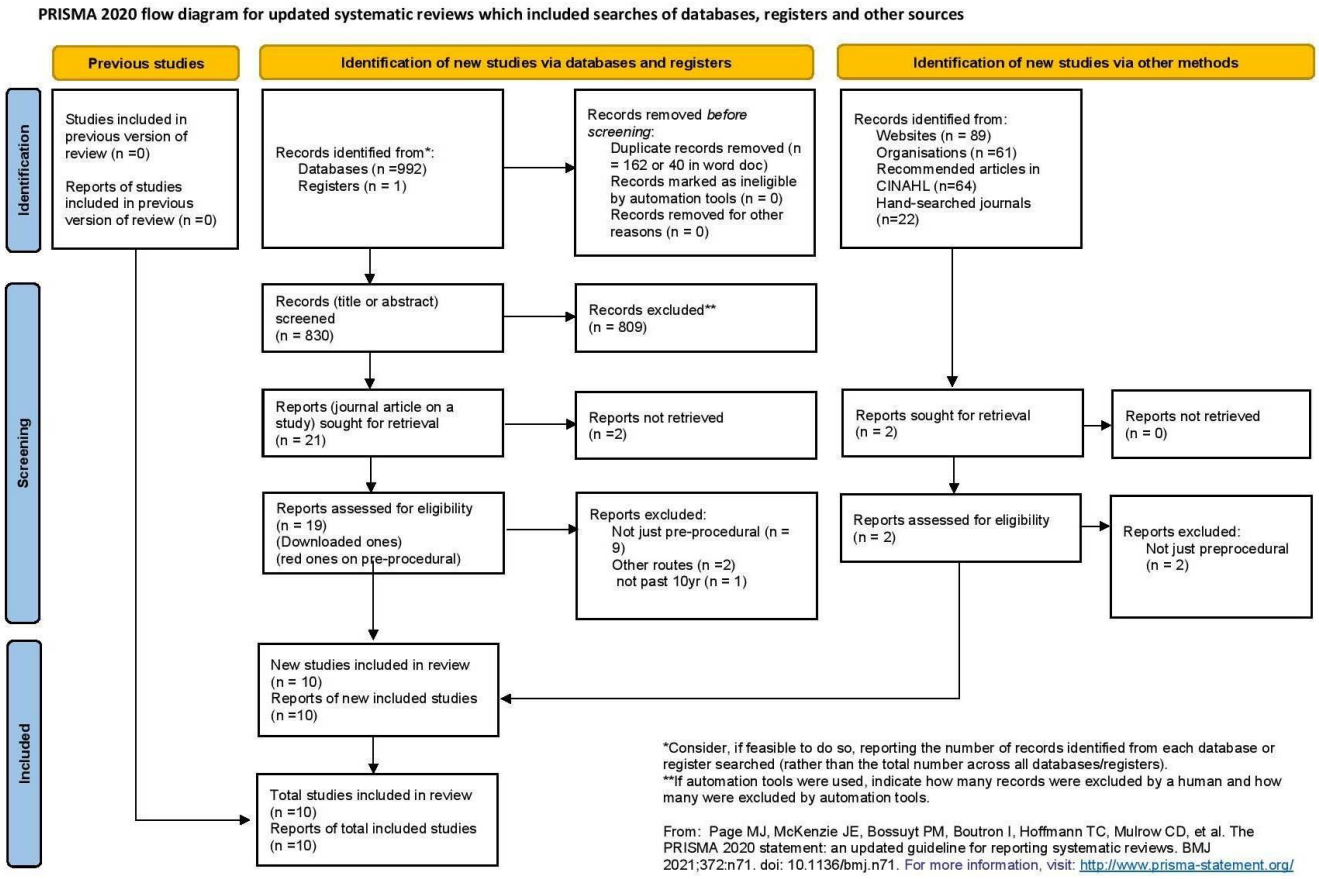
Due to limited resources, the databases were then searched again from 2011 to 2015 to cover the past 10 years. PubMed yielded seven results with one containing the inclusion criteria. Ovid yielded 31 results, none of which fit the criteria. Cochrane Library yielded one trial and one review, neither of which fit the criteria. MedLine had six results all of which were either duplicates or did not fit the criteria. Scopus yielded three results, all duplicates or excluded by criteria. Springer yielded 382 results, of which, two conference abstracts fit the inclusion criteria, but the full text could not be retrieved. Google Scholar had 1490 articles, in the first forty, one trial fit the inclusion criteria, one review had some preprocedural trials included, and another

review had a reference that fit the criteria. PsychInfo had one result that did not fit inclusion criteria. Clinicaltrials.gov did not have any results.

No additional articles that fit the inclusion criteria were found by hand-searching *Evidence Based Complementary and Alternative Medicine*, *Complementary Therapies in Medicine*, *Journal of Evidence-Based Integrative Medicine*, or *Journal of Alternative and Complementary Medicine*.

Search Organization and Reporting Strategies

Each article's abstract that fit the topic and inclusion and exclusion criteria was read and



if it still fit, downloaded. RefWorks was used to help manage search findings. Results are reported using the PRISMA flow diagram in Figure 1 (Page, et al., 2021).

Figure 1

PRISMA Flow Diagram

Note: Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., . . . Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Journal of Clinical Epidemiology, 134*, 178-189. https://doi.org/10.1016/j.jclinepi.2021.03.001

Terminology

Essential Oil is abbreviated as EO

Spielberger's state-trait anxiety inventory: STAI

Gas chromatography: GC

Anxiolytic is the elimination of anxiety.

Section Three: Managing the Collected Data

RefWorks was chosen to help manage the data because of the convenience of the subscription Liberty University has with RefWorks. All the records identified from the databases and registers were entered into a "dump" folder. Once they were screened, the reports that were retrieved were put into a separate folder. A word document keeping track of the searches highlighted the ones that seemed to be "preprocedural" and listed the citations of the retrieved articles. At this stage, 25 of the retrieved articles seemed to be preprocedural.

The data was then extracted and inserted into a table like the one used by in Perry, et al. (2012). When read completely, one of the sources was found to be post-procedural and was excluded, and one that was not strictly pre-procedural was also excluded. One source by Mannucci, et. al. (2018), a review, was not strictly on humans or pre-procedural. A source was taken from the references used in the review, but only the abstract was available. In another review by Kemper (2020), a source specifically on preprocedural anxiety (Abdelkhakim 2020)

was found. In total, ten were excluded for not being solely preprocedural, one was not in the past 10 years, two did not have the full text available in English, and two included other routes other than inhalation.

Section Four: Quality Appraisal

Each article was ranked according to the John Hopkins Nursing Evidence Level and Quality Guide (©The Johns Hopkins Hospital/The Johns Hopkins University). Sources of bias in the review process and in each article were identified and inserted into a table, and the Johns Hopkins Nursing Evidence-Based Practice Research Evidence Appraisal Tool (n.d.) (©The Johns Hopkins Hospital/The Johns Hopkins University) was used to analyze the quality of each source.

Sources of Bias

Bias was diminished by completing a comprehensive search including ten databases, google scholar, clinicaltrials.gov, the clinical trials EMA registry, a google search, and four journals. All the trials randomized their participants into the groups, and they all had a control group. All the trials minus three calculated a minimum sample size required. The State Trait Anxiety Inventory (STAI), a reputable tool in which the validity and reliability has been confirmed, was used in all studies except two, in which a stress scale like the numeric rating scale (NRS) and visual analog scale (VAS) were used. Only three studies performed gas chronometry analysis to test the actual components of the essential oils to ensure the therapeutic components are present and can cause the anxiolytic effect. Four of the studies listed the attrition rate ranging from 0 to 12. Since all of the studies used EOs which have a scent, it was not possible to blind any of the studies. Some of the studies used the same procedure but with the control using distilled water or unscented oil, while other studies only used standard care for the

control group. In Hasanzadeh, et al. (2016) the aromatherapy group was asked to breath slowly for 20 min, while the others were not, which could impact anxiety. The transferability is not very broad because all of the studies were very specific with a specific procedure, population, and essential oil. More research needs to be done with different EOs and units of the hospital.

Internal Validity

Internal validity was fairly consistent among the trials. Instrumentation was not given much detail in the reports, but some did include statements about using the same administrator, and most included the brand/source of EO that they used, which is assumed to be the same for all patients. None, however, included the method of STAI administration for all patients; the most likely is a paper questionnaire. They all compared pre- and post- intervention scores with a control group to increase validity, except for Yayla and Ozdemir (2019), who only compared the post-intervention scores between the intervention and control groups. Due to testing threat of taking a pre-test, the patients could focus more on the symptoms of their anxiety which could increase their anxiety as their focus is directed toward their anxiety. Selection bias was minimized by determining statistically significant differences between the groups before intervention, in which all of them had none except Hozumi, et al. (2017), who did not report statistical difference. Since extremes in population were not sought after, regression threat was less likely, and history threat was not considered high due to the short interval between pre- and post-tests.

In Franco, et al. (2016), age, ethnicity, ASA classification, severity, nor type of surgery were significantly different between the groups, but there was a significant difference between oncological versus plastic surgery, with oncological surgeries taking precedence in the lavender

fleur oil (LFO) group. Even though oncological surgery might be thought to exacerbate anxiety, no difference was found in preintervention anxiety between the two groups.

Hozumi, et al. (2017) described the demographic homogeneity of the groups as a mean, and did not calculate statistical significance. The estimated sample size needed was 300, and they had 361 patients for the study with an attrition rate of three. All the EOs used were from the same Japanese company, Seikatsunoki. The same endoscopist performed all the colonoscopies, and they were all done under no sedation and with 10mg scopolamine butylbromide IM as an antispastic. The patients were asked to grade their anxiety and abdominal discomfort of the procedure on a numeric rating scale (NRS), but it is not stated in what form it was given or if it was the same person assessing each patient. In addition, the NRS is not so commonly used as the STAI for anxiety in such trials, and no validity of the NRS was explained.

Hosseini, et al. (2016) found no significant difference between the control and lavender EO intervention group with sex, age, racial group, education, and marital status, and no significant difference in preintervention anxiety. They did not calculate the required sample size. The lavender EO was from Kashan Barich essence company, but no gas chronometry was performed. The cortisol test kits were from Monobind, made in USA with a sensitivity of 62.5 pg (0.25 μg/dl). The interventions were all performed in the same hour on the day of surgery. The study may be generalized to other heart surgeries but not those on psychiatric medications, such as those with anxiety disorders.

Moradi et al. (2021) had as part of their inclusion criteria the ability to smell to ensure the citrus oil had the same effect on all patients since they could not blind it. No significant difference between the intervention and control group was found in regards to preintervention anxiety and demographic info including anxiety-related diseases. A pilot study was completed to

determine that 40 participants per group were required. Forty participants were in each group but six from each group withdrew. The intervention was performed 60 minutes before angiography by the same person and the pre- and post-tests in both groups were by the same person. Each patient in the intervention group received 4mL of citrus aurantium in which the density of aurantium acid was determined by the School of Pharmacy, Kermanshah University of Medical Sciences, Iran.

Yayla and Ozdemir (2019) also included in their criteria that participants could not have a problem smelling to even out the effects. Demographic characteristics between groups did not have any significant difference, but the authors did not list the difference between pre-intervention anxiety scores. They calculated the sample size to be 123, which is exactly as many as they had. For instrumental threats, the authors specified that face-to-face interviews were used but did not say if it was the same interviewer for every patient. In addition, specific information on the EO supplier was not given, and they just say the EOs were of "good quality" based on the GC analysis certificates and give the top ingredients. Of the external variability, the authors conclude that since it is only from one hospital and only with those with an implantable venous port catheter, it cannot be generalized.

Selection bias was ruled out in the study by Hasanapour, et al. (2017) with the finding of no significant difference in demographic nor anxiety scores before intervention. Demographic information included history of hospitalization and operation waiting time which were not included in all other studies but could have an effect on anxiety. Their calculation of sample size resulted in 50 required participants per group, which is the number they had. The lavender essence was from Kandelos Co., and instrumentation treats were reduced by having the same two researchers administer the surveys. All were handwritten unless the patient could not write due to

an injured hand in which case the researcher asked each question and recorded the answers for him, introducing some bias.

Hasanzadeh et al. (2016) did not calculate the sample size required for their study but used 80 participants. Between the four groups (one being a control group), there was no significant difference in demographical information, time the chest tube had been in, or pre-intervention anxiety. The lavender EO was from Giah Essence Pharmaceutical Company, with lavender grown in Southeast Gorgan, in Iran. The specific details of collection, identification, and GC and GC-Mass Spectrometry are recorded with findings of linalool being the highest concentration of any other component at 21%. The method of STAI administration is not recorded. An ICU nurse assessed the patients, and it is unlikely to have been the same nurse each time, but they do not specify. Smell deficits were also excluded from this study, but a source of bias, the aromatherapy group was asked to inhale slowly for 20 min., which could impact anxiety scores. Generalizability would be only in patients with chest tubes being removed post-coronary artery bypass graft (CABG) surgery excluding patients with a BMI>30, unstable vital signs (VS), on mechanical ventilation (MV) or sedatives, on analgesics, patients with a psychiatric disorder, or smokers.

Fayazi, et al. (2011) did a pilot study to find that they needed 36 patients per group, which is what they recruited. No significant difference was found in demographic and hospitalization information or in anxiety before the intervention. The brand or where the oil was sourced from is not listed. Also not listed are the number of researchers administering STAI or the method by which they administered it. For external validity, the results cannot be generalized because the study took place only in two specific hospitals in Iran with specific criteria.

Kim, et al (2011) completed a pilot study to find a minimum of 10 subjects per group would be required. They recruited 30 volunteers to split between the two groups randomly. No significant difference was found between the patients' heights, ages, sex, weight, or stress scores with the first needle insertion, before intervention. Lavandula angustifolia from Plant Life Natural Body Care was used, but a GC was not obtained. Instrumentation rigor was increased by using a study-blinded anesthesiologist for all patients to measure bispectral index scores (BIS) and ask patients to verbally rate their pain and rate their stress on a scale of 0 to 10. Rating stress on a scale from 0 to 10 is not commonly used, and it may be hard for some patients to recognize how stressed they are without including rating of their symptoms or an objective measurement.

Appraisal Tools

The Johns Hopkins Nursing Evidence-Based Practice Research Evidence Appraisal Tool (n.d.) was used to evaluate each article and the John Hopkins Nursing Evidence Level and Quality Guide to score each article with permission from ©The Johns Hopkins Hospital/The Johns Hopkins University. All of the studies graded at a Level 1. Gaps were not addressed in Franco, et al. (2016) and none of the articles had the literature review with resources mostly from the last five years. Four of the articles, Franco, et al. (2016), Hosseini, et al (2016), Hasanpour, et al. (2017), and Hasanzadeh, et al. (2016), did not give a rationale for their sample size or state that they calculated the minimal size needed. Two studies used something other than STAI and did not discuss instrument reliability (Franco, et al., 2016; Kim, et al., 2011). Two studies did not discuss instrument validity (Hozumi, et al., 2017; Kim, et al., 2011). One study, by Hassanpour, et al. (2017), did not include the results on the vital signs (VS) of the groups, like they described in the methods section. Two did not address limitations (Fayazi, et al., 2011; Kim, et al., 2011). Hasanpour, et al. (2017) and Hasanzadeh (2016) also did not list the statistical results in their

narrative but just put it in tables, so that information could not be compared for consistency, and Hosseini, et al. (2016) had an inconsistency with the p value of the change in anxiety scores between the text and the table. None of the studies were in more than one setting, so that did not apply. Everything else on the Hopkins appraisal tool was answered in the affirmative, including: stated what is known/unknown about the problem and identifies gaps, clear purpose stated, sample size sufficient based on design and rationalization, characteristic/demographics was similar in control and intervention groups, all groups were treated equally except the intervention group, data collection was described clearly, Instruments were reliable (α>0.70), instrument validity was discussed, response rate on questionnaires was >25%, results are presented clearly, limitations are addressed, and conclusions are based on results. Abdelhakim, et al. (2020), a review, underwent a different part of the Hopkins appraisal tool. It was graded a level 1 systematic review with meta-analysis, and answered everything in the affirmative, except that it did not include the limitations/strengths of each study included. There was no theoretical or gray literature included in the present integrated review.

Table 1

The Johns Hopkins Nursing Evidence-Based Practice Research Evidence Appraisal Tool

	Franco	Hozumi	Hosseini	Moradi	Yayla	Hasanpour	Hasanzadeh	Fayazi	Kim	
Manipulation of independent variable	√	√	√	√	√	√	√	√	√	all√= Level 1
Control group	√	√	√	√	√	√	√	√	√	
Randomly assigned to groups	√	√	√	√	√	√	√	√	√	
Known/unknown about the problem and identifies gaps	x-gaps not addressed	√	√	√	√	√	√	√	√	=consistent results (not generalizable outside of specific procedure), sufficient sample size
Purpose clear	√	√	√	√	√	√	√	√	√	
Lit review current (last 5 years/classic)	X	X	X	X	X	X	X	X	X	

	Franco	Hozumi	Hosseini	Moradi	Yayla	Hasanpour	Hasanzadeh	Fayazi	Kim	
Sample size sufficient based on design and rationalization	No rationale	√	No rationale	√	√	No rationale	No rationale	√	√	for study design, adequate control, definitive conclusions, consistent recommendations based on comprehensive literature review that includes thorough reference to scientific evidence
Characteristic/demographics similar in control and intervention groups	√	√	√	√	√	√	√	√	√	
If multiple settings, similar	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
All groups treated equally except intervention	√	√	√	√	√	√	√	√	√	
Data collection described clearly	√	√	√	√	√	√	√	√	√	
Instruments=reliable (α≥0.70)	√ (but not VS)	√	√	√	√	√	√	√	Not discussed	
Instrument validity discussed	√	x	√	√	√	√	√	√	x	
Response rate on questionnaires >25%	√	√	√	√	√	√	√	√	√	
Results presented clearly	√	√	√	√	√	x-VS not reported	√	√	√	
Narrative consistent with the table content	√	√	x	√	√	Only stated info in table, not narrative	Only stated info in table, not narrative	√	√	
Limitations addressed	√	√	√	√	√	√	√	x	x	
Conclusions based on results	√	√	√	√	√	√	√	√	√	

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Applicability of Results

The results of the appraisal have been made into a table including appraisal of the introduction, design, sampling, data collections, results, discussion, tables/graphs, and relevance to the guiding questions. The preamble and ethical matters were not critiqued by the John Hopkins critical appraisal tool. All of the articles were ranked as high quality except for the lack of generalizable results.

Reporting Guidelines

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) has been used to document and show the systematic nature of the literature search process in this integrative review (Page, et al., 2021). The data was extracted and categorized into tables. Comparison was made and the data were coded, analyzed, and synthesized (Whitmore & Knafl, 2005).

Section Five: Data Analysis and Synthesis

Data Analysis Methods (Constant Comparison)

Multiple tables were created to look at different aspects of the articles and manually code the data. Data reduction was completed first by choosing aspects of each report to focus on and finding specific information from each report. The data was then inserted it into matrices and graphs as part of the data display stage, rearranging it in different ways to be able to better understand and analyze it. Data was compared, and patterns and themes were identified. Questions that came up were addressed with a librarian or the thesis chair. Conclusions were made from the generalizations noted, and throughout the process, the information was verified with the original sources.

Descriptive Results

Ten reports were included from 2011 to 2021 with a total of 1685 patients, nine of which were randomized controlled trials (RCT) and one a systematic review with meta-analysis. Five of the studies were conducted in Iran, and four of those were on patients undergoing coronary procedures. One study was conducted in Korea, one in the United States, one in Japan, one in Turkey, and the systematic review was completed in Egypt, but most of the trials were from Iran. There was one study with patients undergoing abdominal surgery and one colonoscopy. The one in the US was with patients undergoing breast surgery, and the one in Turkey with patients undergoing chemotherapy. Table 2 summarizes the design, authors, location, population, and limitations of each study.

Table 2

Descriptive Results and Limitations

	Year	**Design**	**Authors: MD or RN**	**Country**	**Population**	**Limitations**
Fayazi	2011	RCT	nursing	Iran	Preop heart and abdominal surgery	Not listed
Kim	2011	RCT	Interdisc: MDs and PhDs-informatics and nursing	Korea	preoperative	Not listed
Franco	2016	RCT	Interdisc: MDs and MS and PhD research coordinators	US (NY)	Adult women scheduled for breast surgery	-All females (have higher anxiety) -Lack of a third group with nothing added to face mask
Hasanzadeh	2016	RCT	Interdisc: Nursing, anesthesiology, pharmacognosy, Biotech, MD researcher	Iran	CABG pts with a CT in for >24 h undergoing CTR	-Small sample size -CABG only -Subjective (STAII) -Not blinded
Hosseini	2016	RCT	Interdisc: Nursing, medical, pharm, research, anesthesiology, psychiatry	Iran	Candidates for open-heart surgery	-variables such as different levels of understanding, culture, beliefs,

	Year	Design	Authors: MD or RN	Country	Population	Limitations
						and religious beliefs
Hozumi	2017	RCT	Not listed, most likely doctors	Japan	Male patients undergoing colonoscopy	-Males age 40-50s -Other demographics -Not elucidated how it physiologically affects the body
Hasanpour	2017	RCT	Interdisc: nursing, med, plastic reconstructive and burn surgery, biostats, trauma and injury research center	Iran	undergoing upper limb reconstruction surgery	none
Yayla	2019	quasi-randomiz-ed controlled quasi pilot study	Nursing, PhD	Turkey	cancer patients with implantable venous port catheters scheduled to undergo chemotherapy	-only during 1 cycle of chemo=no long-term effects studied -too specific to generalize
Abdelhakim	2020	SR and meta-analysis of RCTs	MDs	Egypt, but most of the RCTs were from Iran	Patients undergoing any cardiovascular surgery	-small sample -not blinded -did not examine different stress hormones in the plasma -concentration and exposure time have not been estimated -differences in placebo
Moradi	2021	RCT	Interdisc: Med, nursing, health, nursing school research,	Iran	Patients undergoing coronary angiography	-not blinded -pt backgrounds affect anxiety

Synthesis

All of the studies on coronary procedures were studied in Iran, interestingly. Six of the studies used solely lavender EO (LEO), one used LEO for one intervention group and eucalyptus for the other, another had three intervention groups: one with LEO, one with grapefruit oil, and the last with tea olive oil, and one study just used neroli oil. Three used *Lavandula angustifolia*, all with a statistically significant improvement in anxiety. *Lavandula officinalis* was only used in one study with no significant difference in anxiety. In the same study by Yayla and Ozdemir (2019), *Eucalyptus globulus* was used in a separate group but also did not have any significant decrease in anxiety as measured by the STAI. One study used *Citrus aurantium* and had a significant difference in anxiety level between the intervention and control group. Four of the reports used LEO but did not specify the species, and all of those showed a significant decrease in anxiety on the STAI. Table 4 outlines the statistical differences between the studies.

Table 4

Statistical results

	EO	***Instrument***	***Intervention group***			***Control group***			***P***
			Pre-	*Post-*	*difference*	*Pre-*	*Post-*	*difference*	
Fayazi 2011	Lavandulan	STAI	51.00	38.61	12.39	50.67	49.53	1.14	0.001
		VS	No significant difference						>0.05
Kim 2011	*Lavandula angustifolia*	VAS	5	2	3	4	4	0	<0.001
		BIS	95	80	15	95	95	0	<0.001 at 5,10,15,20 min
Franco 2016	Lavender fleur oil (containing *Lavandula angustifolia*)	STAI	Not listed, sign diff for positive scores negative scores						0.001 <0.0001 in LFO, 0.0007 in UO
		HR & BP	Not significant						
Hasanzadeh 2016	*Lavandula angustifolia*	STAII	38.2	23.2	15	33.9	27.5	6.4	<0.001 or 0.0001 (in-consistent)
Hosseini 2016	lavender	STAI	56.73	54.73	2	55.18	54.07	1.11	<0.0001
		Serum cortisol	16.76	14.88	1.88	16.19	15.77	0.42	<0.001
		VS	BP & RR as covariates to confirm the effect of intervention on						0.001 0.002

	EO	***Instrument***	***Intervention group***			***Control group***			***P***
			Pre-	*Post-*	*difference*	*Pre-*	*Post-*	*difference*	
			cortisol						
Hozumi 2017	lavender oil, grapefruit oil, and *Osmanthus fragrans*	NRS	Hard to read graph						<0.05
Hasanpour 2017	Lavender essence	STAI:State anxiety	55.80	41.86	13.94	55.76	55.56	0.2	<0.001
		STAI: trait anxiety	53.93	45.66	8.27	55.90	55.90	0	>0.001 (0.89)
		VS	Results not listed						
Yayla & Ozdemir 2019	*Lavandula officinalis*	STAI-I	Did not compare pre- v post	37.24 (69.9% = "mild" 34.1% moderate)			37.73 (61% mild 39% mod)		>0.05
	Eucalyptus globulus			35.24 (75.6% mild, 24.4% mod)					>0.05
Abdelhakim 2020 (meta-analysis)	8: lavender 1: rose	STAI						MD=-3.21, MD=-1.67 after resolving heterogenity	0.03, 0.02 after resolving heterogenity
		DASS						MD= -1.78	0.33 (no sig diff)
		HR						MD= -5.49	0.003
		SBP						MD= -1.66	0.69 (no sig diff)
		DBP						MD= -2.40	0.30 (no sig diff)
Moradi 2021	*Citrus aurantium*	STAII	53.30	42.37	10.93	52.04	51.66	0.38	<0.01
		SBP	134.82	124.49	10.33	133.86	133.76	0.1	<0.01
		DBP	84.49	79.23	5.26	83.79	83.51	0.28	<0.01
		RR	17.87	14.54	3.33	17.54	17.97	-0.43	<0.01
		PR	76.48	70.03	6.45	76.44	76.13	0.31	<0.01

Anxiety scores were measured with STAI in nine of the studies, with two not giving specific results, but all except Yayla and Ozdemir (2019), who did not give any results on the

STAI, had a significant decrease in scores before and after intervention in the intervention group and between the intervention and control groups. Yayla and Ozdemir (2019) were the only ones who did not compare pre-intervention and post-intervention scores but only compared between groups. Among the ones that did not use STAI, Kim (2011) used the VAS to rate stress and Hozumi, et al. (2017) used the NRS as the primary instrument to rate stress. With both the VAS and NRS, significant decreases in anxiety scores were noted. Hosseini, et al. (2016) were, perhaps surprisingly, the only ones to use cortisol as a measurement. They found a significant decrease in serum cortisol before and after intervention and between the groups. Even though Abdelhakim, et al. (2020), found a drop in anxiety scores on the STAI, they did not find a significant difference on the depression anxiety stress scale (DASS). Fayazi, et al. (2011) and Yayla and Ozdemir (2019) compared the severity of anxiety as mild, moderate, or severe, but the results are conflicting. Fayazi, et al. (2011) found a significant difference in the post-intervention scores in the intervention group as compared to the control group while Yayla and Ozdemir (2019) did not. Significant reductions in anxiety were noted in all studies except Yayla and Ozdemir on the STAI, VAS, NRS, and in serum cortisol, but not in the DASS or in the severity of anxiety in two of the studies.

Six incorporated the measurement of vital signs. Hassanpour, et al. (2017) did not list the results. Five of the ones that did include results measured blood pressure, of which, three found a significant difference, with Fayazi, et al. (2011) only finding a significant difference in systolic BP (SBP) but not diastolic (DBP), and the other two did not any significant difference. Five studies assessed heart/pulse rate with three finding no significant difference and two finding a significant difference. Respiratory rate was assessed in three studies, with no significant difference in two studies and a significant difference in one. Hosseini, et al. (2016) entered serum

cortisol levels, SBP, DBP, pulse, and respiratory rate values into ANOVA to find that around 70% of the cortisol drop was due to lavender. VS results are conflicting and need further research.

The procedures were similar in many of the studies with measurements of anxiety right before intervention and after intervention ranging from immediately after to 25 minutes after. Five of the studies used either a cotton ball or gauze to deliver the aromatherapy, two used an oxygen mask, one used a handkerchief, one used a commercial aroma diffuser, and Abdelhakim, et al. (2020) used various methods of inhalation in the different studies included. Table 4 shows the different and ratio of oil to diluent, if used. Hozumi, et al. (2017) used a blending ratio to determine how much of each oil to use. An average of two drops were used in the studies that did not use a diluent. Time of inhalation varied from three minutes to twenty minutes in the majority of the trials. Many of the reports used an object such as a cotton ball to directly put two drops, on average, of EO on, which was pinned or held close to the patient's nose and inhaled for three to twenty minutes before the procedure.

Table 5

Oil and Diluent Ratios

	Oil	**Diluent**	**Ratio**
Franco (2016)	LFO (*Lavandula angustifolia*)	oxygen	2 drops:2L/min
Hozumi (2017)	Lavender oil	tap water	0.05mL: 70mL
	Grapefruit oil		0.03mL: 70 mL
	Osmanthus fragrans oil		0.05mL: 70 mL
Abdelhakim (2020)	varies		
Hosseini (2016)	Lavender essence	None (sterile gauze)	2 drops
Moradi (2021)	*Citrus aurantium*	Not listed	Not listed
Yayla (2019)	*Lavender officialis*	None (cotton swab)	3 drops
	Eucalyptus globulus		
Hasanpour (2017)	Lavender essence	None (gauze)	Not listed
Hasanzadeh (2016)	LEO	None (cotton ball)	1-2 drops
Fayazi (2011)	Lavendulan oil	None (handkerchief)	2 drops
Kim (2011)	*Lavandula angustifolia*	Jojoba oil	2 drops:100 drops

Four studies also measured pain along with anxiety. All showed a significant decrease in preprocedural pain intensity, but Hasanzadeh, et al. (2016) did not find a change in the quality of pain. All of the studies used lavender EO, and Abdelhakim, et al. (2020) had one rose EO in their review. Yayla and Ozdemir (2019) found that only the LEO, not the eucalyptus EO significantly decreased pre-procedural pain during needle insertion into an implantable central venous catheter. Three used the VAS for pain, and one, Kim, et al. (2011) used the NRS.

Two other studies included other measurements related to anxiety, as seen in tables C1 and D1 (See Appendix C and D). Bispectral Index Scores (BIS) were measured by Kim, et al. (2011) to see the impact of lavender on brain activity and sedation. BIS decreased significantly for 20 min. after inhalation. Hozumi, et al. (2017) looked at abdominal discomfort, which may increase with increased anxiety, and found Grapefruit, and *Osmanthus fragrans* to attenuate abdominal discomfort using the NRS in patients with high anxiety levels. A reduction in anxiety may also be related to the reduction in brain activity and in abdominal discomfort reported by these two studies.

Adverse effects can be of concern, but none were reported in the included reports. Four of the reports stated that there were no adverse effects. The other six did not mention adverse effects at all.

Common limitations include the lack of blinding in patients due to the odor of EOs, small sample sizes, variables including patient's background and demographics, and a specific population and location that make the results hard to generalize. Franco, et al. (2016) only included females due to the population undergoing breast surgery, and Hozumi, et al. (2017) only included males in their fourth and fifth decade due to the population available and the fact that they are at greater risk of having more severe abdominal discomfort. Another limitation

included lack of a control group without a placebo in five of the studies, such as face mask with no unscented oil (UO) in Franco, et al. (2016), however, the other studies used distilled water instead of an UO. Franco, et al. (2016) saw a significant improvement in anxiety scores with the UO (control group), whereas none of the other studies did. Hasanzadeh, et al. (2016) noted that using a survey was subjective, however, many of the other studies used vital signs or cortisol measures to reduce subjectivity. Limitations were noted in seven of the reports, many of which applied to all of the studies.

Table 6 shows the conclusions varied from confidence in aromatherapy to wariness. Three reports concluded stating the simplicity/easy use of aromatherapy, and two used the term effective to describe aromatherapy. Five recommended its use in the clinical setting, with three putting the limitation of use in the specific setting of their study, and Hasanpour, et al. (2017) recommended it in the pre-surgical setting. Moradi, et al. (2021) recommended a program for nurses and staff with in-service education for coronary angiography. Kim, et al. (2011) said that the results are hard to interpret but may be helpful in the ambulatory setting, and Franco, et al. (2016), who found decreased anxiety in the placebo, UO group, as well, added that the placebo effect of the LEO likely impacts the attenuation in anxiety due to added attention the patients receive. Six out of the ten stated that further research is required.

Table 6

Introductions and conclusions: How anxiety affects patients and mechanisms of the EOs

	Effects of preprocedural anxiety (Introductions)	Effects of the EO (Conclusion/discussions)
Fayazi, et al. (2011)	-Severe preoperative anxiety can delay post-op wound healing -Associated with more pain -increased risk of infection -increased post-op analgesic requirements	Psych and physical: -odor activates olfactory nerves entering the limbic system. -Depending on the EO, neurons release neurotransmitters such as encephalin, norepinephrine and

	Effects of preprocedural anxiety (Introductions)	Effects of the EO (Conclusion/discussions)
	-lengthened hospitalization	serotonin. -association between olfactory and psyche -linalool and linalyl acetate activate the parasympathetic system. Linalyl acetate also acts as a narcotic and linalool as a sedative -some studies: GABAnergic effect like BZDs
Kim, et al. (2011)	-increase intraoperative anesthesia requirements -affects recovery from anesthesia	-preop anxiety can increase anesthesia requirements (anxiety and BIS-sedation) so when anxiety decreases, the need for sedatives may also decrease -will not prolong sedation after surgery -no increase in N/V -cost effective -noninvasive -glutaminergic: potentiates γ-aminobutyric acid
Franco (2016)	-increases anesthetic requirements, increasing risks -many anxiolytic meds cause "excessive and prolonged amnesia, sedation, and, infrequently, respiratory depression" which is inappropriate because pt must sign informed consent -LEO: one of the least toxic and allergenic of the EOs	- "A national survey suggests that the estimated number of visits to complementary alternative medicine practitioners exceeded the number of visits to all primary care physicians" (p. 247). -lavender affects voltage-sensitive calcium channels
Hasanzadeh, et al. (2016)	Not much about anxiety	Anxiety has not been studied much in CTR
Hosseini, et al. (2016)	-increases cortisol and epinephrine (E) -decreases cognitive function -destruction of thyroid function -hyperglycemia -HTN -suppresses immune and inflammatory responses -delays wound healing -reduces muscle mass	-several other studies have shown aromatherapy to decrease cortisol levels -psychological aspect of open-heart surgery=higher anxiety, so any intervention may decrease stress and increase trust in the staff
Hozumi, et al. (2017)	-increases abdominal discomfort -try not to use sedatives during colonoscopy d/t AEs (CV depression, respiratory	-grapefruit oil may suppress the insular cortex or the anterior cingulate gyrus by stimulating olfactory neurons

	Effects of preprocedural anxiety (Introductions)	Effects of the EO (Conclusion/discussions)
	depression, anterograde amnesia)	
Hasanpour, et al. (2017)		-the second most used therapy by nurses clinically -introduced by the US State Boards of Nursing
Yayla and Ozdemir (2019)	-decreases compliance -anxiolytic EOs: LEO, eucalyptus, sage, lemon, majoram	-eucalyptus in a blend may decrease anxiety d/t the synergism of the oils
Abdelhakim, et al. (2020)	-anxiety=a complication of cardiac surgery	-decreases SNS and the concentration of E -the limbic system influences HR, BP, and the respiratory system
Moradi, et al. (2021)	-increases RR and HR -increases myocardial oxygen use, E and NE, and plasma density causing interstitial damage and platelet aggregation	-Citrus aurantium has anti-depressant effects and increases blood flow

Section Six: Discussion

Answering the question, “How do inhaled essential oils affect pre-procedural anxiety of adults in acute care settings?” this review finds conflicting evidence. However, the majority of the findings support the hypothesis that aromatherapy can attenuate anxiety even without all the oils containing a level of linalool and linalyl in the 30-40% range (Franco, et al., 2016). There was more variation in VS measurements with three out of five favoring a drop in blood pressure, and more showing no significant difference in regards to heart rate and respiratory rate. However, BIS levels significantly decreased in Kim, et al. (2011), perhaps signifying the reduced impact of stimulation to the brain due to decreased anxiety levels and the improvement in sedation. Since pain and anxiety are linked, it is interesting to note that all four of the studies that included pain as a measurement found it decrease after lavender inhalation, and a fifth measuring

discomfort in the abdomen also found it to decrease with aromatherapy in those with high anxiety levels. No adverse effects were present in any of the reports. Although further research is required, finding a therapy to decrease anxiety, BIS, pain, and improve sleep without the adverse effects of anxiolytic drugs may prove very helpful.

Kang, et al. (2019) found in their meta-analysis of studies focusing on the anxiolytic effects of lavender through various routes, that lavender is effective in reducing symptoms of anxiety of healthy patients and those with anxiety disorders. LEO was found to decrease SBP but not DBP, heart rate, and serum cortisol, similar to the findings of the present review. Perry, et al. (2012) did a review of randomized controlled trials on the efficacy of lavender EO and found seven out of fifteen trials favoring lavender and one finding it as effective as lorazepam. Ghiasi, et al. (2019) also found aromatherapy to be effective in significantly reducing anxiety in fifteen of the sixteen included studies during the first stage of labor. However, all of the reviews included studies in a wide variety of places and hospitals, using various EOs for differing amounts of time, with different routes, which makes it hard to compare findings.

Wang and Heinbockel (2018) found that Citrus aurantium affects 5-HT_1A receptors to cause the anxiolytic effect presented in Moradi, et al. (2021). *Lavandula angustifolia* also affects the serotonergic system, but they did not think it likely that it interacts with GABA receptors. Lopez, et al. (2017) also found no effect on GABA receptors, but they suggest that lavender inhibits the N-methyl-D-aspartate (NMDA) receptor and the serotonin transporter (SERT), similar to SSRIs but may also have a neurotoxic effect due to hydrogen peroxide. Schuwald, et al. (2013) found in preclinical trials that LEO inhibits voltage dependent calcium channels (VOCCs) in mostly hippocampal neurons and has some similarities with pregabalin but does not use the same binding site. Malcolm and Tallian (2017) support the research that LEO works by

reducing $5HT1_A$ receptor activity and inhibiting VOCC through linalyl acetate which is converted to linalool in the liver. The known mechanism of action of LEO supports the findings of reduced cortisol levels and anxiety scores.

Wang and Heinbockel (2018) also list popular oils for anxiety as *Anthemis nobilis* (chamomile), *Salvia sclarea* (clary), *Rosmarinus officinalis* (rosemary), *Lavandula angustifolia* (lavender), and *Rosa damascena* (rose) of which, only two were found in the present review. *Rosa damascena*, used in one of the studies included in the review by Abdelhakim, et al. (2020), decreased anxiety to a significant degree. Dhakad, et al. (2017) explains that eucalyptus oil, which was used in Yayla and Ozdemir's (2019) study with no benefit in anxiety score, has a largely unknown mechanism of action, but 1,8-Cineole is assumed to be the therapeutic component, metabolized by the CYP2A6 pathway. Hozumi, et al. (2017), who found *Osmanthus fragrans* to attenuate anxiety, describes the effect of it on the lateral hypothalamus to reduce orexin secretion, a hormone involved in wakefulness and mood. They also explain that grapefruit oil may suppress the anterior cingulate gyrus or insular cortex. However, Hozumi, et al. (2017) used the NRS as the only method to rate anxiety and did not discuss instrument validity. LEO has the most research, but there is some evidence of *Rosa damascene* and *Osmanthus fragrans* oils being effective in reducing anxiety.

Although most of the trials in the present review reported aromatherapy as safe with few adverse effects, Posadzki, et al. (2011) searched five databases plus departmental files to find adverse effects of EOs with no time limit, and only found two cases with inhaled EO causing an adverse effect. One study with inhaled roman chamomile caused lightheadedness, tachycardia, and nausea, and another case with eucalyptol in children caused dyspnea, loss of consciousness, and metabolic acidosis. Matthew, et al. (2017) reported ten cases of acute seizures due to

inhalation of eucalyptus oil in three hospitals over two years. However, Malcolm and Tallian (2017) note that LEO has been deemed Generally Recognized as Safe by the FDA. Out of 1685 patients in this review, no adverse effects were reported, which may indicate a lower risk compared to anxiolytic medications, but as a limitation, six of the studies did not specifically include a statement about adverse effects as part of the results. More research should be done to determine the risks of inhalation aromatherapy.

Malcolm and Tallian (2017) also note the emotional memory associated with smells, which may have impacted the preprocedural patients's anxiety, especially since LEO affects the hippocampus. They note that the smell of a dentist office that may produce anxiety in some patients can be covered up to some extent by aromatherapy. Participants may also expect LEO to reduce their anxiety, creating further bias. The fact that the smell of aromatherapy cannot be blinded likely had an impact on the studies included here.

Some gaps in the research include experimenting with other EOs that might have an anxiolytic effect. No studies with large sample sizes, recording adverse effects have been seen in this search process. A large gap is the lack of a regulating organization to certify the purity and therapeutic qualities of various EO companies. Further research using serum or salivary cortisol as an objective measurement is indicated, along with more studies measuring vital signs. There is also a lack of long-term studies looking at the beneficial and adverse effects of aromatherapy. A major limitation is the diverse background of patients, their experiences, religious beliefs, smell-associative memory, etc.

Limitations of the current integrative review would include only one researcher, the different dates of database searches, and the fact that two of the articles that fit the inclusion criteria could not be retrieved in English even with the help of a librarian. Better organization of

the results for the PRISMA flow diagram is also recommended. A strength would be the use of a librarian and the thesis chair to check areas of conflict or areas of lack of knowledge about the review process. Another strength includes the number of databases searched and the gray literature that was searched. The PRISMA flow chart and John Hopkins tools also added rigor to this review. This review makes a contribution to the growing body of literature by suggesting that aromatherapy could make an impact in the pre-procedural setting to reduce anxiety and by bringing together the methods, types and quality of EO, and limitations of recent research to further the discussion and encourage new studies that address the gaps noted.

Implications for Practice/ Future Work

Since there is conflicting evidence, further research must be completed before aromatherapy can be accepted into practice for pre-procedural anxiety. More settings need to be studied, and more experiments in each of those settings need to be done with rigor. Since there is no governing body for the quality of EOs, a certification approval establishment needs to form to test the GC of oils from different companies and create a database for consumers and practitioners alike. The next step would be to do a pilot study, followed by a study with a large sample size looking at many different procedures in one hospital. More studies around the world must emerge with more reviews to better assess the efficacy and safety of aromatherapy for pre-procedural anxiety.

In conclusion, anxiety before procedures can impact the requirements of sedatives and analgesics and recovery, but most anxiety medications have undesirable side effects and may interfere with adequate understanding of the procedure for informed consent. After comparing ten RCTs before various procedures, it is seen that aromatherapy, specifically lavender EO inhalation, may attenuate pre-procedural anxiety in patients as measured by self-reported

anxiety, serum cortisol levels, and pain, abdominal discomfort, and BIS levels. Further research is needed in the area of aromatherapy and its impact on anxiety scores, vital signs, and adverse effects.

Dissemination

The present integrative review will be presented at Liberty University's research week. A podium presentation was chosen to disseminate the information at research week. It will also be submitted to Scholar's Crossing, the journal to publish Liberty University's honor's theses.

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Appendix A

Permissions

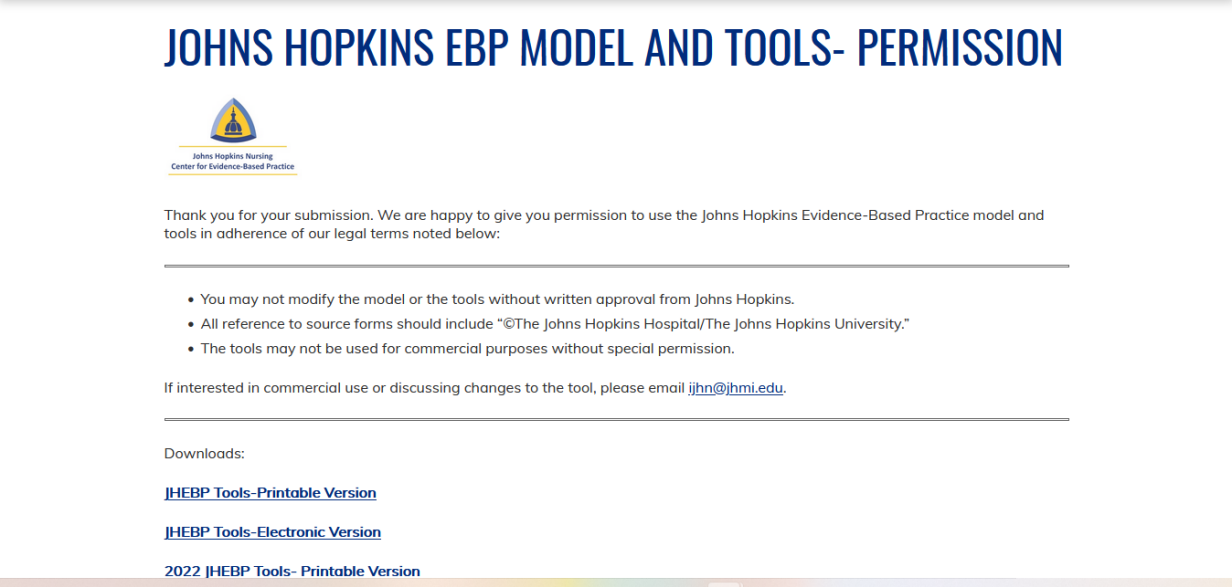

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Figure A1

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Appendix B

Literature Matrix

Table B1

Literature Matrix

First author (year)	Study design	Condition (sample size: analyzed)	Experimental treatment	Control treatment	Anxiety outcome measurement	Main result (between groups)	Author's conclusion
Franco (2016)	Level 1 (RCT)	Adult women scheduled for breast surgery (93:93)	2 drops Lavender fleur oil (LFO) in an oxygen face mask <2L/min	Unscented oil (UO)	1. Speilberger State Anxiety Inventory for Adults (STAI) before and after the 10 min treatment 2. HR and BP measured 5 min before and after	1. Both LFO and UO decreased STAI negative score totals and increased positive score totals, with the LFO group having a slightly, but statistically significant, greater effect 2. no change in VS	"Both LFO and UO aromatherapy treatments lowered anxiety before surgery despite no significant changes in vital signs" (p. 204).
Hozumi (2017)	Level l (RCT)	Male patients undergoing colonoscopy (364:361)	1.Vapor diffusion using 70 mL of tap water with 0.05 mL of lavender oil 2.vapor diffusion with 0.30 mL	No inhalation	graded anxiety and abdominal discomfort during colonoscopy on the Numeric Rating Scale (NRS) from 0 to 10	significant reduction in anxiety in the *Osmanthus fragrans* group compared to the control, significant difference or abd discomfort with grapefruit and *Osmanthus fragrans*	"These results suggest the likelihood that aromatherapy using grapefruit oil and *Osmanthus fragrans* oil could serve as a complementary treatment for anxious patients undergoing colonoscopy" (p. 167).

First author (year)	Study design	Condition (sample size: analyzed)	Experimental treatment	Control treatment	Anxiety outcome measurement	Main result (between groups)	Author's conclusion
			of grapefruit oil 3.vapor diffusion with 0.05 mL of *Osmanthus fragrans* oil 4.Vehicle group: EO-less vapor				
Abdelhakim (2020)	Level 1: Systematic review and meta-analysis of RCTs	Patients undergoing any cardiovascular surgery (656)	Inhalation aromatherapy	patients did not receive inhalation aromatherapy or received placebo	1. anxiety via Spielberger questionnaire. 2.stress: Depression Anxiety stress scale (DASS) 3.pain: Visual analog scale (VAS) 4.vital signs	1. The pooled MD significantly favored inhalation aromatherapy group compared with control group 2. no significant difference 3. pooled MD significantly favored aromatherapy 4.HR: significant difference BP: no significant difference	"Inhalation aromatherapy especially with lavender is effective in reducing anxiety, pain and HR in cardiac surgery. However, it has no significant effect on stress, SBP and DBP" (p. 7).

First author (year)	Study design	Condition (sample size: analyzed)	Experimental treatment	Control treatment	Anxiety outcome measurement	Main result (between groups)	Author's conclusion
Hosseini (2016)	Level 1: RCT	Candidates for open-heart surgery (90)	Patients were asked to inhale two drops of lavender essence on a sterile gauze for 20 min. before and again 5 min. after the intervention	Patients were asked to inhale two drops of distilled water on gauze for 20 min	1. VS (BP, pulse, RR) 2.Spielberger anxiety questionnaire 3.Measurement of serum cortisol levels	1. significant difference but not between groups 2.significant difference in mean scores 3.significant difference correlated with VS, and about 70% reduction in cortisol level due to lavender	"Inhalation of lavender could reduce the level of anxiety and cortisol in open-heart surgery patients before surgery" (p. 401).
Moradi (2021)	Level 1: RCT	Patients undergoing coronary angiography (92:80)	inhaled *Citrus aurantium* essential oil for 15–20 min about 60 min before angiography	Following same procedure but with distilled water	1. STAI 2. VS (BP, RR, HR) Before and 20 min. after intervention	1-2. all had a significant decrease in the experimental groups with no change in the control group	"Inhalation of *Citrus aurantium* was effective in reducing anxiety and stress levels in patients undergoing coronary angiography" (p. 181).
Yayla (2019)	Level 1: quasi-randomized control	cancer patients with implantable venous port catheters scheduled to	**Lavender group:** "3 drops of lavender essential oil were placed	No intervention	1. pain: VAS	1. the average score was lower in the lavender than control group 2. There was no significant	"inhalation aromatherapy with lavender oil is feasible to decrease procedural pain levels during needle insertion into an implantable venous port

First author (year)	Study design	Condition (sample size: analyzed)	Experimental treatment	Control treatment	Anxiety outcome measurement	Main result (between groups)	Author's conclusion
	led quasi pilot study	undergo chemotherapy in an oncology unit (123)	on a cotton swab and fixed at a 10-cm distance from the patient's nose. The lavender group inhaled the essential oil for 3 minutes with normal breathing before needle insertion into an implantable venous port catheter" **eucalyptus group:** eucalyptus EO inhalation using the same procedure as the lavender		2. STAI	difference in anxiety levels among all groups	catheter. However, further randomized controlled clinical trials are needed to validate the findings of this study" (p. 40).

First author (year)	Study design	Condition (sample size: analyzed)	Experimental treatment	Control treatment	Anxiety outcome measurement	Main result (between groups)	Author's conclusion
			group before needle insertion.				
Hasanpour (2017)	Level 1: RCT	undergoing upper limb reconstruction surgery who were admitted to the 15-Khordad Plastic and Reconstructive Surgery Hospital in 2017 (100)	The lavender essence was poured onto a non-sterile 2 × 2 gauze, and the patient was asked to breathe in for 20 minutes.	three drops of distilled water onto a non-sterile gauze of 2 × 2, inhaled for 20 minutes	1. VS 2. STAI Before and 5 minutes after intervention	1.not listed 2.lavender aromatherapy decreased state and trait anxiety	"The results of present study show the significant effect of aromatherapy on reducing the anxiety level of patients undergoing surgical reconstruction of the upper limb" (p. 228).
Hasanzadeh (2016)	Level 1: RCT	CABG pts with a CT in for ≥24 h undergoing Chest tube removal (CTR) (80)	1.applied cold with cooling gel pack 2**. inhaled lavender essential oil:** 1-2 drops on a cotton ball 10cm from nose x20min 3.both together	Neither cold nor EO	1.pain: VAS 2. pain: short form and modified-McGill pain	1.significant difference between all groups and the control group 2. no significant difference in pain quality 3.anxiety decreased in all groups with a sig difference between the cold-aromatherapy and control	all three types of interventions (cold application, inhalation of lavender essential oil, and combination of cold and lavender essential oil inhalation) could reduce pain and anxiety associated with CTR

First author (year)	Study design	Condition (sample size: analyzed)	Experimental treatment	Control treatment	Anxiety outcome measurement	Main result (between groups)	Author's conclusion
			Each group: n=20		questionnaire (SFM-MPQ) Before, immediately after, 5,10, and 15min after 3.STAII before and immediately after CTR		
Fayazi (2011)	Level 1: RCT	Preop heart and abdominal surgery (72)	2 drops lavendulan oil on a handkerchief Inhaled 20 min	2 drops water on handkerchief Inhaled 20 min	1.STAI 2.VS Before and after intervention	1.Mean anxiety of the intervention group dropped from 51.00 to 38.61 and in the control group from 50.67 to 49.53 2. only SBP dropped significantly after intervention	"inhalation aromatherapy had positive effects on reducing anxiety in patient before the surgery which is recommended as a new and easy alternative for nurses in order to reduce anxiety in the patients" (p. 282)
Kim (2011) ILL	Level 1: RCT	Preoperative patients (30)	Oxygen face mask with 2 drops of lavender oil diluted to 2% in jojoba oil wiped onto the inside of the face mask for 5	Oxygen via face mask x 5min	1.stess scale 0-10 2.bispectral index (BIS) 3.NRS (pain) Taken as baseline after 5 min of rest, after needle insertion with no	BIS levels dropped at 5,10.15, &20 min after inhalation, stress levels significantly reduced after inhalation, and pain decreased after 2nd needle insertion	Findings may help control preop fear and stress, particularly in the ambulatory setting.

First author (year)	Study design	Condition (sample size: analyzed)	Experimental treatment	Control treatment	Anxiety outcome measurement	Main result (between groups)	Author's conclusion
			min		interventions, after lavender intervention BIS at 5, 10, 15, 20, and 25 min and stress at 6 min, pain only after 2nd needle insertion		

Appendix C

Chronological Table

Table C1

Chronological table examining the methods, results, and conclusions

	2011 Fayazi	2011 Kim	2016 Franco	2016 Hasanzadeh	2016 Hosseini	2017 Hozumi	2017 Hasanpour	2019 Yayla	2020 Abdelhakim	2021 Moradi
Instrument for anxiety	STAI VS	Stress scale (0-10) BIS	STAI HR, BP	STAII	VS STAI Serum cortisol	NRS (0-10 anxiety)	STAI VS (BP, pulse, RR)	STAI VS	STAI DASS VAS VS	STAI VS (BP, HR, RR)
route	Handkerchief	Wiped on inside of O_2 face mask	O_2 face mask	Cotton 10cm from nose, slow breathing	Inhale from sterile gauze	Commercial aroma diffuser	Gauze, inhaled	Cotton swab 10cm from nose breathed normally	Inhalation, various	Cotton wool pinned to collar breathed normally
Time inhaled	20 min	5 min	10 min	20 min	20 min	Not listed	20 min	3 min	Various	15-20 min
EO used	Lavandulan	*Lavandula angustifolia*	Lavender fleur oil (containing *Lavandula angustifolia*)	*Lavandula angustifolia*	lavender	lavender oil, grapefruit oil, and *Osmanthus fragrans*	Lavender essence	*Lavandula officinalis* and *Eucalyptus globulus*	8: lavender 1: rose EO	*Citrus aurantium*
GC?	X	x	√	√	x	x	x	√	x	x
Control or placebo	Placebo: H20	Control: just O2	Placebo (UO)	control	Placebo: distilled H20	Placebo/vehicle: vapor & control	Placebo: distilled H20	control	both	Placebo: distilled water
Anxiety results	√	√	√ (control group did also, but LFO group was sig lower than control)	√	√ Anxiety √cortisol √STAI	√ *Osmanthus fragrans*	√	X with either	√	√
Other effects	Only SBP √	Stress, pain, & BIS √	VS x	Pain √ (also cold decr both)	√ BP, pulse, & RR but in both	Abd discomfort only decr. In high anxiety group with	VS not listed	Pain √ with lavender	√Pain decreased HR decreased Did not	√VS (SBP, pulse, RR)

	2011 Fayazi	2011 Kim	2016 Franco	2016 Hasanzadeh	2016 Hosseini	2017 Hozumi	2017 Hasanpour	2019 Yayla	2020 Abdelhakim	2021 Moradi
					groups	grapefruit and *Osmanthus fragrans* (anxiety was shown to sign. Incr abd discomfort)			decrease BP No sign difference in stress	
conclusion	"recommended as a new and easy alternative for nurses in order to reduce anxiety in patient" (p. 282)	"although difficult to interpret, may prove to be important in controlling preoperative fear and stress, particularly in the ambulatory setting." "a simple, low risk, cost-effective nursing intervention " (p. 825)	"It is probable that the beneficial effect observed was due to both aromatherapy with LFO and a placebo effect related to the added attention given to the patients" (p. 244)	"Given the simplicity and inexpensive nature of such approaches, their application in clinical practice could be suggested to the nursing staff" (p. 73)	"aromatherapy with lavender can be adopted as a branch of complementary medicine to control anxiety before surgeries in clinical settings" (p. 401)	"aromatherapy can serve as an effective complementary treatment for making colonoscopy procedures more tolerable" (p. 168)	"suggested to use lavender essential oil in similar clinical situations to control surgical anxiety" (p. 228)	"lavender essential oil administered by inhalation decreased VAS scores during needle insertion into an implantable venous port catheter" (p. 40)	"Inhalation aromatherapy especially with lavender is effective in reducing anxiety, pain and HR in cardiac surgery. However, it has no significant effect on stress, SBP and DBP" (p. 7).	"conducting in-service educational programs for health advisers and treatment staff, including nurses, and considering this intervention as a part of a healthcare program of coronary patients undergoing angiography are needed" (p. 181).

	2011 Fayazi	2011 Kim	2016 Franco	2016 Hasanzadeh	2016 Hosseini	2017 Hozumi	2017 Hasanpour	2019 Yayla	2020 Abdelhakim	2021 Moradi
Stated: more research necessary	√	√	x	√	x	√	x	√	√	x

Note: √=significant decrease or answer in the affirmative

Appendix D

Other Effects of Aromatherapy Table

Table D1

Other reported effects of the aromatherapies: Beneficial and adverse

Authors (year)	Purpose	Sample	Hopkin's Level of Evidence	EO used	Significant improvement in anxiety?	Other beneficial effects	Adverse Effects
Franco, Blanck, Dugan, Kline, Shanmugam, Galotti,von Bergen Granell, Wajda (2016)	"to determine whether lavender fleur oil (LFO) aromatherapy would reduce anxiety when administered to women before undergoing breast surgery" (p. 243)	Adult women scheduled for breast surgery (93:93)	1:RCT	LFO	√	**VS**: no reduction of HR or BP **STAI**: decreased feelings of fright, worry, and worry over possible misfortunes. Both LFO and UO decreased feelings of tension, jitteriness, negative attitudes, increasing feelings of well-being	Not listed (states that they were recorded, but does not present the findings in the results section)
Hozumi,, Hasegawa, Tsunenari, Sanpei, Arashina, Takahashi, Konnno, Chida, & Tomimatsu (2017).	To investigate the "effectiveness of aromatherapy for reducing anxiety and abdominal discomfort during colonoscopy" (p. 166)	Male patients undergoing colonoscopy (364:361)	1:RCT	Lavender, Grapefruit, and *Osmanthus fragrans* (tea olive)	√ (LEO and *Osmanthus fragrans*)	abdominal discomfort decreased in the high anxiety group but not in the general sample (with grapefruit and *Osmanthus fragrans*)	none
Abdelhakima, Husseinb, Doheimc, Sayed (2020)	"to synthesize evidence regarding the efficacy of inhalation	Patients undergoing any cardiovascular	Level 1: Systematic review and	8 studies used LEO 1 used rose	√	Pain decreased HR decreased Did not decrease BP No sign difference in stress	Not listed

Authors (year)	Purpose	Sample	Hopkin's Level of Evidence	EO used	Significant improvement in anxiety?	Other beneficial effects	Adverse Effects
	aromatherapy in patients undergoing cardiac surgery" (p. 1)	surgery (656)	metaanalysis of RCTs	EO			
Hosseini, Heydari, Vakili, Moghadam & Tazyky (2016)	"to determine the effect of lavender essence on the levels of anxiety and blood cortisol in candidates for open-heart surgery" (p. 397)	Candidates for open-heart surgery (90)	Level 1: RCT	LEO	√	VS: no mean difference between the groups in SBP, pulse, and RR (ANOVA: 70% correlation between cortisol levels and VS)	Not listed
Moradi, Ashtarian, Danzima Saeedi, Bijan, Akbari, Mohammadi (2021)	"To determine the effectiveness and safety of essential oil from *Citrus aurantium* on anxiety in patients undergoing coronary angiography" (p. 177)	Patients undergoing coronary angiography (92:80)	Level 1: RCT	*Citrus aurantium*	√	VS: SBP, pulse, RR had a significant difference	none
Yayla & Ozdemir (2019)	"to determine the effects of inhalation aromatherapy on procedural pain and anxiety after needle insertion into an implantable central venous port	cancer patients with implantable venous port catheters scheduled to undergo chemotherapy in an oncology unit (123)	Level 1: quasi-randomized controlled quasi pilot study	**Lavender** in one group, **eucalyptus** in other	x	Pain: reduced severity in the lavender group	Not listed

Authors (year)	Purpose	Sample	Hopkin's Level of Evidence	EO used	Significant improvement in anxiety?	Other beneficial effects	Adverse Effects
	catheter" (p. 35)						
Hasanpour, Begloo, Jafarian, Aliyari, Moghadam,Haghani, & Otaghvar (2017).	"to determine the effect of aromatherapy on the anxiety of patients undergoing surgical reconstruction of the upper limb" (p. 228)	undergoing upper limb reconstruction surgery who were admitted to the 15-Khordad Plastic and Reconstructive Surgery Hospital in 2017 (100)	Level 1: RCT	LEO	√	None listed	None
Hasanzadeh, Kashouk, Amini, Asili, Emami, Vashani, Sahebkar (2016)	"To determine the effects of cold application, inhalation of lavender essential oil, and their combination on pain and anxiety during CTR" (p. 64)	CABG pts with a CT in for ≥24 h undergoing Chest tube removal (CTR) (80)	Level 1: RCT	LEO	√	Pain intensity but not quality improved	Not listed
Fayazi, Babashahi, Rezaei (2011)	"to investigate the effects of inhalation aromatherapy on anxiety level in preoperative patients" (p. 278)	Preop heart and abdominal surgery (72)	Level 1: RCT	lavandulan	√	SBP dropped significantly, but mean pulse rate, respiratory rate, temperature, and diastolic blood pressure did not	Not listed
Kim, Kim, Yeo, Hong, Lee, Jeon	"to investigate whether lavender oil aromatherapy	Preoperative patients (30)	Level 1: RCT	LEO	√	BIS decreased significantly for 20 min. after lavender inhalation (an EEG	None

Authors (year)	Purpose	Sample	Hopkin's Level of Evidence	EO used	Significant improvement in anxiety?	Other beneficial effects	Adverse Effects
(2011)	can reduce bispectral index (BIS) values and stress and decrease the pain of needle insertion in 30 volunteers" (p. 823)					derivative used to assess LOC with sedation with midazolam or acupressure) Pain significantly decreased	