PRELIMINARY INTEGRATIVE GUIDELINES FOR AROMATHERAPY:

A TOOL FOR HEALTHCARE PROVIDERS

by

Ruth Elizabeth King

A scholarly project submitted in partial fulfillment
of the requirements for the degree

of

Doctor of Nursing Practice

in

Family and Individual Health

MONTANA STATE UNIVERSITY
Bozeman, Montana

April 2018

DEDICATION

This project is dedicated to my husband Jonathan for being the most supportive partner on the planet while I have pursued my education, my daughter Naomi, who supplied copious hugs and notes of encouragement to me when I had to work long hours studying or in clinic, and my sons Elijah and Isaiah, for cuddles and never ending comic relief.

ACKNOWLEDGEMENTS

There have been many people who have supported me and guided me along my nurse and nurse practitioner journey that deserve acknowledgment. First, my deepest gratitude to my project committee chairperson, Jean Shreffler-Grant, who helped me turn my lofty desire of making something useful into reality. I would also like to thank my committee members, Jennifer Sofie, Laura Marx, and Mindy Opper – thank you for supporting me and encouraging me with this non-traditional DNP project idea. I would also like to thank several people who were instrumental in my nursing journey, including Jeanne Hebl, CNM, whose care gave me the confidence to pursue nursing and who was the first to help spark an interest in me in holistic care and complementary therapies. I would also like to thank all of my instructors in my undergraduate and graduate education at Montana State University, particularly Linda Torma, who was the first to encourage me to pursue my goal of becoming a family nurse practitioner in my own timing and manner. Lastly, I would like to thank my parents, who taught me how to work hard and pursue excellence.

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ABSTRACT

Aromatherapy has a long history of use for medicinal purposes. In recent years, aromatherapy has increased in popularity among the general public yet many healthcare providers are unsure of its efficacy and safety. Although there are many resources for the general public and trained aromatherapists, currently no clinical guideline or evidence-based aromatherapy resource exists for the busy healthcare provider. The purpose of this project was to explore the state of the evidence available for the ten most commonly used essential oils and synthesize this evidence into integrative summaries in order to improve general healthcare providers' knowledge of this topic. The top 10 most commonly purchased essential oils were first identified as lavender, peppermint, eucalyptus, tea tree, rosemary, patchouli, lemon, rose, frankincense, and roman chamomile. Peer-reviewed journals were searched for the most current research available on human research on each oil. The student summarized the evidence in each study, conducted an initial evaluation of the evidence, and created an evidence table. This data was then converted to evidence profiles for each use that was studied for each oil, where data was pooled when appropriate and an overall quality of evidence was assessed for each use. This information was then transferred into a one-page integrative summary for each oil, which not only contains a short summary of human research available on the use(s) of the oil, but also safety considerations, how the oil was used historically, suggested mechanisms of action, any other pertinent data on the oil, and the student's overall impression. These integrative summaries may be used as an evidence-based reference tool for healthcare providers, and this project may be used as a model to build upon as new research emerges.

CHAPTER ONE

INTRODUCTION

Background

Aromatherapy is defined as "the therapeutic use of essential oils (also known as volatile oils) from plants (flowers, herbs, or trees) for the improvement of physical, emotional, and spiritual well-being" (American Cancer Society, 2014). In the literature, the terms "aromatherapy" and "essential oils" are commonly used interchangeably and therefore, this is the case in this scholarly project as well. The use of essential oils (EO) for therapeutic purpose dates back to use by ancient Chinese, Indian, Egyptian, Greek, and Roman cultures (Erlich, 2011). The popularity of aromatherapy grew in the United States during the 1980's, and continues to rise today (Erlich, 2011). There are many health claims related to aromatherapy use, including therapy for health concerns such as constipation, skin issues, insomnia, infections, pain, and anxiety (Erlich, 2011), however limited evidence exists to support the efficacy of aromatherapy to treat these health concerns.

A call for evidence-based treatments supported by high-quality research has not escaped the realm of aromatherapy. Good high quality research on aromatherapy is particularly needed due to the fact that essential oil production and sales are not federally regulated in the United States (PDQ Integrative Alternative and Complementary Therapies Editorial Board, 2015).

Challenges in Aromatherapy Research

Research involving human uses of aromatherapy is challenging for numerous reasons. Price and Price (2012) offer several theories on why essential oils have not been heavily researched with humans participants, including the high cost of pure essential oils, botanical crop variation, difficulty with blinding, and numerous confounding factors that arise in research related to the multi-effectual nature of essential oils in the body. Price and Price (2012) further conjecture that clinical testing of essential oils done in the same manner as mainstream pharmaceuticals would cost billions of dollars to test each oil's therapeutic effect due to the fact that essential oils are comprised of many components and may have numerous therapeutic effects on the body. Some essential oils have been studied extensively in vitro and in animal studies, however in vitro and animal studies do not always translate into therapeutic effect in humans due to the complex nature of the human response (Price & Price, 2012). Despite a general lack of human research, essential oils are widely available for purchase and directions for consumer use are varied and often based on anecdotal experience and not empirical evidence. At the same time, many essential oils do carry a small amount of risk with use just as any other over-the-counter pharmaceutical. Most of these risks are not life-threatening but rather include conditions such as dermal irritation, toxic doses if ingested or used on children, photosensitivity, damage to the eyes, and concerns about use during pregnancy (National Association of Holistic Aromatherapy, 2017a). Another limitation of aromatherapy research is difficulty blinding study participants to the therapy. Aromatherapy uses the sense of smell as the vehicle for many applications, making it is extremely difficult and

sometimes impossible to blind the participant to the therapy – much different from ingesting pills or applying odorless creams.

Emotion and Physiology

Comparing the physiological and emotional effects essential oils may have in the body is worth discussing as a specific challenge in aromatherapy research. As a natural substance, essential oils have a synergistic effect due to the complexity of the oil components and the complexity of the human response (Price & Price, 2012). Several studies have been conducted in which the researchers studied the comparative effects of expectation, emotion, and physiological factors of aromatherapy. Köteles and Babulka (2014) conducted a randomized experimental crossover study that explored the roles that expectations and pleasantness of essential oils played in physiological and psychological response. The participants in the study inhaled rosemary, eucalyptus, and lavender on three separate occasions and found that there was no identifiable connection between the perceived pleasantness and expectations of a particular oil and a measurable physical response (heart rate and blood pressure variation) (Köteles & Babulka, 2014). Similar conclusions were found in a study by Goepfert et al. (2017) where the effect of lemon oil inhalation was examined in 30 conscious and unconscious patients. They found that not only did lemon oil inhalation produce an increase in respiratory rate, heart rate, and diastolic blood pressure, but there was also no difference between those who were conscious versus those who were unconscious (Goepfert et al., 2017). Although these are only two studies, they suggest that essential oils may have physiological effects independent of emotional expectations or response.

On the other hand, there is also a theory that effects of some essential oils are more closely tied to emotional response than an actual physiological benefit. This is especially worth mentioning when exploring the response to pain. The International Association for the Study of Pain defines pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (International Association for the Study of Pain, 2017, p. 1). Since multiple oils may induce feelings of relaxation, it therefore becomes difficult to differentiate the exact mechanism by which pain is reduced. Shirazi et al. (2017) conjecture a possible rationale for the pain-reducing effect of rose oil inhalation in their 2017 study:

> "The exact mechanism of rose oil for pain relief is not clear, but possible mechanisms involve stimulating the olfactory system and reduction of sympathetic activity, increase in parasympathetic activity, and release of endorphin by Rosa damascena essential oil, which resulted in an increase in pain threshold" (p. 124).

Purpose

At this time, no evidence-based clinical guideline exists for aromatherapy for healthcare providers. The purpose of this project was to explore the state of the evidence available for the ten most commonly used essential oils and synthesize this evidence into integrative summaries in order to improve general healthcare providers' knowledge of this topic. An evidence synthesis approach was used to produce integrative summaries of these ten essential oils for clinicians and lay the groundwork for future guidelines. The

intent of the integrative summaries was to improve the quality of healthcare providers' care through increasing their evidence-based knowledge on the topic of aromatherapy.

Theoretical Framework

This project focused on an end product (the integrative summaries) that has the potential to improve healthcare practitioners' care; therefore Dorothea Orem's Self-Care Deficit theory was chosen to guide this project. Orem's theory centers on the basic concept that humans operate at a personal degree of self-care and when that person is no longer able to operate at this degree, nursing enters and takes steps to remedy it (Masters, 2014). Regarding self-care, Orem (as cited in Masters, 2015, p. 155) stated that the "therapeutic self-care demand consists of the summation of care measures necessary to meet all of an individual's known self-care requisites." Pursuing further clarification on treatments such as aromatherapy may fall into the category of an individual's self-care requisites. Regarding self-care deficit, Orem mentioned five methods nurses use to help patients in their self-care needs: (a) acting for and doing for others, (b) guiding and directing, (c) providing physical or psychological support, (d) providing an environment promoting personal development in relation to meet future demands, and (e) teaching (Masters, 2015, p. 156). Among these methods, the three that most applicable to this project include: "Guiding and directing, providing physical or psychological support, [and] teaching" (Masters, 2015, p. 156).

Orem's theory and promotion of evidence-based practice go hand in hand. Conducting an integrated review of aromatherapy for general healthcare providers is

grounded in the assumptions that patients are either already using or interested in using aromatherapy (as a part of their own self-care), and there is a deficit in aromatherapy knowledge on the part of both the patient and provider (self-care deficit). Prioritizing evidence-based recommendations further exemplifies a conscientious effort by the provider to be guided by practice that will be of maximum efficacy for facilitating patient health goals, of which self-care is a part.

Orem's Self-care deficit theory guided both the underlying values of the project as well as use of the end product of the integrative summaries themselves. The review of literature is heavily guided by the need for high-quality evidence, when possible, in order to satisfy the provider and patient's deficit in knowledge about aromatherapy.

In this project, the intervention was the development and dissemination of the evidence-based integrative summaries and the methods were both the location and synthesis of available evidence, therefore these two processes were interwoven. Orem's theory (Masters, 2014) supports bridging deficit gaps, and the highest-quality evidence was prioritized in this project. In turn, this project can not only provide knowledge, but also support the helping relationship of the provider and patient to promote the patient's need for self-care.

Assumptions and Definitions

It was assumed that as a general rule healthcare providers desire to offer evidence-based recommendations to their clients as a part of their care. Therefore, if a client chooses to utilize aromatherapy, it is important for the provider to have access to

evidence-based knowledge about aromatherapy safety and utilization. Furthermore, the busy healthcare provider is in need of simplified evidence summaries in order for quality evidence to be translated into patient care.

Integrative Summary: A new type of summary created by the student. These summaries contain not only a summary of the most current evidence on the treatment (oil), but also integrates information on safety, historical uses, suggested mechanisms of action, and other potentially useful information. The integrative summary may be used as a tool by the healthcare provider to expand their knowledge and it may be used as a starting point to guide future evidence-based summaries.

Healthcare Provider: A trained professional who provides care to clients that may include medical doctors, physician assistants, advanced practice nurses, nurses, nursing assistants, and personal care assistants.

In vitro: In vitro studies are studies done in a controlled environment outside of a living organism (The Marshall Protocol Knowledge Base, 2015). These studies may be done in test tubes, agar plates, dressing models, etc.

CHAPTER TWO

LITERATURE REVIEW

Overview

In this literature review, general attitudes toward complementary medicine (CAM) among consumers and healthcare practitioners, the historical use of essential oils, and the current utilization of essential oils were explored. This can not only provide a broader perspective of essential oil use in healthcare, but will also demonstrate that clear and concise research and resources about complementary and alternative therapies can be valuable.

General Attitudes Toward CAM

In order to obtain a better understanding of the general state of CAM attitudes among clients and providers that might relate to aromatherapy, research on this subject was explored. It was found that clients have a generally positive attitude toward CAM and a desire for informed choices. Siahpush (1999) conducted an exploratory study by selecting random phone numbers from a telephone book and asked questions about health in general as well as attitudes toward CAM. Through these telephone surveys, 98.7 % of 209 respondents strongly agreed that it is ultimately the individual who is responsible for his/her health and 97.7% strongly agreed that it is good to have so many different types of therapies from which to choose (Siahpush, 1999). Regarding natural remedies, 82% in

the same study responded they prefer natural remedies to pharmacologic drugs and 67.5% agreed that most prescription drugs have negative side effects (Siahpush, 1999).

Concerning provider knowledge and attitudes about CAM integration, Flannery, Love, Pearce, Luan, and Elder (2006) emailed 102 surveys to rural primary care practitioners and received 65 responses regarding their education and perspectives on CAM. From these surveys 91% reported it was either "very important" or "somewhat important" to receive further education on CAM because "[their] patients are asking about CAM and [they are] unsure how to advise them" (Flannery et al., 2006, p. 57). Only 14 out of the 65 providers surveyed (21%) had education on CAM and only two clinicians out of 65 (3%) practiced it (Flannery et al., 2006). Despite this, Flannery et al. (2006) found these providers were interested in CAM and the main motivator for further CAM education was patient safety. The clinicians "expressed a generally positive attitude toward CAM and an interest in learning more" (p. 60). A cross-sectional descriptive research study by Sohn and Loveland Cook (2002) specifically explored CAM knowledge in nurse practitioners through mailed surveys. These investigators found that among 151 nurse practitioners (NPs), 83% recommended CAM, but only 24% reported NP education contributed to knowledge on these treatments. Additionally, even though 90% of NPs surveyed recommended CAM to their clients, greater than 60% of these NPs relied on personal experiences to fuel their recommendations (Sohn & Loveland Cook, 2002).

This limited review of literature on CAM attitudes showed that consumers desire to be involved in care and that providers generally lack knowledge on CAM therapies and how to advise their clients regarding CAM. The integrative summary on aromatherapy developed in this project will serve as a resource to assist in this knowledge gap.

Historical Essential Oil Use

Aromatherapy has a long history of human utilization and was originally a part of the herbal medicine paradigm, meaning it was originally used for medicinal purposes alongside mainstream herbal remedies (Buckle, 2015). Essential oils were used worldwide and not confined to one geographical area, showing up in manuscripts dated as early as 2800 B.C. in the Middle East, China, India, Tibet, Greece, Eastern Europe, and North America (Buckle, 2015). Ancient Egyptians used them for antiseptic properties during the mummification process and Hippocrates fought the plague in Athens by using aromatic essences for fumigation (Price & Price, 2012). Aromatherapy was used in the middle ages as well: St. Hildegard of Bingen was using lavender oil in the 12th century and by the year 1500, many oils were documented to be used by pharmacists: benzoin, calamus, cedarwood, cinnamon, frankincense, myrrh, rose, rosemary, sage, spikenard, and turpentine (Price & Price, 2012). Even Shakespeare mentions the "perfumes of Arabia," referring to plant absolutes and essential oils. The renaissance of aromatherapy occurred in France in the 1930s among three health professionals: chemist Maurice Gattefosse discovered that a rinse of lavender essential oil virtually stopped a gas gangrene infection, Jean Valnet, MD, documented numerous

clinical case studies on aromatherapy for ailments such as wound care and insomnia, and nurse Margeurite Maury documented and eventually wrote a book on her use of essential oils on many health conditions (Freeman, 2009). These three professionals pioneered the use of essential oils in specific clinical contexts and laid the groundwork for modern clinical aromatherapy (Freeman, 2009).

Current Essential Oil Use

In recent years, aromatherapy has exploded into use by the general public. Currently, the term "aromatherapy" in the general public can mean everything from aromatics used in soaps and candles to the use of essential oils for therapeutic purposes. It is not uncommon to find essential oils for sale in local stores carrying natural products, online, and sold from person to person through multi-level marketing. The amount of available literature on aromatherapy has also expanded and the layperson can now locate books on aromatherapy, computer applications to guide use, or use web searches to find information on the many conditions that essential oils assert to help. According to Buckle (2015), there are three types of aromatherapy today: aesthetic, clinical, and holistic. Aesthetic aromatherapy is using essential oils for the pleasurable smell, such as burning aromatic waxes or home air fresheners (Buckle, 2015). Clinical aromatherapy involves the use of essential oils to target a specific symptom or complaint (such as pain) and may include internal or topical use, and holistic aromatherapy typically entails the use of essential oils for mind-body-spirit uses, such as the use of an essential oil mixture by a massage therapist (Buckle, 2015).

In recent years, use of all types of CAM including aromatherapy has grown. In 2012, approximately 59 million individuals in the United States had some kind of expenditure on complementary and alternative medicine (Nahin, Barnes, & Stussman, 2016). As of 2012, it was estimated that 34% of U.S. adults used some kind of complementary or alternative treatment as a part of their health care regime (Clarke, Black, Stussman, Barnes, & Nahin, 2015). This means that approximately one in three clients who walks into a health care clinic at any time is currently using some type of complementary health approach. In 2012, out-of-pocket CAM expenditures in the United States amounted to approximately $30.2 billion (Nahin et al., 2016).

Essential oils specifically have had a consistent 13% annual growth in retail demand as of a 2013 survey conducted by the International Trade Centre (International Trade Centre, 2014). In the research focused on EOs, many available studies are characterized by small sample sizes, less rigorous methods, bias, or difficulties masking placebo controls versus the active oil (Scott, 2015). A search conducted on November 13, 2016 on ClinicalTrials.gov produced a mere 30 clinical trials related to the term "aromatherapy" despite the numerous options of essential oils on the market as well as the even larger group of conditions many claim to treat (U.S. National Institutes of Health, 2016). It is clear there is a need for increased research and knowledge on the topic of aromatherapy.

In 2016, Rebecca Boesl, a DNP candidate at North Dakota University, created an online continuing education (CE) module on aromatherapy and administered it through the AANP's CE program as a part of her DNP scholarly project. Boesl (2016) found that

although 73% of the 231 participants either rarely or never discuss CAM/essential oils with their clients, after the CE module, 63% stated they agreed that they now intended to ask their clients about their use of CAM/essential oils (Boesl, 2016). This further affirms that there is an increased need and desire for provider education on CAM/essential oils.

CHAPTER THREE

METHODS

The purpose of this project was to explore the state of the evidence available for the ten most commonly used essential oils and synthesize this evidence into integrative summaries in order to improve general healthcare providers' knowledge of this topic. According to Whittemore and Knafl (2005), an integrative review contains five stages: problem identification, literature search, data evaluation, data analysis, and presentation. This model was followed for the purposes of this project and ventured one step further in the analysis phase to produce integrative summaries for each of the selected oils to be used as tools by healthcare providers.

Data Collection

The primary tools for data collection were peer-reviewed journals. In order to ensure systematic and rigorous evidence acquisition, synthesis articles were sought as well as high quality randomized clinical studies as a priority. Although randomized controlled trials (RCTs) provide the highest level of evidence, when this type of research was not available, other less rigorous forms of evidence were included in searches, which is in agreement with the integrative review model. Furthermore, evidence was categorized in a series of tables, including search methods (see Appendix A) and a preliminary evidence table (see Appendix B).

Essential Oil Selection

Lists of the most commonly used essential oils from sources with minimal commercial interest were first located, then cross-referenced to determine the most common oils among them to include in this project. The primary resource was determined to be a market insider report from the International Trade Center (ITC), an independent development agency that analyzes and supports international trade enterprises and is also a joint agency of the World Trade Organization and the United Nations (International Trade Centre, 2014). As a part of the ITCs most recent report on characteristics of the aromatherapy market in the United States, they produced a list of the "Top selling essential oils in the US retail aromatherapy market, by value" (International Trade Centre, 2015, p. 4), and it is from this list the top 10 most commonly used essential oils were determined for this project. The ITC list has two essential oil "blends" in the top 11 oils, so this list was cross-referenced with the most commonly used essential oils identified from the National Association of Holistic Aromatherapy (2017a)(NAHA). Every oil found in the IHI's top 10 list was also found in the NAHA list. The final list of 10 most commonly used essential oils (see Table 1) was presented to the student's committee and approved before proceeding.

Table 1. Ten Most Commonly Used Essential Oils

#	Essential Oil	Source
1	Lavender	IHI
2	Peppermint	IHI
3	Eucalyptus Globulus	IHI

Table 1 Continued

4	Tea Tree	IHI
5	Rosemary	IHI
6	Patchouli	IHI
7	Lemon	IHI
8	Rose	IHI
9	Frankincense	IHI
10	Roman Chamomile	NAHA*

*replaced "blend – calming" from IHI list

Search Methods

Article searches were conducted online, first using peer-reviewed journals to find the highest-quality research studies and reviews, and then branching out to other sources as needed for supplemental information. The primary databases used were the Cochrane Library, CINAHL, Joanna Briggs Institute EBP Database, Medline, and PubMed. UpToDate and National Guideline Clearinghouse were also searched both for aromatherapy in general and the name of each individual oil however no results were found in these resources. General search criteria included use of the name of the individual oil (no mixtures or blends), a preference toward studies of the therapeutic effect of the oil, and general exclusion of aromatherapy used in conjunction with massage therapy due to a high probability of confounding. Aromatherapy and massage are commonly linked and although massage has a host of widely recognized benefits, some of these benefits are similar to the desired effect of aromatherapy (e.g. stimulation of circulation, deep relaxation, digestion enhancement, etc.) (Price & Price, 2012). For this reason of unclear attribution possible with massage treatment, studies involving massage

were excluded. Additionally, it became apparent the most useful studies for this particular project were studies conducted with humans, therefore both in vitro and animal in vivo studies were excluded. See Appendix A: Aromatherapy Search Log for further details on specific searches.

Quality Assessment

The general framework used for evaluating the quality of evidence was the GRADE method. GRADE stands for the "Grading of Recommendations Assessment, Development and Evaluation" and is used for evaluating both the quality of evidence as well as developing grades for recommendation into practice (Grade Working Group, 2016). This highly structured system emerged as an attempt to standardize the multitude of quality assessment systems guideline developers have used in the past and minimize confusion (Guyatt et al., 2008).

The GRADE approach is a labor intensive process designed for teams of researchers, therefore the approach was modified slightly for this project due to student labor, training, and time constraints, however the general approach of evidence gathering and assessment was followed according to the basic tenets of GRADE. The student searched for articles and completed an initial evaluation of the quality of evidence in each article according to one of the four quality of evidence grades (see Appendix B for complete evidence table). These four grades and their definitions are shown in Table 2. According to the GRADE criteria, the quality of evidence grade may be reduced or

increased by various factors. A summary of these factors are shown in Table 3 and Table 4, respectively.

Maintaining objectivity in the review of research studies in this project was a challenge due to the wide variation of design and execution of the research as well as the different writing styles and quality of writing in the research publications. To provide rigor and consistency in the review process, the student used several strategies similar to those implemented in qualitative research. Criteria for determining trustworthiness of qualitative data include demonstrating credibility, dependability, and transferability (Lincoln & Guba, 1985; Morse, 2015). Credibility refers to the overall believability of the data and results, dependability refers to the consistency of the process used to achieve the results, and transferability refers to the ability to transfer the process and results to other situations.

Credibility was addressed in this project by Prolonged Engagement and Persistent Observation of the data before conclusions were drawn (Houghton, Casey, Shaw, & Murphy, 2013). The student had prolonged engagement with the data and persistently observed while reading and rereading publications multiple times. After this extensive review, she proceeded with categorizing the studies, rating the quality of the evidence, and developing the integrative summaries.

Creating an Audit Trail is a method used to contribute to credibility, dependability, and transferability. It involves outlining the data and the decisions made and providing rationale for interpretative judgments (Houghton et al., 2013). This technique is used to provide sufficient details so that others can follow the evidence and

make their own interpretations and conclusions. In this project, an audit trail was kept to document a summary of the studies reviewed, the quality of evidence, and rationale for the conclusions. The tables that contain the audit trail include the Search Log, Evidence Table, and Evidence Use Profiles, and are available in Appendices A, B, and C, respectively. An External Audit was also conducted by the student's committee chairperson to contribute to credibility, dependability, and transferability. The chairperson reviewed 10 randomly selected publications from the total included in the project (approximately 12.5% of the total). This audit was conducted independently of the student's review and prior to reading details of the student's results. The chairperson used the categories of data in the Aromatherapy Evidence Table as a guide while conducting the external audit. While some of the details noted in the 10 research publications were somewhat different between the reviews done by the student and chairperson, the resulting ratings of the quality of the evidence in the publications were nearly identical.

Table 2. Quality of Evidence Grades

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

(Grade Working Group, 2016)

Table 3. Factors that can reduce the quality of the evidence

Factor	Consequence
Limitations in study design or execution (risk of bias)	↓ 1 or 2 levels
Inconsistency of results	↓ 1 or 2 levels
Indirectness of evidence	↓ 1 or 2 levels
Imprecision	↓ 1 or 2 levels
Publication bias	↓ 1 or 2 levels

(Grade Working Group, 2016)

Table 4. Factors that can increase the quality of the evidence

Factor	Consequence
Large magnitude of effect	↑ 1 or 2 levels
All plausible confounding would reduce the demonstrated effect or increase the effect if no effect was observed	↑ 1 level
Dose-response gradient	↑ 1 level

(Grade Working Group, 2016)

Summarizing the Evidence

A decision was made to cease searching for evidence when the student found multiple repeat articles in large databases (PubMed, for example) with minimal-to-no new articles meeting inclusion criteria. Evidence was then categorized further by identifying uses for each oil that were included in the research studies. For example, research concerning frankincense included evaluation of its effect on cognition in people with multiple sclerosis, pain, gingivitis, cerebral edema, and osteoarthritis. These uses were organized into evidence use profile tables for each individual oil, where each use for

the oil includes a pooled number of participants (n=) from the included studies, and a summary of the studies' findings (see Appendix C: Evidence Use Profiles). For uses that had multiple studies to inform their use, quality of evidence scores for the individual studies were taken and averaged to make an overall quality of evidence score for each essential oil use. This was calculated by listing the quality of evidence for each study and determining which quality was assigned to the majority of the studies. For example, the student found nine studies on lavender used for pain relief. Seven were low quality evidence, one was moderate quality, and one was very low quality, therefore the overall quality of evidence was averaged as low quality (see Appendix C). The format for the Evidence Use Profile tables was based on the suggested evidence use profiles used in the GRADE method (Grade Working Group, 2016), as adapted to fit the scope and aim of this project. Quality assessment for pooled data and outcomes included (a) the number of participants in each study pooled for each category (total pooled n=), (b) limitations and identified biases, (c) overall quality of evidence averaged from evidence table, (d) summary of findings, and (e) a preliminary conclusion and strength.

The strength of the conclusion was categorized as either weak, moderate, strong, or no conclusion. These strengths were adapted from the GRADE approach to recommendations (strong and weak). Definitions of these conclusions are shown in Table 5. It should be noted that it is possible to have low quality evidence yet still have an associated conclusion (typically weak) if the reason for the lower quality rating is due to a factor such as a study design flaw yet the study results are noteworthy. This was assessed on a case-by-case basis. For example, Woelk and Schläfke (2010) found an oral

preparation of lavender to be comparable if not better than lorazepam for reducing anxiety in general anxiety disorder. Although this study was well designed and had statistically significant results supporting the effect of lavender, the student assessed the evidence to be low quality due to the fact that there was no mention of how often the lavender or lorazepam were taken by each group. These preliminary conclusion ratings also take into account the relative risk of each therapy compared to the possible outcome, which is detailed further in chapter four. In general, the design of the study was used to inform the quality of the study and both the study itself and the results of the study were used to inform the conclusion.

Table 5. Strength of Conclusion Definitions

Strength	Definition
Strong	The student is confident that the desirable effects of using the oil for the specified condition outweigh its undesirable effects (strong likelihood the therapy is helpful for the condition).*
Weak	The student has assessed the desirable effects of using the oil for the specified condition *probably* outweighs the undesirable effects (the evidence is weak, however the risk of using the oil is also very low).*
No Conclusion	There appears to be evidence an oil may or may not have a desirable effect, however the quality is too low to formulate a conclusion for use.

* Adapted from GRADE Handbook (Grade Working Group, 2016)

The final step in this project was to take the summarized conclusions and present them in single-page evidence summary and oil information sheets that may be used as references by healthcare providers. These summaries not only include the conclusions found from the research, but also include useful information such as various names of

each oil, historical use, possible routes of use (oral, topical, inhalation), safety considerations, frequently suggested mechanisms of action (MOA), any additional useful notes on the oil, and the student's overall impression. Since these integrative summaries are intended to be used as tools for healthcare providers not only as evidence summaries but also to be aware of how each oil has been used historically and how the general public may view these oils, a lay literature source on essential oils was used for the "historical uses" and "frequently suggested MOA" categories (Life Science Publishing, 2014). *Essential Oil Safety* by Tisserand and Young (2014) was the primary source for all safety parameters noted in each integrative summary.

CHAPTER FOUR

RESULTS

The purpose of this project is to explore the state of the evidence available for the ten most commonly used essential oils and synthesize this evidence into integrative summaries in order to improve general healthcare providers' knowledge of this topic. These integrative summaries may be used as a reference for healthcare providers. Through a rigorous process involving multiple steps of evidence gathering, summarizing, and evaluating based on the GRADE method, integrative summaries were developed and are presented in this chapter. Each integrative summary contains the name(s) of the oil, historical uses, typical routes of administration, safety parameters, frequently suggested mechanisms of action, evidence summary, further notes, and the student's overall impression. Regarding safety, it is mentioned whether the oil is generally recognized as safe (GRAS) from the United States Food and Drug Administration (FDA). A food or drug may achieve GRAS status when the FDA has assessed it is safe for human consumption under typical use (U.S. Food & Drug Administration, 2017). It should be noted that since no studies were found that demonstrated significant harm from use of the oils investigated, no evidence conclusions were made against using any essential oil in its entirety, however side effects and cautions are listed in the summaries. Individual safety parameters for possible harms and contraindications were added to the evidence summary sheets as stated from the text by Tisserand and Young (2014), "Essential Oil Safety." A

brief summary of the findings from each oil are discussed in this chapter followed by the integrative summaries themselves.

Lavender

Lavender is by far the most common essential oil to be studied in humans and has also been studied extensively in in vitro and in animal studies. Safety-wise, it has GRAS status and the most common routes include inhalation and topical use, however, some individuals take lavender orally (Tisserand & Young, 2014). Although the most common side effect of lavender is skin sensitization, Tisserand and Young (2014) noted the actual reports of adverse skin reactions is quite low, particularly compared to the high usage of this oil.

The general trend that emerged in the student's search of research publications about lavender were directed at pain relief, anxiety, and sleep quality. Lavender aromatherapy was also found in a systematic review by Forrester et al. (2014) aimed at evaluating essential oils for agitation in people with dementia, however the investigators were unable to compare agitation scores due to design flaws and biases. From an initial group of 48 studies gathered, 25 met inclusion criteria and were summarized. These 25 articles were then organized into eight studied uses: Pain relief (9 studies), anxiety (7 studies), sleep quality (3 studies), fatigue (1 study), restless leg syndrome (1 study), dysmenorrhea (2 studies), dementia (1 review), and menopause hot flushing (1 study). After further evaluation, the strongest evidence available for lavender use was determined and added to the integrative summaries: Pain relief, anxiety, sleep quality, dysmenorrhea, and menopause hot flushing. The student's overall impression of lavender essential oil is:

Lavender is generally safe to use and there is a moderate amount of evidence demonstrating its usefulness as an analgesic, anxiolytic, and sedative..

Peppermint

Peppermint is a popular food additive and is also used as an essential oil either inhaled, topically, or for oral use. Peppermint has GRAS status however has several safety hazards and contraindications, most notably avoiding use on or near the face of infants/children due to risk of neurotoxicity, and avoiding use in individuals with cholestasis (oral route) or with cardiac fibrillation. Standard 1% peppermint oil is generally safe used topically, but Tisserand and Young state there have been occasional reports of mucous membrane sensitivity, most likely related to the menthol component (and thought to be very rare due to the high use of peppermint in dental products) (Tisserand & Young, 2014).

From an initial group of 24 studies gathered, nine met inclusion criteria and were summarized. These nine articles were then organized into four studied uses: Dysmenorrhea (1 study), irritable bowel syndrome (IBS) (1 study, 3 systematic reviews), nausea/vomiting (3 studies), and stress (1 study). The most studied use of peppermint oil is oral use for IBS symptoms, which contributes to it having the strongest evidence for this use with many individuals experiencing partial or complete relief of symptoms such as abdominal pain and distention (see “Peppermint” in Appendix C). The student’s overall impression of peppermint oil is that oil is generally safe when used topically or internally in enteric-coated capsules, however it should not be applied to the face or chest

of small children due to the risk of neurotoxicity from menthol. Peppermint oil may improve IBS symptoms.

Eucalyptus

Eucalyptus comes in several forms; the most commonly used and purchased form is the cineole-rich eucalyptus globulus, a commonly considered remedy for respiratory problems. Safety-wise, eucalyptus globulus should not be applied near the face of children under ten years old and may cause central nervous system (CNS) depression and breathing problems if used under the age of two (Tisserand & Young, 2014). Eucalyptus does not have GRAS status and there are reports of toxicity in humans if ingested in high doses, particularly children ingesting 2-30 mL of eucalyptus oil with symptoms ranging from minor CNS depression to loss of consciousness (Tisserand & Young, 2014).

In the research, an initial group of eight studies were gathered from which five met inclusion criteria and were summarized. These five articles were then organized into seven studied uses: Anxiety (1 study), pain (1 study), inflammation (2 studies), tuberculosis (1 case study), asthma (1 review), rhinosinusitis (1 review), and chronic obstructive pulmonary disorder (COPD) (1 review). The student's overall impression is that the most common use for eucalyptus globulus is for respiratory problems and there is some evidence showing use for asthma, rhinosinusitis, and COPD. Caution should be used around children, as there is a risk of neurotoxicity.

Tea Tree

Historically, tea tree oil (TTO), also known as melaleuca oil, has been considered to be a powerful antimicrobial agent, touted as an antibacterial, antifungal, antiviral, antiparasitic, and anti-inflammatory (Life Science Publishing, 2014). TTO is generally applied topically, is safe at 15% maximum concentration, and does not have GRAS status (Tisserand & Young, 2014). Many studies found in the literature focus on wound healing, inflammation, and specifically treatment of methicillin-resistant staphylococcus aureus (MRSA). In fact, "Tea tree oil has been claimed to have anti-bacterial, analgesic and anti-inflammatory effects that have been suggested in many in-vitro studies to have good efficacy against MRSA" (Lee, Leung, & Wong, 2014, p. 7). Despite a wealth of in vitro data on TTO, human studies have shown mixed results.

From an initial group of 17 studies gathered on tea tree oil, 11 met inclusion criteria and were summarized. These 11 articles were then organized into seven studied uses: Burns (1 study), MRSA (3 studies, 2 reviews), dental plaque (1 study), acne (1 study), wound healing (2 studies, 1 review), and ocular discomfort (1 study). The student's general impression is that although tea tree oil has historically been used as an anti-infective and has shown in vitro success, studies to date on humans have produced generally weak evidence for its efficacy as an antimicrobial agent.

Rosemary

Rosemary has a long history of human use, from medicinal to nutritional. Traditionally, it has been thought be an anti-inflammatory, antimicrobial, antidepressant, hypertension moderator, and to enhance mental clarity (Life Science Publishing, 2014).

Rosemary has GRAS status however may be neurotoxic in high doses (particularly in children younger than two) depending on camphor concentrations (Tisserand & Young, 2014). The student did elect to review one well-written abstract (Panahi, Taghizadeh, Marzony, & Sahebkar, 2015) on the use of rosemary for alopecia since the full article was unable to be found, however, the quality of the source was deemed too weak for inclusion in the summary.

From an initial group of 12 studies gathered, 10 met inclusion criteria and were summarized. These 10 articles were then organized into eight studied uses: Alopecia (1 study), blood pressure (2 studies), asthma (1 study), cognition (2 studies), and anxiety (2 studies). The student's overall impression is that there is some evidence that rosemary may be helpful to increase low blood pressure when taken orally and enhance a sense of alertness in individuals when inhaled.

Patchouli

Patchouli has historically been used as a remedy for multiple health complaints, including use as a relaxant, digestive aid, anti-inflammatory, antimicrobial, insecticide, and for dry/itchy skin (Life Science Publishing, 2014). It does not have GRAS status and although it is more commonly used topically or inhaled, individuals should be cautious or avoid oral use due to the possibility of inhibiting blood clotting (Tisserand & Young, 2014). Extensive searches were conducted on patchouli and its pseudonyms (pogostemon, pogostemon cablin) in the literature, however only three studies were found for initial evaluation, as most of the studies found were directed toward the use of patchouli as an insecticide and antimicrobial in vitro. Among these three studies, one

concerning use of patchouli as an insect repellent met inclusion criteria and was summarized. The student's overall impression of patchouli is that topical and inhaled patchouli appear to be safe and patchouli may have use as an insect repellent, however human studies with patchouli are severely lacking.

Lemon

Lemon oil is a citrus oil and is expressed from the peel of the lemon fruit. Lemon oil has a long history of use not only as a food additive, but also for skin care needs as an antiseptic, a vascular stimulant, and digestive aid (Life Science Publishing, 2014). Lemon oil has GRAS status, however can be phototoxic if applied to the skin in high concentrations (Tisserand & Young, 2014). Initial searches for lemon oil research resulted in very few studies on humans (only three meeting inclusion criteria), so in this case the student searched for its primary constituent, limonene, which yielded a systematic review done on medicinal limonene uses. Overall, four met inclusion criteria and were summarized. These four articles were then organized into five studied uses: Nausea/vomiting (2 studies), anxiety (1 study), gallstones (2 studies within an evidence review), GERD (2 studies within an evidence review), and as an anticancer treatment (4 case studies in an evidence review). The student's overall impression is: Limited studies exist on lemon oil, however its main constituent, limonene, shows weak positive effects for treating gallstones, GERD, and possibly as an antitumoral agent.

Rose

Rose oil is extracted from rose flowers and has a history of use not only in the cosmetic industry, but is also thought to have properties including use as an anti-inflammatory, antioxidant, anxiolytic, anti-ulcer, and even as a cancer treatment (Life Science Publishing, 2014). The most common form of rose oil is rosa damascena, which has GRAS status and is generally safe for topical, inhaled, and oral use. Initially, six studies were found on rosa damascena and from these studies four met inclusion criteria and were summarized. The three primary studied uses that emerged include pregnancy-related low back pain (1 study), dysmenorrhea (1 study), and anxiety (1 study). The student's general impression of rose oil is: Rose oil is generally safe, pleasant, and may have mild pain relieving and anxiolytic effects.

Frankincense

Frankincense has a long history of use from biblical references to documentation of use by pharmacists in the 1500s (Price & Price, 2012). An internet search on frankincense reveals a recent upsurge in interest in its possible use against cancer cells, however there is no clinical research that supports this to date (Tisserand, 2016) Not only are most of the studies done in vitro and not on humans, but they are in fact mostly done with frankincense extract from gum resin, and specifically boswellic acid, which frankincense oil does not contain (Tisserand, 2016). The most frequently suggested uses for frankincense are as an antimicrobial, an immune-stimulant, antidepressant, and muscle relaxant (Life Science Publishing, 2014).

Searches for studies on frankincense revealed an initial group of 19 studies from which seven met inclusion criteria and were summarized. These seven studies were organized into five uses: Cognition in patients with multiple sclerosis (1 study), pain (1 study), gingivitis (1 study), cerebral edema (1 study), and osteoarthritis (3 studies within a review). The student's overall impression is: Frankincense has most commonly been studied for its anti-inflammatory and analgesic effects, however evidence is weak for its efficacy. Although it does not have official GRAS status, it is generally safe when stored correctly to allow for minimal oxidation.

Roman Chamomile

Although chamomile generally brings to mind uses as a calmative substance, Roman chamomile has historically been used as a cardiac calmative, for ophthalmic issues, and as an anti-infective (Price & Price, 2012). It has GRAS status and no known hazards or contraindications (Tisserand & Young, 2014). It should be noted that there are several types of chamomile that are used therapeutically, specifically German chamomile, which not only has different therapeutic effects than Roman chamomile but also has multiple drug interactions (Tisserand & Young, 2014). In human research, an initial group of nine studies on Roman Chamomile were gathered, four of which met inclusion criteria and were summarized. These studies were then organized into three uses: Incontinence (1 study), carpal tunnel syndrome (2 studies), and osteoarthritis (1 study). The student's overall impression is: Roman chamomile is generally safe. There is some weak evidence to support the anti-inflammatory action of roman chamomile, including treatment of osteoarthritis and carpal tunnel syndrome.

Table 6. Evidence gathering and summarizing flow

Oil	Initial Search	Summarized	Topics identified in the research
Lavender	48	25	Pain, anxiety, sleep, fatigue, RLS, dysmenorrhea, dementia, menopause hot flushing
Peppermint	24	9	Dysmenorrhea, irritable bowel syndrome, nausea/vomiting, stress.
Eucalyptus	8	5	Anxiety, pain, inflammation, tuberculosis, asthma, rhinosinusitis, COPD
Tea Tree	17	11	Burns, MRSA, dental plaque, acne, wound healing, ocular discomfort
Rosemary	12	10	Alopecia, blood pressure, asthma, cognition, anxiety
Patchouli	3	1	Insect repellent
Lemon	8	4	Nausea/vomiting, gallstones, GERD, anticancer
Rose	6	4	Pregnancy-related low back pain, dysmenorrhea, anxiety during labor
Frankincense	19	7	Cognition (MS), pain, gingivitis, cerebral edema, osteoarthritis
Chamomile	9	4	Incontinence, carpal tunnel syndrome, osteoarthritis.
Total	154	80	

Aromatherapy Integrative Summaries

The following ten pages include the ten integrative summaries, in order of popularity:

1. Lavender
2. Peppermint
3. Eucalyptus
4. Tea Tree
5. Rosemary
6. Patchouli
7. Lemon
8. Rose
9. Frankincense
10. Chamomile

LAVENDER

Common Names	English lavender, French lavender, true lavender, common lavender
Latin Name	Lavendula angustifolia, lavandula vera, lavandula officinalis
Historical Uses	Respiratory infections, high blood pressure, arteriosclerosis, PMS, skin conditions, burns, hair loss, insomnia, anxiety
Route	Inhalation, topical, oral
Safety	"Generally Recognized as Safe" Status: Yes No known hazards or contraindications. Some people may experience dermal sensitivity, particularly with repeated exposure (Tisserand & Young, 2014, p. 327).
Frequently Suggested MOAs	Antiseptic, antifungal, analgesic, anticonvulsant, vasodilator, relaxant, anti-inflammatory, reduces blood lipids, reduces excess sebum on skin

Summary of Human Research on Lavender

USE	EVIDENCE SUMMARY	STRENGTH
Pain Relief	According to nine clinical trials there is a probability that lavender application and/or inhalation may be used to temporarily reduce mild-moderate pain.	Strong
Anxiety	Studies on lavender for anxiety report mixed results, however there is a general trend supporting inhalation to relieve mild-moderate anxiety.	Weak
Sleep Quality	There is moderate evidence that lavender inhalation may assist in reducing time to fall asleep and perception of sleep quality.	Strong
Dysmenorrhea	Lavender inhalation may temporarily reduce pain and mood symptoms related to primary dysmenorrhea.	Weak
Menopause Hot Flushing	Lavender inhalation may have a positive effect on reduction of menopause-related hot flushes	Weak

Further notes on this oil

- There are several other forms of lavender, notably "Spike Lavender" (lavandula latifolia, lavandula spica), which may function as an expectorant, mucolytic, and possibly as a stimulant (Buckle, 2015)
- Woelk and Schläfke (2010) found an internal preparation of lavender was at least as effective as lorazepam for anxiety when taken long-term.

Overall Impression

Lavender is generally safe to use and there is a moderate amount of evidence demonstrating its usefulness as an analgesic, anxiolytic, and sedative.

PEPPERMINT

Common Names	Peppermint oil
Latin Name	Mentha x piperita
Historical Uses	IBS, Respiratory infections, viral infections, nausea, headaches, skin conditions, rheumatism/arthritis, obesity, digestive problems
Route	Inhalation, topical, oral
Safety	"Generally Recognized as Safe" Status: Yes Hazards: Choleretic, neurotoxicity (especially in children), mucous membrane irritation Contraindications: Cardiac fibrillation, G6PD deficiency, cholestasis (oral), do not use on or near face of infants/children. Caution: GERD (oral use). Most common side effect is heartburn. (Tisserand & Young, 2014, p. 387)
Frequently Suggested MOAs	Anti-inflammatory, antitumoral, antiparasitic, antibacterial, antiviral, antifungal, digestive stimulant, analgesic, curbs appetite.

Summary of Human Research on Peppermint

USE	EVIDENCE SUMMARY	STRENGTH
IBS	There is not an established dose and frequency, but numerous studies suggest ingested peppermint oil via enteric-coated capsules can significantly improve IBS symptoms such as pain, abdominal distention, and bowel frequency/ flatulence. The most common side effect is heartburn.	Strong
Nausea/Vomiting	Despite little clinical evidence to support peppermint oil inhalation to relieve nausea, it is generally safe and may provide mild short-term symptom relief.	Weak
Stress	Peppermint oil inhalation may be used to decrease short-term stress perception.	Weak

Further notes on this oil

- Tisserand and Young (2014) recommend a maximum adult oral dose as 152 mg/day based on an 8.0% menthofuran and 3.0% pulegone content.
- Internal doses from studies range from 330mg/day to 540 mg/day with minimal to no side effects.

Overall Impression

Peppermint oil is generally safe when used topically or internally in enteric-coated capsules, however it should not be applied to the face or chest of small children due to the risk of neurotoxicity from menthol. Peppermint oil may improve IBS symptoms.

EUCALYPTUS

Common Names	Eucalyptus oil
Latin Name	Eucalyptus globulus, eucalyptus camaldulensis (cineole)
Historical Uses	Respiratory/sinus infections, decongestant, rheumatism/arthritis, muscle soothing
Route	Inhalation, topical, oral
Safety	"Generally Recognized as Safe" Status: No Hazards: Can cause central nervous system and breathing problems in children (do not use for children under 2 years old) Contraindications: Avoid on or near the face of children under ten years old. Dose: 600mg max/day (adults). May use up to 20% concentration for dermal use. (Tisserand & Young, 2014, p. 273)
Suggested MOAs	Expectorant, mucolytic, antimicrobial, antibacterial, antifungal, antiviral, antiaging, antiulcer, antidiabetic

Summary of Human Research on Eucalyptus

USE	EVIDENCE SUMMARY	STRENGTH
Anxiety	Eucalyptus may have a short-term effect reducing anxiety before surgery	Weak
Asthma	Eucalyptus inhalation may temporarily reduce asthma symptoms, including increased FEV1 and decreased airway restriction.	Weak
Rhinosinusitis	Oral eucalyptus oil may help reduce symptoms of rhinosinusitis, including malaise, nasal congestion, headache, and facial tenderness.	Weak
COPD	High-dose oral eucalyptus may decrease frequency, severity, and duration of COPD exacerbations.	Weak

Further notes on this oil

- Eucalyptus globulus should be avoided in children under two years old, however eucalyptus radiata may be used in this population (National Association of Holistic Aromatherapy, 2017a).
- Studies were found on pain, inflammation, and tuberculosis, however evidence was too weak to formulate a recommendation for use.

Overall Impression

The most common use for eucalyptus globulus is for respiratory problems and there is some evidence showing use for asthma, rhinosinusitis, and COPD. Caution should be used around children, as there is a risk of neurotoxicity.

TEA TREE

Common Names	Tea tree oil, Melaleuca oil, Australian tea tree oil
Latin Name	Melaleuca alternifolia
Historical Uses	Fungal infections, sinus/lung infections, tooth/gum disease, water retention/hypertension, skin conditions (acne)
Route	Topical, oral
Safety	"Generally Recognized as Safe" Status: No Hazards: skin sensitization with high doses and/or repeated use. Cautions: Old/oxidized tea tree oil should be avoided for topical use. Dose: 15% concentration maximum (topical) (Tisserand & Young, 2014, p. 440)
Frequently Suggested MOAs	Antibacterial, antifungal, antiviral, antiparasitic, anti-inflammatory

Summary of Human Research on Tea Tree Oil

USE	EVIDENCE SUMMARY	STRENGTH
Dental plaque	Tea tree oil used in toothpaste may decrease the number of harmful bacteria in dental biofilm and reduce the risk of periodontal disease compared to mainstream toothpastes without tea tree oil.	Weak
MRSA	TTO as a treatment for MRSA has mixed results in human studies, from complete eradication to no difference in MRSA bacteria count after treatment.	Uncertain
Wound Management	There is conflicting evidence for efficacy of TTO for wound healing and as an antimicrobial agent, however cases exist that suggest topical TTO may have expedited wound healing time compared to no treatment	Weak
Ocular Discomfort	Topical TTO may be an effective treatment for ocular symptoms related to the demodex parasite.	Weak

Further notes on this oil

- Ingestion of tea tree oil is generally not recommended.
- Studies were found on acne and burns, however evidence was too weak to formulate a recommendation for use.

Overall Impression

Although tea tree oil has historically been used as an anti-infective and has shown in vitro success, studies on humans have produced generally weak evidence for its efficacy as an antimicrobial agent to date.

ROSEMARY

Common Names	Rosemary
Latin Name	Rosmarinus officinalis L.
Historical Uses	Infectious disease, liver conditions, throat/lung infections, hair loss, acne, memory impairment, weight loss
Route	Inhalation, topical, oral
Safety	"Generally Recognized as Safe" Status: Yes Hazards: Neurotoxic depending on camphor content Contraindications: Do not apply to or near the face of infants or children. Dose: Based on individual oil's camphor content (Tisserand & Young, 2014, p. 409)
Frequently Suggested MOAs	Anti-inflammatory, antifungal, antibacterial, anticancer, antidepressant, hypertension moderator, enhances mental clarity

Summary of Human Research on Rosemary

USE	EVIDENCE SUMMARY	STRENGTH
Hypotension	Oral and inhaled rosemary may be a safe and effective method of increasing systolic & diastolic blood pressure (by 4%-21%).	Weak
Cognition	Low-dose oral intake of rosemary oil may increase alertness and memory speed in the elderly. Inhalation may improve subjective sense of alertness, but does not appear to have an effect on actual performance.	Weak
Anxiety	Rosemary may have an effect on increasing alertness, however it also may increase feelings of anxiety and tension in some individuals.	Weak

Further notes on this oil

- Studies were found on alopecia and asthma, however evidence was too weak to formulate a recommendation for use.

Overall Impression

There is some evidence that rosemary may be helpful to increase low blood pressure when taken orally and enhance a sense of alertness in individuals when inhaled.

PATCHOULI

Common Names	Patchouli
Latin Name	Pogostemon cablin
Historical Uses	Hypertension, IBS, skin conditions (eczema, acne), fluid retention, insect repellent, listeria infection.
Route	Topical, inhalation, oral
Safety	"Generally Recognized as Safe" Status: No Hazards: Possibility of inhibiting blood clotting Cautions: Caution if taking orally and on anticoagulant medication or have high bleeding risk. (Tisserand & Young, 2014, p. 382)
Frequently Suggested MOAs	Relaxant, antitumoral, digestive aid, anti-nausea, anti-inflammatory, antimicrobial, antifungal, insecticidal, wrinkle and chapped skin prevention, itch relief.

Summary of Human Research on Patchouli

USE	EVIDENCE SUMMARY	STRENGTH
Insect Repellent	Patchouli may have mosquito-repellency properties that are concentration dependent (50% concentration gave 60 minutes of complete repellency in one trial by Trongtokit)	Weak

Further notes on this oil

- No restriction on dermal use.

Overall Impression

Topical and inhaled patchouli appear to be safe and patchouli may have use as an insect repellent, however human studies with patchouli are severely lacking.

LEMON

Common Names	Lemon oil
Latin Name	Citrus limon
Historical Uses	Skin care (cleanser, wrinkle-reducer, acne), flavoring. Lemon peel has a history of use as an antiseptic, carminative, diuretic, eupeptic, vascular stimulant/protector, and as a vitamin
Route	Oral, inhalation, topical
Safety	"Generally Recognized as Safe" Status: Yes Hazards: Skin sensitization if oxidized, phototoxic Contraindications: Sunlight should be avoided for 12 hours if applied to skin over maximum concentration recommendations Dose: 2.0% maximum concentration for dermal use. (Tisserand & Young, 2014, p. 331)
Frequently Suggested MOAs	Antiseptic, microcirculation improvement, immune stimulant (WBC production), memory improvement, relaxation, antitumoral (limonene content)

Summary of Human Research on Lemon Oil

USE	EVIDENCE SUMMARY	STRENGTH
Nausea/Vomiting	Lemon oil inhalation may help relieve mild nausea, however more studies are needed.	Weak
Gallstones	Oral d-limonene may be used as a treatment to assist in dissolution of gallstones	Weak
GERD	Oral use of d-limonene has shown clinical efficacy at relieving heartburn and GERD (up to 89% achieving complete relief by day 14)	Weak
Anticancer	Several cases exist that suggest d-limonene may have antitumoral effects when taken orally.	Very weak

Further notes on this oil

- The primary active component in lemon oil is limonene (56.6%-76%)
- One study was found on lemon oil and anxiety, however evidence was too weak to formulate a recommendation for use.

Overall Impression

Limited studies exist on lemon oil, however its main constituent, limonene, shows weak positive effects for treating gallstones, GERD, and possibly as an anticancer agent.

ROSE

Common Names	Rose
Latin Name	Rosa damascena
Historical Uses	Hypertension, hearth strengthening, anxiety, viral infections, skin conditions, ulcers.
Route	Topical, oral, inhalation
Safety	"Generally Recognized as Safe" Status: Yes Hazards: May contain menthyleugenol, which has shown toxicity in animal studies. Contraindications: None known Dose: 0.6% dermal or 21mg oral/day based on 3.3% methyleugenol content. (Tisserand & Young, 2014, p. 405)
Frequently Suggested MOAs	Anti-inflammatory, antioxidant, anxiolytic, hepatoprotective, relaxant, scar reducer, antiulcer, immunomodulating, cancer treatment, DNA damage prevention.

Summary of Human Research on Rose Oil

USE	EVIDENCE SUMMARY	STRENGTH
Low Back Pain during Pregnancy	Topical rose oil to the low back may have an analgesic effect for pregnancy-related low back pain.	Weak
Anxiety During Labor	Using rose oil aromatherapy alongside a footbath may reduce labor-related anxiety.	Weak

Further notes on this oil

- There are several types of rose oils, the 2nd most common one being rosa centifolia (Provence), which is high in phenyl ethanol and has very different therapeutic uses than rosa damscena.
- One study was found on rose oil and dysmenorrhea and suggest possible efficacy, however results were not included due to poor study design.
- According to older studies and empirical reports, may also have sedative effects to treat insomnia (Buckle, 2015).

Overall Impression

Rose oil is generally safe, pleasant, and may have mild pain relieving and anxiolytic effects.

FRANKINCENSE

Common Names	Frankincense
Latin Name	Boswellia frereana
Historical Uses	Depression, cancer, respiratory infection, inflammation, immune-stimulation
Route	Oral, topical, inhalation
Safety	"Generally Recognized as Safe" Status: No Hazards: Skin sensitization if oxidized Contraindications: Avoid old/oxidized oils. Dose: None given (Tisserand & Young, 2014, p. 288)
Frequently Suggested MOAs	Antimicrobial, immunostimulant, antidepressant, muscle relaxant

Summary of Human Research on Frankincense

USE	EVIDENCE SUMMARY	STRENGTH
Cognition (in MS patients)	Frankincense taken orally may have a positive effect on memory for people with multiple sclerosis.	Weak
Pain	Frankincense taken orally may have a prophylactic analgesic effect.	Weak
Gingivitis	Topical frankincense may have a positive effect on dental plaque reduction and gingivitis, either used alone or with scaling and root planing.	Weak
Osteoarthritis	Frankincense taken orally may produce improvement in OA symptoms, including pain, flexion, walking distance, and OA symptom scores.	Weak

Further notes on this oil

- There are several types of boswellia, however it is believed differences between these variations are minimal (Tisserand & Young, 2014).

Overall Impression

Frankincense has a long history of recorded use and has gained increasing interest in its therapeutic properties. In humans, it has most commonly been studied for its anti-inflammatory and analgesic effects, however evidence is weak for its efficacy. Although it does not have official GRAS status, it is generally safe when stored correctly to allow for minimal oxidation.

ROMAN CHAMOMILE

Common Names	Roman chamomile
Latin Name	Chamaemelum nobile
Historical Uses	Cardiac calmative, healing, ophthalmic use, anti-inflammatory, anti-infective, calming (Price & Price, 2012)
Route	Topical, inhalation
Safety	"Generally Recognized as Safe" Status: Yes Hazards: None known Contraindications: None known (Tisserand & Young, 2014, p. 244)
Frequently Suggested MOAs	Relaxant, antispasmodic, anti-inflammatory, antiparasitic, antibacterial, anesthetic

Summary of Human Research on Chamomile

USE	EVIDENCE SUMMARY	STRENGTH
Incontinence	There is some evidence that chamomile applied topically may be used as a short-term treatment for day or nighttime enuresis in children.	Weak
Carpal Tunnel Syndrome	Topical application of chamomile oil may have a positive effect on overall carpal tunnel syndrome symptoms, including pain and functionality, particularly in mild-moderate carpal tunnel syndrome.	Weak
Osteoarthritis	Topical Chamomile may decrease the need for analgesics for those with OA as well as improve physical function and stiffness.	Weak

Further notes on this oil

- There are other types of chamomile, the most popular being German chamomile, which has different therapeutic effects and may have interactions with certain drugs due to CYP enzyme action (Tisserand & Young, 2014).

Overall Impression

Roman chamomile is generally safe. There is some weak evidence to support the anti-inflammatory action of roman chamomile, including treatment of osteoarthritis and carpal tunnel syndrome.

CHAPTER FIVE

DISCUSSION

The purpose of this DNP project was to explore the state of the evidence available for the ten most commonly used essential oils and synthesize this evidence into integrative summaries in order to improve general healthcare providers' knowledge of this topic. Included in this chapter are: an overall summary of the project, the limitations of the project, implications for use of the results of the project, as well as recommendations for future essential oil research and future evidence summaries.

The ten most commonly used essential oils were first identified as lavender, peppermint, eucalyptus, tea tree, rosemary, patchouli, lemon, rose, frankincense, and chamomile. These oils were then approved by the student's committee, then an intensive literature review was implemented to find research articles on the selected oils that involved human subjects. The student utilized a modified version of the GRADE approach when reviewing and summarizing articles. After articles were reviewed they were categorized by uses identified in the research. Preliminary summaries and conclusions were presented in ten evidence use profile tables (one per oil) and the evidence was categorized as (a) strong evidence to support conclusion, (b) weak evidence to support conclusion, or (c) no conclusion. These preliminary conclusions were then placed in the final integrative summaries. The integrative summaries not only provide a summary of the conclusions from the evidence use profiles, but also other information potentially useful for healthcare providers, including alternative names for each oil,

safety issues, a list of conditions the oil has been used to treat in the past, a list of suggested mechanisms of action from a literature source intended for the lay public, further notes on the oil, and the student's overall impression from the research.

The conceptual framework that guided this project was Dorothea Orem's Self-Care Deficit theory. Orem's theory is grounded in the idea that when there is some degree of needed self-care that can no longer be met by an individual on his/her own, nursing steps in to assist the individual so that he/she may be able to remedy the deficit (Masters, 2014). Some ways that nurses help remedy deficits are through actions such as guiding, directing, teaching, and providing support (Masters, 2014), and the use of evidence-based practice goes hand-in-hand with these concepts. As stated in chapter one of this project, the intervention of creating the integrative summaries for healthcare providers supports bridging knowledge deficits of healthcare providers regarding aromatherapy, which will in turn help the provider meet the patient's own self-care needs through enhanced knowledge of aromatherapy.

It was found that although there is a general interest in CAM therapies among the general population, many healthcare providers are unsure how to advise their clients when asked about CAM therapies (Flannery et al., 2006). To date, there are numerous ways to obtain information on aromatherapy. Literature sources intended for the lay public range from websites with a wide and often undefined degree of credibility, essential oil guides and references published by for-profit companies and individuals, Internet wellness blogs, and a large selection of books to be used as personal references for interested individuals. Professionally, the National Association for Holistic

Aromatherapy (NAHA) not only offers membership and continuing education, but also lists NAHA approved schools of aromatherapy, where one can go to obtain official aromatherapy training (National Association of Holistic Aromatherapy, 2017b). There are even textbooks on aromatherapy for healthcare providers. Although resources exist for the healthcare provider who is able to spend the required time to read a textbook or take a course in aromatherapy, there is no current simplified guideline for aromatherapy in general practice. Additionally, no known research summaries exist which include conclusions based on research on aromatherapy conducted with humans. This project, though limited in scope, aimed to create a new kind of resource to be used by healthcare providers that may help fill the gap between the lay literature of variable reliability and highly structured aromatherapy training.

Limitations of the Project

To begin, the most obvious limitation of this project is the limited amount of clinical aromatherapy research on humans. The initial number of available articles to review ranged from 48 studies for lavender to three for patchouli. Among these studies, even fewer met final inclusion criteria to review for this project. The student employed an alternative approach in evidence gathering. Instead of the traditional approach used in guideline development of identifying a singular health problem and finding research on treatments for the problem, the student began with the treatment (oil) and explored the research literature on all the conditions/problems for which the oil had been used to treat. Although this backwards approach provided a wide variety of types of research for some

of the oils, in many cases only one or two small studies were available and weak conclusions resulted due to the small number of studies.

Further limitations of this project stem from student limitations including limitations on training, resources, and time. The student is not a professional researcher nor is the student an expert on aromatherapy, though these may also be viewed as strengths that enhanced objectivity. Additionally, the student was the only person reviewing the evidence in this project aside from a limited review by the student's committee chairperson for rigor, whereas typical guideline and evidence-based practice committees are usually comprised of panels of experts and reviewers.

Implications for Practice

Healthcare providers use a variety of resources when providing care for clients, including learned knowledge, personal experience, online and text references, and clinical guidelines. The recent upsurge in evidence-based practice initiatives has increased the need for a variety of evidence-based reviews and summaries (Whittemore & Knafl, 2005). Additionally, these tools must be easily accessible in order for the healthcare provider to incorporate them into client care. Essential oils are widely available and utilized by the general public, therefore it is valuable for healthcare providers to expand their knowledge of essential oils in order to better serve their clients who may be using them. The integrative summaries presented in this project may be used as a stepping stone to both further provider knowledge on the topic of essential oils and also lay the groundwork for further summaries of evidence on this topic.

Recommendations for Future Research

This project provides a new summary of evidence about essential oils that also integrates valuable background and safety information on each of the 10 selected oils. This tool is only the first step in the larger mission to bring aromatherapy research to the forefront to better understand the complex mechanisms that occur between the human body and these natural substances. As was mentioned in chapter one, the DNP project by Boesl (2016) also found limited research involving human subjects on essential oils, making full recommendations difficult if not impossible to formulate. Boesl's conclusion is not dissimilar from the student's experience in this project.

One of the challenges in aromatherapy research is translation of research from trial conditions to real life conditions. In fact, many clinical trials found by the student were characterized as exploratory studies or designed as RCTs but left to the participant and his/her environment for the execution of the treatment itself. Subsequently, many of these studies were graded as low quality in this project (and other systematic reviews) due to the inability to attain the tight control required in a randomized controlled trial (RCT). It is possible that human clinical research in aromatherapy might benefit from a different approach than the typical RCT. One solution might be the utilization of pragmatic trial design, which differs from the traditional controlled "explanatory trial" (such as the RCT) in a way that studies the effect of an intervention in real-life environments (Patsopulos, 2011). Pragmatic trials involve evaluation of the intervention in everyday settings through the use of simple study designs, large sample sizes, and may measure a wider spectrum of outcomes than explanatory trials (Patsopulos, 2011).

According to Patsopulos (2011), pragmatic trial design might be more beneficial in studying treatments with moderate outcomes as the lack of blinding may effect the participant's values and beliefs and alter the overall results of the study. The student suggests that personal beliefs and preferences are not confounding factors but factors existing in the real world that can affect real-world outcomes. There is room for and different uses for both traditional explanatory studies and the newer more generalized pragmatic studies in the world of research. More human research is needed for aromatherapy uses, and an increase in human research, particularly in real-world circumstances, will provide benefit to the continuing science of aromatherapy research.

The purpose of this project was to synthesize the available evidence on aromatherapy in a way that may be useful for healthcare providers and this was done through creating the integrative summaries presented in this project. Others could add upon this summary as new research emerges for these ten oils or additional oils in order to continually expand evidence-based knowledge of aromatherapy. Additionally, this project may be replicated and additional studies may be included that the student did not include in this project, such as in vitro and animal studies. As stated in chapter one, there are challenges that arise with translating in vitro and animal study data, but including this data may also give an even wider perception of how these oils may function.

Conclusion

The purpose of this project was to explore the state of the evidence available for the 10 most commonly used essential oils and synthesize the evidence into integrative

summaries in order to improve general healthcare providers' knowledge of this topic. Although there is limited clinical research on humans available, the research that was found was summarized and presented in a way that may potentially be useful for healthcare providers who have clients using essential oils and asking their healthcare providers about their uses. Objective five of the National Center for Complementary and Integrative Health's 2016 strategic plan is to "Disseminate Objective Evidence-based Information on Complementary and Integrative Health Interventions," further stating "It is critical that the public, health care providers, researchers, and policymakers be informed and knowledgeable about the safety and effectiveness of complementary and integrative health interventions" (National Center for Complementary and Integrative Health, 2017, p. para. 1). The integrative summaries presented in this project serve as a step toward promotion of evidence based practice and knowledge of aromatherapy, laying the groundwork for continued development of clinical practice guidelines. As Americans continue to use complementary therapies such as essential oils, clinical research and dissemination of results should continue in a way that is useful for healthcare providers to enhance whole-client care.

REFERENCES CITED

Abdel-Tawab, M., Werz, O., Schubert-Zsilavecz, M., Abdel-Tawab, M., Werz, O., & Schubert-Zsilavecz, M. (2011). Boswellia serrata: An overall assessment of in vitro, preclinical, pharmacokinetic and clinical data. *Clinical Pharmacokinetics, 50*(6), 349-369. doi:10.2165/11586800-000000000-00000

Akcan, E., & Polat, S. (2016). Comparative effect of the smells of amniotic fluid, breast milk, and lavender on newborns' pain during heel lance. *Breastfeeding Medicine, 11*(6), 309-314. doi:10.1089/bfm.2015.0174

American Cancer Society. (2014). Aromatherapy and essential oils. Retrieved from http://www.cancer.gov/about-cancer/treatment/cam/patient/aromatherapy-pdq

Bagheri-Nesami, M., Shorofi, S., Nikkhah, A., Espahbodi, F., & Ghaderi, K. F. (2016). The effects of aromatherapy with lavender essential oil on fatigue levels in haemodialysis patients: A randomized clinical trial. *Complementary Therapies in Clinical Practice, 22*, 33-37. doi:10.1016/j.ctcp.2015.12.002

Bikmoradi, A., Seifi, Z., Poorolajal, J., Araghchian, M., Safiaryan, R., & Oshvandi, K. (2015). Effect of inhalation aromatherapy with lavender essential oil on stress and vital signs in patients undergoing coronary artery bypass surgery: A single-blinded randomized clinical trial. *Complementary Therapies in Medicine, 23*(3), 331-338. doi:10.1016/j.ctim.2014.12.001

Blackwood, B., Thompson, G., McMullan, R., Stevenson, M., Riley, T., Alderdice, F., . . . McAuley, D. (2013). Tea tree oil (5%) body wash versus standard care (johnson's baby softwash) to prevent colonization with methicillin-resistant staphylococcus aureus in critically ill adults: A randomized controlled trial. *The Journal of Antimicrobial Chemotherapy, 68*(5), 1193-1199. doi:10.1093/jac/dks501

Boesl, R. R. (2016). *Essential oil education for healthcare providers.* (DNP Scholarly Project), North Dakota State University, Available from ProQuest Dissertations & Theses Global (1794656559). ProQuest Dissertations & Theses Global database. (10112564)

Buckle, J. (2015). *Clinical aromatherapy: Essential oils in healthcare*. St. Louis, MO: Elsevier.

Burnett, K., Solterbeck, L., & Strapp, C. (2004). Scent and mood state following an anxiety-provoking task. *Psychological Reports, 95*(2), 707-722. doi:10.2466/pr0.95.2.707-722

Cash, B., Epstein, M., & Shah, S. (2016). A novel delivery system of peppermint oil is an effective therapy for irritable bowel syndrome symptoms. *Digestive Diseases and Sciences, 61*(2), 560-571. doi:10.1007/s10620-015-3858-7

Chin, K. B., & Cordell, B. (2013). The effect of tea tree oil (melaleuca alternifolia) on wound healing using a dressing model. *Journal of Alternative & Complementary Medicine, 19*(12), 942-945. doi:10.1089/acm.2012.0787

Cho, Y., & Choi, Y. (2017). Comparison of three cooling methods for burn patients: A randomized clinical trial. *Burns, (no pagination)*. doi:10.1016/j.burns.2016.09.010

Clarke, T. C., Black, L. I., Stussman, B. J., Barnes, P. M., & Nahin, R. L. (2015). Trends in the use of complementary health approaches among adults: United States, 2002-2012. *National Health Statistics Report, 79*.

Edmondson, M., Newall, N., Carville, K., Smith, J., Riley, T. V., & Carson, C. F. (2011). Uncontrolled, open-label, pilot study of tea tree (melaleuca alternifolia) oil solution in the decolonisation of methicillin-resistant staphylococcus aureus positive wounds and its influence on wound healing. *International Wound Journal, 8*(4), 375-384. doi:10.1111/j.1742-481X.2011.00801.x

Edwards-Jones, V., Buck, R., Shawcross, S. G., Dawson, M. M., Dunn, K., Edwards-Jones, V., . . . Dunn, K. (2004). The effect of essential oils on methicillin-resistant staphylococcus aureus using a dressing model. *Burns (03054179), 30*(8), 772-777.

Erlich, S. D. (2011). Aromatherapy. Retrieved from http://umm.edu/health/medical/altmed/treatment/aromatherapy

Fernandez, L. F., Palomino, O. M., & Frutos, G. (2014). Effectiveness of rosmarinus officinalis essential oil as antihypotensive agent in primary hypotensive patients and its influence on health-related quality of life. *Journal of Ethnopharmacology, 151*(1), 509-516. doi:10.1016/j.jep.2013.11.006

Flannery, M. A., Love, M. M., Pearce, K. A., Luan, J. J., & Elder, W. G. (2006). Communication about complementary and alternative medicine: perspectives of primary care clinicians. *Alternative Therapies in Health and Medicine, 12*(1), 56-63.

Flaxman, D., & Griffiths, P. (2005). Is tea tree oil effective at eradicating MRSA colonization: A review (structured abstract). *British Journal of Community Nursing, 10*(3), 123-126.

Ford, A. C., Talley, N. J., Spiegel, B. M. R., Foxx-Orenstein, A. E., Schiller, L., Quigley, E. M. M., & Moayyedi, P. (2008). Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: systematic review and meta-analysis. *British Medical Journal (International Edition), 337*(7683), 1388-1392. doi:10.1136/bmj.a2313

Forrester, L. T., Maayan, N., Orrell, M., Spector, A. E., Buchan, L. D., & Soares-Weiser, K. (2014). Aromatherapy for dementia. *Cochrane Database of Systematic Reviews,* (2). doi:10.1002/14651858.CD003150.pub2

Freeman, L. (2009). *Complementary & alternative medicine: A research-based approach*. St. Louis, MO: Mosby Elsevier.

Ghods, A., Abforosh, N., Ghorbani, R., & Asgari, M. (2015). The effect of topical application of lavender essential oil on the intensity of pain caused by the insertion of dialysis needles in hemodialysis patients: A randomized clinical trial. *Complementary Therapies in Medicine, 23*(3), 325-330. doi:10.1016/j.ctim.2015.03.001

Gnatta, J., Pinto, F., Bruna, C., Souza, R., Graziano, K., & Silva, M. (2013). Comparison of hand hygiene antimicrobial efficacy: Melaleuca alternifolia essential oil versus triclosan. *Latin American Journal of Pharmacology, 21*(6), 1212-1219. doi:10.1590/0104-1169.2957.2356

Goepfert, M., Liebl, P., Herth, N., Ciarlo, G., Buentzel, J., & Huebner, J. (2017). Aroma oil therapy in palliative care: a pilot study with physiological parameters in conscious as well as unconscious patients. *Journal of Cancer Research and Clinical Oncol*ogy. doi:10.1007/s00432-017-2460-0

Grade Working Group. (2016). Grade handbook. Retrieved from http://gdt.guidelinedevelopment.org/app/handbook/handbook.html - h.9rdbelsnu4iy

Gupta, I., Gupta, V., Parihar, A., Gupta, S., Ludtke, R., Safayhi, H., & Ammon, H. P. (1998). Effects of boswellia serrata gum resin in patients with bronchial asthma: results of a double-blind, placebo-controlled, 6-week clinical study. *European Journal of Medical Research, 3*(11), 511-514.

Guyatt, G. H., Oxman, A. D., Kunz, R., Vist, G. E., Falck-Ytter, Y., & Schünemann, H. J. (2008). What is "quality of evidence" and why is it important to clinicians? *British Medical Journal, 336*(7651), 995-998. doi:10.1136/bmj.39490.551019.BE

Hasanzadeh, F., Kashouk, N., Amini, S., Asili, J., Emami, S., Vashani, H., & Sahebkar, A. (2016). The effect of cold application and lavender oil inhalation in cardiac surgery patients undergoing chest tube removal. *EXCLI Journal, 15*, 64-74. doi:10.17179/excli2015-748

Hashemi, S. H., Hajbagheri, A., & Aghajani, M. (2015). The effect of massage with lavender oil on restless leg syndrome in hemodialysis patients: a randomized controlled trial. *Nursing & Midwifery Studies, 4*(4), 1-5. doi:10.17795/nmsjournal29617

Hashempur, M., Ghasemi, M., Daneshfard, B., Ghoreishi, P., Lari, Z., & Homayouni, K. (2017). Efficacy of topical chamomile oil for mild and moderate carpal tunnel syndrome: a randomized double-blind placebo-controlled clinical trial. *Complementary Therapies in Clinical Practice, 26*, 61-67.

Hashempur, M. H., Lari, Z. N., Ghoreishi, P. S., Daneshfard, B., Ghasemi, M. S., Homayouni, K., & Zargaran, A. (2015). A pilot randomized double-blind placebo-controlled trial on topical chamomile (matricaria chamomilla L.) oil for severe carpal tunnel syndrome. *Complementary Therapies in Clinical Practice, 21*(4), 223-228. doi:10.1016/j.ctcp.2015.08.001

Heshmati, A., Dolatian, M., Mojab, F., shakeri, N., Nikkhah, S., & Mahmoodi, Z. (2017). The effect of peppermint (mentha piperita) capsules on the severity of primary dysmenorrhea. *Journal of Herbal Medicine, 6*(3), 137-141. doi:10.1016/j.hermed.2016.05.001

Hines, S., Steels, E., Chang, A., & Gibbons, K. (2012). Aromatherapy for treatment of postoperative nausea and vomiting. *Cochrane Database of Systematic Reviews,* (4). doi:10.1002/14651858.CD007598.pub2

Hongratanaworakit, T. (2009). Simultaneous aromatherapy massage with rosemary oil on humans. *Scientia Pharmaceutica, 77*(2), 375-387. doi:10.3797/scipharm.0903-12

Houghton, C., Casey, D., Shaw, D., & Murphy, K. (2013). Rigour in qualitative case-study research. *Nursing Research, 20*(4), 12-17.

Igarashi, M., Ikei, H., Song, C., & Miyazaki, Y. (2014). Effects of olfactory stimulation with rose and orange oil on prefrontal cortex activity. *Complementary Therapies in Medicine, 22*(6), 1027-1031. doi:10.1016/j.ctim.2014.09.003

International Association for the Study of Pain. (2017). International association for the study of pain taxonomy. Retrieved from https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698

International Trade Centre. (2014, August 2014). Essential oils and oleoresins. *Market Insider.* Retrieved from http://www.intracen.org/uploadedFiles/intracenorg/Content/Exporters/Market_Data_and_Information/Market_information/Market_Insider/Essential_Oils/Monthly report 2014 August.pdf

International Trade Centre. (2015). Aromatherapy: Characteristics of the market. Retrieved from http://www.intracen.org/uploadedFiles/intracenorg/Content/Exporters/Market_

Data_and_Information/Market_information/Market_Insider/Essential_Oils/Aromatherapy - characteristics of the market.pdf

Irmak Sapmaz, H., Uysal, M., Taş, U., Esen, M., Barut, M., Somuk, B. T., . . . Ayan, S. (2015). The Effect of Lavender Oil in Patients with Renal Colic: A Prospective Controlled Study Using Objective and Subjective Outcome Measurements. *Journal of Alternative & Complementary Medicine, 21*(10), 617-622. doi:10.1089/acm.2015.0112

Johnson, C. E. (2014). Effect of aromatherapy on cognitive test anxiety among nursing students. *Alternative & Complementary Therapies, 20*(2), 84-87. doi:10.1089/act.2014.20207

Jun, Y., Kang, P., Min, S., Lee, J.-M., Kim, H.-K., & Seol, G. (2013). Effect of eucalyptus oil inhalation on pain and inflammatory responses after total knee replacement: A randomized clinical trial. *Evidence-based Complementary and Alternative Medicine*. doi:10.1155/2013/502727

Karadag, E., Samancioglu, S., Ozden, D., & Bakir, E. (2017). Effects of aromatherapy on sleep quality and anxiety of patients. *Nursing in Critical Care, 22*(2), 105-112. doi:10.1111/nicc.12198

Kaviani, M., Azima, S., Alavi, N., & Tabaei, M. H. (2014). The effect of lavender aromatherapy on pain perception and intrapartum outcome in primiparous women. *British Journal of Midwifery, 22*(2), 125-128 124p.

Kazemzadeh, R., Nikjou, R., Rostamnegad, M., & Norouzi, H. (2016). Effect of lavender aromatherapy on menopause hot flushing: A crossover randomized clinical trial. *Journal of the Chinese Medical Association, 79*(9), 489-492. doi:10.1016/j.jcma.2016.01.020

Keating, A., & Chez, R. A. (2002). Ginger syrup as an antiemetic in early pregnancy. *Alternative Therapies in Health and Medicine, 8*(5), 89-91.

Kheirkhah, M., Setayesh, V. P. N., Nisani, L., & Haghani, H. (2014). Comparing the effects of aromatherapy with rose oils and warm foot bath on anxiety in the first stage of labor in nulliparous women. *Iranian Red Crescent Medical Journal, 16*(9). doi:10.5812/ircmj.14455

Kim, K., Seo, H., Min, S., Park, M., & Seol, G. (2014). The effect of 1,8-cineole inhalation on preoperative anxiety: A randomized clinical trial. *Evidence-based Complementary and Alternative Medicine*. doi:10.1155/2014/820126

Kim, S., Kim, H., Yeo, J., Hong, S., Lee, J., & Jeon, Y. (2011). The effect of lavender oil on stress, bispectral index values, and needle insertion pain in volunteers. *Journal*

Of Alternative And Complementary Medicine (New York, N.Y.), 17(9), 823-826. doi:10.1089/acm.2010.0644

Kimmatkar, N., Thawani, V., Hingorani, L., & Khiyani, R. (2003). Efficacy and tolerability of boswellia serrata extract in treatment of osteoarthritis of knee: A randomized double blind placebo controlled trial. *Phytomedicine, 10*(1), 3-7. doi:10.1078/094471103321648593

Kirste, S., Treier, M., Wehrle, S., Becker, G., Abdel-Tawab, M., Gerbeth, K., . . . Momm, F. (2011). Boswellia serrata acts on cerebral edema in patients irradiated for brain tumors: a prospective, randomized, placebo-controlled, double-blind pilot trial. *Cancer, 117*(16), 3788-3795. doi:10.1002/cncr.25945

Koo, H., Kim, T., Kim, K., Wee, S., Chun, Y., & Kim, J. (2012). Ocular surface discomfort and demodex: effect of tea tree oil eyelid scrub in demodex blepharitis. *Journal of Korean Medical Science, 27*(12), 1574-1579. doi:10.3346/jkms.2012.27.12.1574

Köteles, F., & Babulka, P. (2014). Role of expectations and pleasantness of essential oils in their acute effects. *Acta Physiologica Hungarica, 101*(3), 329-340. doi:10.1556/APhysiol.101.2014.3.8

Kwon, H., Yoon, J., Park, S., Min, S., & Suh, D. (2014). Comparison of clinical and histological effects between lactobacillus-fermented chamaecyparis obtusa and tea tree oil for the treatment of acne: An eight-week double-blind randomized controlled split-face study. *Dermatology (Basel, Switzerland), 229*(2), 102-109. doi:10.1159/000362491

Laccourreye, O., Werner, A., Laccourreye, L., & Bonfils, P. (2017). Benefits, pitfalls and risks of phytotherapy in clinical practice in otorhinolaryngology. *European annals of otorhinolaryngology, head and neck diseases, (no pagination)*. doi:10.1016/j.anorl.2016.11.001

Lee, R., Leung, P., & Wong, T. (2014). A randomized controlled trial of topical tea tree preparation for MRSA colonized wounds. *International Journal of Nursing Sciences, 1*(1), 7-14. doi:10.1016/j.ijnss.2014.01.001

Life Science Publishing. (2014). *Essential oils pocket reference* (6th ed.). Lehi, UT: Life Science Publishing.

Lillehei, A., Halcón, L., Savik, K., & Reis, R. (2015). Effect of inhaled lavender and sleep hygiene on self-reported sleep issues: A randomized controlled trial. *Journal Of Alternative And Complementary Medicine (New York, N.Y.), 21*(7), 430-438. doi:10.1089/acm.2014.0327

Lillehei, A. S., & Halcon, L. L. (2014). A systematic review of the effect of inhaled essential oils on sleep. *Journal of Alternative & Complementary Medicine, 20*(6), 441-451. doi:10.1089/acm.2013.0311

Lincoln, Y. S., & Guba, E. G. (1985). *Naturalistic inquiry*. Thousand Oaks CA: Sage Publications.

Liu, C., Chien, L.-W., & Cheng, S. (2012). The effect of lavender aromatherapy on autonomic nervous system in midlife women with insomnia. *Evidence-based Complementary and Alternative Medicine*. doi:10.1155/2012/740813

Lytle, J., Mwatha, C., & Davis, K. (2014). Effect of lavender aromatherapy on vital signs and perceived quality of sleep in the intermediate care unit: A pilot study. *American Journal Of Critical Care : An Official Publication, American Association Of Critical-Care Nurses, 23*(1), 24-29. Retrieved from doi:10.4037/ajcc2014958

Majdinasab, N., Siahpush, A., Mousavinejad, S., Malayeri, A., Sajedi, S., & Bizhanzadeh, P. (2017). Effect of boswellia serrata on cognitive impairment in multiple sclerosis patients. *Journal Of Herbal Medicine, 6*(3), 119-127. doi:10.1016/j.hermed.2016.05.003

Mann, N. S., & Sandhu, K. S. (2012). Peppermint oil in irritable bowel syndrome: Systematic evaluation of 1634 cases with meta-analysis. *International Medical Journal, 19*(1), 5-6.

Masters, K. (2014). *Nursing theories: A framework for professional practice* (2nd ed.). Burlington, MA: Jones & Bartlett Learning, LLC.

Matsumoto, T., Asakura, H., & Hayashi, T. (2013). Does lavender aromatherapy alleviate premenstrual emotional symptoms?: A randomized crossover trial. *BioPsychoSocial Medicine, 7*. Retrieved from doi:10.1186/1751-0759-7-12

Matthews, A., Dowswell, T., Haas, D. M., Doyle, M., & O'Mathúna, D. P. (2014). Interventions for nausea and vomiting in early pregnancy. *Cochrane Database of Systematic Reviews*(3), N.PAG-N.PAG.

McCaffrey, R., Thomas, D. J., & Kinzelman, A. O. (2009). The effects of lavender and rosemary essential oils on test-taking anxiety among graduate nursing students. *Holistic Nursing Practice, 23*(2), 88-93 86p. doi:10.1097/HNP.0b013e3181a110aa

Mesri, M., Hosseini, S. M., Heydarifar, R., Mirizadeh, M., & Forozanmeher, M. (2017). Effect of lavender aromatherapy on anxiety and hemodynamic changes: A randomized clinical trial. *Qom University of Medical Sciences Journal*, 1-3.

Mirsadraei, M., Tavakoli, A., & Ghaffari, S. (2013). Effects of rosemary and platanus extracts on asthmatic subjects resistant to traditional treatments. *European Respiratory Journal, 42*.

Morse, J. M. (2015). Critical analysis of strategies for determining rigor in qualitative inquiry. *Qualitative Health Research, 25*(9), 1212-1222. doi:10.1177/1049732315588501

Moss, M., Cook, J., Wesnes, K., & Duckett, P. (2003). Aromas of rosemary and lavender essential oils differentially affect cognition and mood in healthy adults. *The International Journal Of Neuroscience, 113*(1), 15-38.

Nahin, R. L., Barnes, P. M., & Stussman, B. J. (2016). Expenditures on complementary health approaches: United States, 2012. *National Health Statistics Report, 95*.

Nasiri, A., Mahmodi, M. A., & Nobakht, Z. (2016). Effect of aromatherapy massage with lavender essential oil on pain in patients with osteoarthritis of the knee: A randomized controlled clinical trial. *Complementary Therapies In Clinical Practice, 25*, 75-80. doi:10.1016/j.ctcp.2016.08.002

National Association of Holistic Aromatherapy. (2017a). Exploring aromatherapy. Retrieved from http://naha.org/explore-aromatherapy/

National Association of Holistic Aromatherapy. (2017b). NAHA approved schools. Retrieved from https://naha.org/education/approved-schools/

National Center for Complementary and Integrative Health. (2017). NCCIH 2016 strategic plan. Retrieved from https://nccih.nih.gov/about/strategic-plans/2016

Panahi, Y., Taghizadeh, M., Marzony, E., & Sahebkar, A. (2015). Rosemary oil vs minoxidil 2% for the treatment of androgenetic alopecia: a randomized comparative trial. *Skinmed, 13*(1), 15-21.

Patsopulos, N. A. (2011). A pragmatic view on pragmatic trials. *Dialogues in Clinical Neuroscience, 13*(2), 217-224.

PDQ Integrative Alternative and Complementary Therapies Editorial Board. (2015). Aromatherapy and essential oils (PDQ): Health professional version. 2015.

Pengelly, A., Snow, J., Mills, S., Scholey, A., Wesnes, K., & Butler, L. (2012). Short-term study on the effects of rosemary on cognitive function in an elderly population. *Journal of Medicinal Food, 15*(1), 10-17. doi:10.1089/jmf.2011.0005

Prabhavathi, K., Chandra, U., Soanker, R., & Rani, P. (2014). A randomized, double blind, placebo controlled, cross over study to evaluate the analgesic activity of

Boswellia serrata in healthy volunteers using mechanical pain model. *Indian Journal Of Pharmacology, 46*(5), 475-479. Retrieved from doi:10.4103/0253-7613.140570

Price, L., & Price, S. (2012). *Aromatherapy for health professionals* (4th ed.). Edinburgh: Elsevier.

Raisi Dehkordi, Z., Hosseini Baharanchi, F. S., & Bekhradi, R. (2014). Effect of lavender inhalation on the symptoms of primary dysmenorrhea and the amount of menstrual bleeding: A randomized clinical trial. *Complementary Therapies in Medicine, 22*(2), 212-219. doi:10.1016/j.ctim.2013.12.011

Ruepert, L., Quartero, A. O., de, W. N. J., van, d. H. G. J., Rubin, G., & Muris, J. W. (2011). Bulking agents, antispasmodics and antidepressants for the treatment of irritable bowel syndrome. *Cochrane Database of Systematic Reviews,* (8). doi:10.1002/14651858.CD003460.pub3

Sadlon, A. E., & Lamson, D. W. (2010). Immune-modifying and antimicrobial effects of eucalyptus oil and simple inhalation devices. *Alternative Medicine Review, 15*(1), 33-47.

Samani, K. M., Mahmoodian, H., Moghadamnia, A. A., Mir, A. P. B., & Chitsazan, M. (2011). The effect of frankincense in the treatment of moderate plaque-induced gingivitis: A double blind randomized clinical trial. *DARU Journal of Pharmaceutical Sciences, 19*(4), 288-294.

Sander, O., Herborn, G., & Rau, R. (1998). [Is H15 (resin extract of boswellia serrata, "incense") a useful supplement to established drug therapy of chronic polyarthritis? Results of a double-blind pilot study]. *Z Rheumatol, 57*(1), 11-16.

Santamaria, M., Petermann, K., Vedovello, S., Degan, V., Lucato, A., & Franzini, C. (2014). Antimicrobial effect of melaleuca alternifolia dental gel in orthodontic patients. *American Journal Of Orthodontics And Dentofacial Orthopedics, 145*(2), 198-202. Retrieved from doi:10.1016/j.ajodo.2013.10.015

Scott, G. N. (2015, September 15, 2015). Essential oils and aromatherapy: Worth the hype? *Ask the Pharmacists.* Retrieved from http://www.medscape.com/viewarticle/850160_2

Sengupta, K., Alluri, K. V., Satish, A. R., Mishra, S., Golakoti, T., Sarma, K. V., . . . Raychaudhuri, S. P. (2008). A double blind, randomized, placebo controlled study of the efficacy and safety of 5-loxin for treatment of osteoarthritis of the knee. *Arthritis Research and Therapy, 10*(4), R85. doi:10.1186/ar2461

Seol, G. H., Lee, Y. H., Kang, P., You, J. H., Park, M., & Min, S. S. (2013). Randomized controlled trial for salvia sclarea or lavandula angustifolia: differential effects on blood pressure in female patients with urinary incontinence undergoing urodynamic examination. *Journal of Alternative & Complementary Medicine, 19*(7), 664-670. doi:10.1089/acm.2012.0148

Sharifi, H., Minaie, M. B., Qasemzadeh, M. J., Ataei, N., Gharehbeglou, M., & Heydari, M. (2017). Topical use of matricaria recutita l (chamomile) oil in the treatment of monosymptomatic enuresis in children. *Journal of Evidence-Based Complementary & Alternative Medicine, 22*(1), 12-17. doi:10.1177/2156587215608989

Sheikhan, F., Jahdi, F., Khoei, E. M., Shamsalizadeh, N., Sheikhan, M., & Haghani, H. (2012). Episiotomy pain relief: Use of lavender oil essence in primiparous iranian women. *Complementary Therapies In Clinical Practice, 18*(1), 66-70. doi:10.1016/j.ctcp.2011.02.003

Sherry, E., & Warnke, P. H. (2004). Successful use of an inhalational phytochemical to treat pulmonary tuberculosis: A case report. *Phytomedicine, 11*(2), 95-97. doi:10.1078/0944-7113-00378

Shirazi, M., Mohebitabar, S., Bioos, S., Yekaninejad, M. S., Rahimi, R., Shahpiri, Z., . . . Nejatbakhsh, F. (2017). The effect of topical rosa damascena (rose) oil on pregnancy-related low back pain. *Journal of Evidence-Based Complementary & Alternative Medicine, 22*(1), 120-126. doi:10.1177/2156587216654601

Shoara, R., Hashempur, M., Ashraf, A., Salehi, A., Dehshahri, S., & Habibagahi, Z. (2015). Efficacy and safety of topical matricaria chamomilla L. (chamomile) oil for knee osteoarthritis: A randomized controlled clinical trial. *Complementary Therapies In Clinical Practice, 21*(3), 181-187. doi:10.1016/j.ctcp.2015.06.003

Siahpush, M. (1999). Postmodern attitudes about health: a population-based exploratory study. *Complementary Therapies in Medicine, 7*(3), 164-169.

Sites, D., Johnson, N., Miller, J., Torbush, P., Hardin, J., Knowles, S., . . . Tart, R. (2014). Controlled breathing with or without peppermint aromatherapy for postoperative nausea and/or vomiting symptom relief: a randomized controlled trial. *Journal Of Perianesthesia Nursing : Official Journal Of The American Society Of Perianesthesia Nurses, 29*(1), 12-19. doi:10.1016/j.jopan.2013.09.008

Sohn, P. M., & Loveland Cook, C. A. (2002). Nurse practitioner knowledge of complementary alternative health care: Foundation for practice. *Journal of Advanced Nursing, 39*(1), 9-16.

Sun, J. (2007). D-limonene: safety and clinical applications. *Alternative Medicine Review, 12*(3), 259-264.

The Marshall Protocol Knowledge Base. (2015). Differences between in vitro, in vivo, and in silico studies. Retrieved from https://mpkb.org/home/patients/assessing_literature/in_vitro_studies

Tisserand, R. (2016). Frankincense oil and cancer in perspective. Retrieved from http://tisserandinstitute.org/frankincense-oil-and-cancer-in-perspective/

Tisserand, R., & Young, R. (2014). *Essential oil safety: a guide for health care professionals* (2nd ed.). Edinburgh: Churchhill Livingstone Elsevier.

Toda, M., & Morimoto, K. (2011). Evaluation of effects of lavender and peppermint aromatherapy using sensitive salivary endocrinological stress markers. *Stress & Health: Journal of the International Society for the Investigation of Stress, 27*(5), 430-435. doi:10.1002/smi.1402

Trongtokit, Y., Rongsriyam, Y., Komalamisra, N., & Apiwathnasorn, C. (2005). Comparative repellency of 38 essential oils against mosquito bites. *Phytotherapy Research : PTR, 19*(4), 303-309. doi:10.1002/ptr.1637

U.S. Food & Drug Administration. (2017). Generally recognized as safe (GRAS). Retrieved from https://www.fda.gov/food/ingredientspackaginglabeling/gras/

U.S. National Institutes of Health. (2016). ClinicalTrials.gov: "Aromatherapy". Retrieved November 13, 2016 from https://clinicaltrials.gov/ct2/results?term=aromatherapy&Search=Search

Uysal, M., Doğru, H. Y., Sapmaz, E., Tas, U., Çakmak, B., Ozsoy, A. Z., . . . Esen, M. (2016). Investigating the effect of rose essential oil in patients with primary dysmenorrhea. *Complementary Therapies In Clinical Practice, 24*, 45-49. doi:10.1016/j.ctcp.2016.05.002

Warnke, P. H., Sherry, E., Russo, P. A. J., Açil, Y., Wiltfang, J., Sivananthan, S., . . . Schubert, S. (2006). Antibacterial essential oils in malodorous cancer patients: clinical observations in 30 patients. *Phytomedicine, 13*(7), 463-467.

Whittemore, R., & Knafl, K. (2005). The integrative review: Updated methodology. *Journal of Advanced Nursing, 52*(5), 546-553. doi:10.1111/j.1365-2648.2005.03621.x

Woelk, H., & Schläfke, S. (2010). A multi-center, double-blind, randomised study of the lavender oil preparation silexan in comparison to lorazepam for generalized anxiety disorder. *Phytomedicine, 17*(2), 94-99. doi:10.1016/j.phymed.2009.10.006

Wound Healing and Management Node Group. (2013). Evidence summary: Wound management: tea tree oil. *Wound Practice & Research, 21*(4), 170-172.

Wu, J. C. Y. (2010). Complementary and alternative medicine modalities for the treatment of irritable bowel syndrome: facts or myths? *Gastroenterology & Hepatology, 6*(11), 705-711.

Yavari Kia, P., Safajou, F., Shahnazi, M., & Nazemiyeh, H. (2014). The effect of lemon inhalation aromatherapy on nausea and vomiting of pregnancy: a double-blinded, randomized, controlled clinical trial. *Iran Red Crescent Medical Journal, 16*(3), e14360. doi:10.5812/ircmj.14360

APPENDICES

APPENDIX A

ESSENTIAL OIL SEARCH LOG

*Multiple oils in study from top 10
All are restricted to single oil studies (no mixes).
Preference to responses to individual oils (several studies found that focus on olfactory response using EO as the tool)

DATE	DATABASE	SEARCH TERMS	RESTRICTIONS	HITS	KEEPER
3/24/17	Cochrane	Lavender	Review; Trials, 2012-2017, RCT	4; 185	Forrester*, Oltean, Shin, Smith; 36 added to Endnote (Akcan, Altael, Bagheri, Bednarek, Bikmoradi, Cetinkaya, Dyer, Franco, Ghods, Hadi, Hanson, Harpreet, Hasanzedeh, Hozumi, Jalalian, Jimbo, Kaviani, Kiani, Kiberd, Kim, Koteles, Kritsidima, Lillehei, Liu, Lytle, Mandras, Marzouk, Matsumoto, Mirmohamad, O'Connor, Ou, Ploeg, Rafie, Seyyed, Soltani, Tirabassi, Tosun)
8/17/17	Cinahl	Lavender oil	2012-2017, NOT "in vitro"	115	14 added to EndNote (Baccaglini, Cohn, Field, Hashemi, Irmak, Jones, Karadag, Lillehei, Mesri, Nasiri, Raisi, Seol, Sheikhan, Woelk) (Many duplicate studies from previous searches)
3/27/17	Cochrane	Peppermint	Review; Trials, 2012-2017, RCT	5; 152	Ruepert, Hines, Dennis, Derry, Forrester*; 28 added to Endnote (Alam, Amjadi, Anderson, Asgarshirazi, Babamohamadi, Capanni, Cash, Cash, Epstein, Heshmati, Lane, Li, Mahdieh, Mosaffa, Papathanasopoulos, Quinn,

8/15/17	Cinahl	Peppermint oil	Academic Journals, CEUs	76	Shavakhi, Sites, Strugala, Talsma, Wu, Zadeh) 9 added to endnote (Ford, Imagawa, Lua, Mann, Oliff, Shen, Tate, Toda, Wu)
3/27/17	Cochrane	Eucalyptus	Trials (No Reviews)	24	5 added to endnote (Gobel, Ishikawa, Jun, Kim, Koteles)
8/15/17	Cinahl	Eucalyptus oil	Academic Journals	46	3 added to endnote (Warnke, Sadlon, & Sherry)
9/12/17	Medline WOS	Eucalyptus oil Eucalyptus globulus 1,8-cineole	Journals	50	None added – all in vitro or plant studies
9/16/17	Medline WOS		Journals, complementary	82	None added – many articles on oil constituents, several in-vitro, several mixed with other EO's, several animal studies, and several crossover articles from previous searches. (poss. r/t use of scientific term?)
3/27/17	Cochrane	Tea Tree	Cochrane Reviews; Other Reviews; Trials, 2012-2017	1; 3; 21;	Cao; Ernst, Flaxman, Martin; 9 added to Endnote (Beheshti, Blackwood, Cho, Gnatta, Koo, Kwon, Lee, Santamaria, Tirabassi)
8/14/17	Cinahl	Tea Tree Oil	2012-2017, academic journals	39	1 added to endnote (Wound healing…). Multiple hits from previous Cochrane searches.
8/15/17	Cinahl	Melaleuca oil		32	2 added to endnote (chin, Edmonson)
3/27/17	Cochrane	Rosemary	(none)	60	12 added to Endnote (Ball, Burnett, Davari, Diego, Hongratana….,

					Koteles, Laccourreye, Mehrabi, Mirsadraei, Moss, Panahi, Pengelly)
8/9/17	Cinahl	Rosemary	2012-2017, journals, essential oils	9	1 added to endnote (Fernandez) *Studies on Rosemary extract excluded
9/18/17	Web of Science	Rosemary oil	Biological applications (various)	31	1 duplicate from previous – all others were in vitro or not r/t humans.
	PubMed	Rosemary oil	Humans, clinical trial	9	None added (a few animal, duplicates)
3/28/17	Cochrane	Patchouli;	(none)	4;	2 added to Endnote (Hansen*, Trongtokit);
		Pogostemon	(none)	4	Wang. Hansen later thrown out r/t in
8/9/17	Cinahl	Patchouli	(none)	14	vitro status
		Pogostemon		6	1 added to Endnote (Edwards-Jones).
9/19/17	PubMed	Patchouli oil;		13	Many combinations and in vitro excluded.
		Pogostemon		27	(no human studies)
	Web of Science	Patchouli oil	(none)	240	(no human studies) (1 repeat from previous search, no human studies)
					Many in-vitro, several animal, 2 repeats, no humans
3/28/17	Cochrane	“Lemon oil”;	Reviews;	2;	Matthews;
		“Lemon oil” NOT balm	Trials, 2012-2017	5	3 added to Endnote (Calabrese, Jantarat, Kia)
8/9/17	Cinahl	lemon oil	“academic journals”	33	1 added to endnote (Johnson)
		“citrus limon”	(none)	24	(no studies added because all in vitro or in mice)
9/21/17	PubMed	“lemon oil” NOT balm			
3/28/17	Cochrane	“Rose Oil”	(none)	6	4 added to Endnote (Han, Hansen*,

		(Rose alone brings up authors' names)			Kheirkhah, Sadeghi)
8/9/17	Cinahl	"rose oil"	(none)	10	2 added to Endnote (Shirazi, Sadeghi)
		rose oil	2010-2017	28	2 added to Endnote (Igarashi, Uysal). Several studies on anxiety/depression with a combination of rose and lavender were excluded
3/28/17	Cochrane	Frankincense; Boswellia	(none); (none. "extract" or "acid" ok)	5	2 added to Endnote (NA, Sturner); 11 added to Endnote (Gerhardt, Holtmeier, Kirste, Kizhakkedath, Liu, Madisch, Majdinasab, Moein, Prabhavathi, Sontakke, Togni)
8/8/17	Cinahl	Frankincense	(none)	45	4 added to EndNote (Abdel, Ernst, Michie, & Samani)(Many in vitro
		Frankincense oil		6	studies not on humans or animals.
9/23/17	Web of Science	Frankincense oil; boswellia	none		These were excluded) Multiple duplicates from previous
8/7/17	Cochrane	Chamomile	(none)	3	1 added to Endnote (Burns). Several studies found where Roman chamomile was used as a relaxant, but no specific results r/t chamomile (Burns is a pilot study)
8/8/17	Cinahl	"Chamomile Oil"		22	9 added to Endnote (Hashempur x2, Sharifi, Shoara, Wilkinson, Zargaran, Moss, Matthews, Henson)
9/24/17	Web of Science	"Chamomile Oil"		48	0 added (several studies duplicates, several plant studies and hypotheses. No new human studies)

APPENDIX B

AROMATHERAPY EVIDENCE TABLE

LEGEND

Abbreviations	APAP: Acetaminophen BAI: Beck Anxiety Index BM: Bowel movement BP: Blood Pressure BS: Boswellia Serratta (Frankincense) EO: Essential oil PSQI: Pittsburgh Sleep Quality Index BAI: Beck Anxiety Index PROMIS: Patient Reported Outcomes Measurement Information System sleep disturbance short form REEDA: Redness, edema, ecchymosis, discharge (score) SFM-MPQ: Short for modified-McGill pain questionnaire OA: Osteoarthritis	P: Pulse PO: Peppermint Oil POMS: Profile of Mood States PONV: Post-operative nausea & vomiting RR: Respiratory rate r/t: Related to Stat. sig.: Statistically significant ($p<0.05$) Sx: Symptom TTO: Tea Tree Oil Tx: Treatment VS: Vital Signs WOMAC: Western Ontario and McMaster Universities Osteo-arthritis Index
General Notes	• Statistical Significance = $p < 0.05$ • Unless otherwise stated, the article mentions there are no statistical demographic or baseline data differences between groups. • Unless otherwise specified, all articles are from peer-reviewed journals. • Unless otherwise noted, all studies state inclusion and exclusion criteria. • Unless otherwise noted, all RCTs note and explain details of randomization. • Studies involving massage were generally omitted due to the confounding of massage therapy and aromatherapy, however several were included and noted due to the nature of the massage use and the goal of the study. • + and – in Preliminary Quality of Evidence columns should be interpreted as factors that might have increased (+) or decreased (-) the quality of evidence	

Citation	Design/ Method	Sample/ Setting	Uses Studied	Interventions	Instruments	Study Findings	Preliminary Quality of Evidence (High/Moderate/ Low/Very Low) & Rationale		Importance and/or Additional Considerations
Mesri, Hosseini, Heydarifar, Mirizadeh, and Forozanmeher (2017)	Single-blind RCT	N= 90 female patients with burns <20% Location: Iranian hospital	Anxiety Pain (burn victims)	Received aromatherapy massage: n=30, Received inhalation aromatherapy : n=30, Control: n=30	2-part questionnaire: 1: demographics 2: STAI & VAS	-Baseline anxiety/pain equal among all groups -massage and inhalation groups both had statistically significant reduced pain and anxiety.	+ -RCT -Use of STAI and VAS insturments -Tight control of intervention	− -Single study -No repetition (done only once) -Unable to blind intervention (risk of bias) **LOW QUALITY**	-Poss. Of pain reduction r/t anxiety reduction - Lavender may redice pain and anxiety when applied topically or inhaled
Karadag (2017), Effects of aromatherapy on sleep quality and anxiety of patients g	RCT	N = 60 patients in a coronary ICU. (30 control and 30 treatment) Setting: Turkish hospital	Sleep Quality, Anxiety	N = 30 patients received inhaled 2% lavender EO for 20 minutes before sleep for 15 days (randomized)	BAI (Beck Anxiety Index) and PSQI (Pittsburgh Sleep Quality Index) scales used on all patients (before and after)	Significant difference found between pretest and post-test (lavender group had improved BAI and PSQI) but not in control	+ -RCT, -Appropriate use of BAI and PSQI	− -Single study -No repetition -No placebo group -Unable to blind intervention (risk of bias) -Type of lavender not specified **LOW QUALITY**	Clinically important for non-pharm anxiety reduction and sleep quality in people in a hospital (increased stress)
Nasiri, A. (2016). Effect of aromatherapy	RCT (single-blinded)	N= 90 patients with OA (osteoarthriti	Topical lavender application for pain	N=30 Massage with lavender oil 3% in sweet	-VAS scale -Measured before 3-week intervention,	-Significant reduction of pain in lavender group	+ -Self-administration instructions	− -Self-administred -All	-Included this study with massage due to fact there

massage with lavender essential oil on pain in patients with osteoarthritis of the knee: a randomized controlled clinical trial		s) of the knee (30 in each group) Outpatient rheumatology patients in Iran	relief (self-massage)	almond oil N= 30 Massage without lavender (only sweet almond oil) (placebo) N=30 No treatment (control)	immediately after intervention, 1 week after intervention, and 4 weeks after intervention *attrition = 3 in treatment and placebo groups each, 4 in control.	immediately after intervention. -No difference in pain between groups at four weeks past intervention	given and weekly reminder calls done -Appropriate use of data analysis instruments	participants were taking pain relief meds (nsaids, apap) from rheumatologist -26% of patients were male -Double blinding impossible r/t fragrance **LOW QUALITY**	was a placebo group as well as a control group. -Confounding factor: lavender smell
Hasanzadeh (2016). The effect of cold application and lavender oil inhalation in cardiac surgery patients undergoing chest tube removal	RCT with factorial design	80 ICU patients with a chest tube for >24h after cardiothoracic surgery (post CABG) Hospital in Iran	Lavender Inhalation for pain/anxiety relief	N=20 cold gel with cooling pack N=20 inhaled lavender N=20 inhaled lavender and cooling gel N=20 control (no cold or lavender)	VAS SFM-MPQ STAI -VAS Pain measured 10 minutes before, immediately during, 5, 10,, and 15 minutes after CTR -STAI measured 10 minutes before and after	Pain: All interventions had a reduced total SFM-MPQ compared to control (but no diff between interventions) -Anxiety: Aroma and cold + aroma had significantly less anxiety post-CTR than cold alone or control	+ -Oil was confirmed to be of good quality -Variables reasonably controlled -Multiple intervention groups to compare	− -Subjective nature of VAS -High variability of pain experiences with CTR -Limited to post-CABG CTR (very specific, how generalizable?) **LOW QUALITY**	- Cold therapy and lavender inhalation did not significantly change pain experience vs. control or cold therapy alone, however the combination did have a decrease in anxiety.
Bagheri-Nesami, M. (2016). The effects of aromatherapy with lavender essential oil on fatigue levels	RCT	N= 60 patients undergoing hemodialysis Two hospitals in	Fatigue levels in hemodialysis patients	n-30 in control (no treatment) N= 29 patients (one lost due to infection) Patients	Fatigue Severity Scale (FSS) used. Measured before intervention, after last intervention in	No difference in fatigue levels between groups during or after	+ FSS widely used in research studies	− -Small study -very small amount of exposure to intervention compared to overall fatigue	Previous studies have shown that lavender may have a positive effect on fatigue, but this study

in haemodialysis patients: A randomized clinical trial		Iran		inhaled lavender during hemodialysis (10 minutes at a time for 3x/week for four weeks)	week 2 and 4.			levels (many counfounding factors) VERY LOW QUALITY	does not support this.
Akcan, E.. (2016). Comparative Effect of the Smells of Amniotic Fluid, Breast Milk, and Lavender on Newborns' Pain during Heel Lance	RCT	N=102 newborns Hospital in Turkey	Pain in newborn (heel stick) -Compared with smelling breast milk (bm) and amniotic fluid	N=27 in lavender inhalation group N=24 in breast milk group N=26 in amniotic fluid group N=25 in control group Newborns smeleed different odors only before, during, and after heel lance	NIPS, heart rate, O2 saturation measured -1 minute before, during, and one minute after.	Statistically significant reduction in pain for all three intervention groups vs. control. -NIPS score in lavender group was lower than the bm or amnio groups during lance, however the bm and amnio groups had lower NIPS than lavender after heel lance. -HR: lowest in BM group, then lavender, amnio, and control respectively	+ -Physical variables measurable -Large sample -Environmental control and consistency	− -No mention of limitations **MODERATE QUALITY**	Smell of lavender decreased pain during heel lance and minimized HR increases (same with BM)
Lillehei, As (2015). Effect of Inhaled Lavender and Sleep Hygiene on Self-Reported Sleep Issues: A Randomized Controlled	RCT Single blinded and steps taken to blind participants	N= 79 college students At patients normal sleep setting (University of Minnesota)	Sleep quantity (fitbit, sleep diary) and Sleep quality. Compared lavender and sleep hygeine to	N=39 used lavender patches plus sleep hygiene N=40 used sleep hygiene alone -Conducted over five consecutive	PSQI and NIH "PROMIS" sleep disturbance short form, Fitbit data, and Sleep Hygeinge Survey.	-No statistically significant differences in sleep quantity between groups (based on sleep diary). -Both groups feel asleep more easily and	+ -Screened roommates and included them when possible for a different wave to assist with blinding -specific sleep hygiene rules	- -No control group -Honor system that all sleep hygiene protocols were used -Wide variation in	Even though quality is very low, Lavender may be used as an aid to achieve more restful sleep and may have a longer-term

Trial			sleep hygiene alone	nights.	Data collected at baseline, during intervention, post-intervention, and 2-week f/u.	number of awakenings decreased. -PSQI scores significantly less for lavender group than SH group. Also less daytime fatigue, even at 2-weeks post intervention	- Methodological strength	what "keep up with school work" and "exercise regularly" means -Technical malfunction of fitbit trackers (only 14% data recoverable) **VERY LOW QUALITY**	effect on sleep quality.
Irmak, S. (2015). The Effect of Lavender Oil in Patients with Renal Colic: A Prospective Controlled Study Using Objective and Subjective Outcome Measurements	RCT (double blinded, placebo-controlled)	N=100 patients diagnosed with renal colic.	Pain due to renal colic (stones)	N=50 received standard care (IM diclofenac sodium) N=50 received standard care plus lavender aromatherapy.	-VAS -Mean arterial pressure (MAP) -Heartbeats per minute (BPM)	-No difference between MAP and BPMs -VAS not statistically significant before or during, however VAS score at 30 minutes was sig. lower in lavender group	+ Compared to physical factors (BPM, MAP)	- -VAS highly subjective -Standard diclofenac dose given (75mg) and patients may have different responses to diclofenac dose **LOW QUALITY**	-Results are unclear, however lavender may help decrease pain in some individuals, particularly women. -The typically smaller weight of women may be a confounding factor due to metabolism of diclofenac.
Hashemi, S. (2015). The Effect of Massage With Lavender Oil on Restless Leg Syndrome in Hemodialysis	RCT	N=70 hemodialysis patients with RLS Two hemodialysis centers in Iran	RLS in patients with chronic renal failure	N=29 received effleurage massage using lavender oil N=30 received routine care	RLS international questionnaire Given before study then one week after study end	-Mean RLS scores no different before study began. -Mean RLS score significantly decreased in the intervention	+ -Severity of RLS measured -Lavender only given certain shifts and never when control group was present	- -No placebo group -Possibility of confounding factor of massage -Longer f/u would be	Lavender massage may be helpful in alleviating RLS symptoms in hemodialysis patients. This may also be

Patients: A Randomized Controlled Trial				(3 week duration) (several dropped out in each group for various reasons)		group (unchanged in control group)		helpful **LOW QUALITY**	r/t anxiety, which was not measured in this study.
Ghods, A. (2015). The effect of topical application of lavender essential oil on the intensity of pain caused by the insertion of dialysis needles in hemodialysis patients: A randomized clinical trial.	Open crossover study	n=34 -Pts admitted to dialysis unit of one hospital. -n=17 placebo, n=17 intervention	Pain	N=Topical lavender application -Placebo state -Control state (no intervention)	Numerical rating score Pt. demographics -Pain intensity before insertion, after inserting venous needle, and after inserting arterial needle.	-Positive statistically significant effect of pain reduction with lavender EO application compared to placebo or control.	+ -All patients were tested in each state (lavender, placebo, and control)	- -Question whether 72h between different states is sufficient -Anxiety not assessed. **LOW QUALITY**	Lavender application may act as an mild-moderate analgesic, however this result may be in part due to fragrance, which also reduces anxiety.
Bikmoradi, A. (2014) Effect of inhalation aromatherapy with lavender essential oil on stress and vital signs in patients undergoing coronary artery bypass surgery: A single-blinded randomized clinical trial	RCT (single-blind)	N=60 patients post-CABG Hospital in Iran	Mental Stress (anxiety) Vital sign improvement	N=35 aromatherapy group N=35 control group Aromatherapy: inhaled lavender oil inside oxygen mask for 20 minutes on the 2nd and 3rd days after surgery (control inhaled 2 drops distilled water)	Vital signs, DASS-21 questionnaire measured before, and 5, 30, and 60 minutes after.	-No difference in vital signs before, during or after. No statistically significant difference in mental stress data before, during, or after. -Mental stress level dropped in both groups.	+ Placebo group present	- -No control group -Duration of treatment time was 20 minutes (would longer have been better?) **LOW QUALITY**	Lavender inhalation does not appear to have a significant effect on vital signs or mental stress levels in hospitalized post-CABG patients. -Intervention is still low-risk
Raisi, Z.	Experim	N=96	Primary	N=48 inhaled	Dysmenorrhea	Dysmenorrhea	+	-	Intereseting

(2014). Effect of lavender inhalation on the symptoms of primary dysmenorrhea and the amount of menstrual bleeding: A randomized clinical trial	ental clinical trial (randomized)	female students University in Iran	dysmenorrhea	lavender on their palms and inhale for 5 minutes 1 hr. after experiencing dysmenorrhea. N=48 inhaled sesame oil	intensity questionnaire (developed by the researcher based on other questionnaires), VAS, Amount of blood on pads and tampons (point system). Study over 4 menstrual cycles	symptoms: Lavender was highly effective in reducing sx score ($p<0.001$) Bleeding: no significant effect of lavender on menstrual bleeding.		-Blood amount difficult to assess accurately -Small sample size **LOW QUALITY**	effect particularly because greater menstrual flow is commonly associated with more pain, but flow was not changed.
Lytle, J. (2014) Effect of lavender aromatherapy on vital signs and perceived quality of sleep in the intermediate care unit: a pilot study	Randomized Controlled Pilot Study	N= 50 patients Teaching hospital	Perceived quality of sleep in a hospital unit	N=25 control (usual care) N=25 usual care plus jar of lavender EO by bedside from 10pm-6am -Done over five nights	Vital signs throughout intervention and sleep questionnaire at 6am (VAS that records ease of falling asleep, frequency of awakening, ease in return to sleep, and sleep quality.)	-No significant differences in VS -Mean sleep scores for depth of sleep, ease of falling asleep, ease in return to sleep, and quality of sleep were higher in intervention group but not significantly.	+ -Vital signs recorded (objective measure)	- -No verification of quality of lavender. - Subjective nature of sleep questionnaire -Multiple reasons for hospitalization -Small sample size (pilot study) **VERY LOW QUALITY**	Although no significant differences were found between these two groups, self-reported improvement in sleep quality may have clinical significance.
Lillehei, A. (2014). A Systematic Review of the Effect of Inhaled Essential Oils on Sleep	Systematic Review	10 studies which studied lavender	Sleep	10 studies	Multiple instruments related to sleep quality	Satistically significant results for improved sleep quality were reported for lavender oil	+ -Systematic review	- Meta-analysis not possible due to wide variety of study designs **VERY LOW QUALITY**	Authors suggest lavender may assist with sleep quality for some individuals. This is in congruence

									with previous studies
Kaviani (2014). The effect of lavender aromatherapy on pain perception and intrapartum outcome in primiparous women	Semi-experimental clinical trial	N=160 primiparous women in active labor at 3-4 cm dilation	Pain (labor)	N= 80 in lavender inhalation group (on pre-made tissues) N=80 in control group (inhaled distilled water on tissues)	-VAS - Pain before intervention, 30 minutes after, and 60 minutes after measured with VAS -Patient contentment -Apgar of baby	-Statisticallhy significant decrease in pain and increase in contentment observed in lavender group -No difference in baby apgar scores	+ -Some inclusion/ exclusion criteria -Relatively large sample size	- -Inability to blind -not tightly controlled -short-term study -No information about duration or frequency of inhalation (x1 time?) **VERY LOW QUALITY**	Use of lavender during labor may assist in decreased perception of pain and increased level of contentment (but does not necessarily have an effect on labor outcome)
Forrester (2014). Aromatherapy for dementia	Cochrane Review	N= 4 studies included with lavender only intervention (Fu, Lin, O'Connor, & Smallwood)	Dementia (primarily agitation)	Fu: RCT, inhalation vs. massage, n=67 Lin: RCT, inhalation at night. O'Connor: RCT crossover (1 week washout), n=66,lavender application to forearm Smallwood: RCT, 21 patients, video recorded for	Most use CMAI (Cohen Mansfield Agitation Inventory)	Fu: Unable to use agitation scores r/t data not reported separately for each group Lin: Unable to use r/t selective reporting O'Connor: unable to use r/t bias Smallwood: Significant interaction with time, but likely high risk for reporting bias	+ Cochrane Review	- lack of long-term follow-up or study, which is preferable with progressive disease, -difficult to compare results r/t wide variety of severity of dementia. **VERY LOW QUALITY**	"There is plenty of non-randomised evidence of both benefit and harm for aromatherapy for dementia. The seven randomised trials included in this review show equivocal evidence for the benefits of aromatherapy, and further evidence for its effectiveness is needed."
Seol, G. (2013)	RCT	N=34	Stress	N= 10 in	Stress scale (30	VS: clary group	+	-	-Aim: to

Randomized Controlled Trial for Salvia sclarea or Lavandula angustifolia: Differential Effects on Blood Pressure in Female Patients with Urinary Incontinence Undergoing Urodynamic Examination		female patients Korean hospital	during uncomfortable examination (acute nxiety)	control group N=12 in clary group N=12 in lavender group Participants breathed 2ml on aroma pads for 60 minutes during urodynamic exam	questions) VS: BP, P, & RR Salivary cortisol	had sig. decrease in systolic BP compared to lavender and control. Diastolic BP increased in the control and lavender groups. No stat sig change in pulse rate (though there were decreases with lav. & clary). Lavender produced stat. sig. reduction in RR compared to control. Cortisol: no stat. sig. difference	-Mass spectrometer used to verify components -Tight variable control	-Small study size -Several dropouts for unexplained reasons VERY LOW QUALITY	examine the effects of inhalation of clary or lavender on stress relief/relaxing blood vessels and therefore BP. -Writers suggest that lavender may have a diuretic effect and may have caused toe bladder to become more sensitive, thus acting as a stress source for these patients. -Lavender may not be the best choice for those undergoing this procedure.
Matsumoto, T. (2013) Does lavender aromatherapy alleviate premenstrual emotional symptoms?: A randomized	RCT (randomized crossover)	N=17 women "in their 20's" – Recruited via college campus advertisement (Japan) (all	Emotional symptoms r/t PMS: Tension-anxiety Depression-dejection, Anger-hostility,	N=17 for each intervention (over two cycles). Lavender or water was inhaled for 10 minutes via	ECG (5 min before ihalation, 5 after, 10 after, 20 after, and 30 after) -POMS done before and after	ECG: baseline and post-intervention HR did not sig differ between trials (both decreased) Mood: All PMS symptoms decreased in	+ -Environment highly controlled -Controlled for basal heart rate and autonomic nervous system variation	- -Very small sample size over only two cycles. -PMS sx highly variable & subjective - Very short-	-Controlled environment may not mimic "real life" mood states without negative stimuli. - Lavender

crossover trial		participants had mild-moderate. No severe PMS or PMDD)	Vigor, Fatigue, Confusion	diffuser in a controlled environment	intervention.	lavender group, however the only depression-dejection and confusion had sig.changes.	-All participants at same point in cycle.	term intervention -Women only had mild-mod PMS and not severe (sampling bias) **VERY LOW QUALITY**	may assist in improving short-term mood sx assoc. with PMS, however this study lacks suggestion for real-life application of these findings.
Sheikhan, F. (2012). Episiotomy pain relief: Use of Lavender oil essence in primiparous Iranian women...	RCT	N=60 primiparous women who underwent episiotomy Teaching hospital in Iran	Pain relief (episiotomy) Wound healing	N=30 control group (routine care, 30 min. warm sitz baths BID for 5d)	VAS, REEDA -Both assessed at 4h, 12h, and 5d post-episiotomy	Pain: 4h: sig. less pain in lavender group 12h: less pain in lavender group, but not sig. 5d: sig. less pain in lavender group and only 33.3% in this group had taken analgesics, whereas 70% in the control had taken analgesics. REEDA: Significantly lower scores in lavender oil group post-intervention	+ Specific inclusion/ exclusion criteria -Participants excluded if elevated analgesic consumption.	- -participants were permitted to take analgesics – data was recorded but not quantified in doses. No mention of what "elevated analgesic consumption" means. **LOW QUALITY**	Although there are some missing components all factors pointed toward lavender as effective pain relief and wound healing may suggest potential clinical significance for this therapy.

Liu, C (2012). The effect of lavender aromatherapy on autonomic nervous system in midlife women with insomnia	RCT (Prospective study)	N=67 female volunteeers from communities in Taipei connected to a healthcare program regarding sleep hygiene.	Insomnia	N=34 experimental group (lavender) N= 33 control group Aromatherapy administered in controlled room for 20 minutes twice a week for 12 weeks.	Chinese PSQI HRV (heart rate variability) analysis using electrodes. -Baseline, 4th week, and 12th week	HRV:Lavender group had significant increase in VLF in the 4th week compared to control (suggesting increase in parasympathetic activity). No other significant differences. PSQI: Stat. sig decrease in total PSQI score in lavender group from before to after as well as between lavender and control groups	+ -12-week duration to study both shor-term and long-term effects. -Sleep hygiene course given	- -Attrition rate: 7 total -No placebo group -polysomnography not used to verify sleep stages and length -Women were both pre and post-menopausal (likelihood for inconsistencies r/t hormonal action) **LOW QUALITY**	The authors suggest that lavender's anxiolytic effects might manifest as modulation of heart rate variability, according to a study by Bradley. -Lavender may help improve sleep quality in midlife women in the short-term, however long-term parasympathetic activity was not shown.
Kim, S., (2011). The Effect of Lavender Oil on Stress, Bispectral Index Values, and Needle Insertion Pain in Volunteers.	RCT	N=30 volunteers Participants blinded to study group, anesthesiologist assessing stress level also blinded.	Stress level, pain intensity of participants before and following needle insertion.	1. Stress level 2. Pt. VAS (Pt. pain level 0-10 on a visual analogue scale) 2. Bispectral index values (BIS) – measures LOC. Independent variables: 5 min. O2 with	Mean VAS, Stress level, and BIS scores before and after inhalation.	.-Lavender inhalation significantly reduced BIS and stress after treatment compared to placebo -Lavender reduced needle pain insertion compared to placebo	+ -Placebo-controlled -Inhalation-only data due to face mask aromatherapy inhalation	- Small study **LOW QUALITY** due to small sample size	Lavender inhalation may have an anxiolytic and analgesic effect for needle insertion pain, however it is unclear whether the pain reduction may also be related to the

				lavender-coated face mask (intervention) –or- 5 minutes O2 without lavender (placebo).					anxiolytic effect.
Woelk, H. (2010). A multi-center, double-blind, randomised study of the Lavender oil preparation Silexan in comparison to Lorazepam for generalized anxiety disorder	RCT (double blind)	N=78 patients Location: Multiple sites in Germany	Anxiety (GAD)	N= 40 to Silexan group N=37 to lorazepam group. Measured at weeks 1, 2, 4, 6, and at week 8 (2 weeks after completion)	HAM-A: Hamilton Anxiety Rating Scale CGI SAS PSWQ	HAM-A score reduced with both groups. Silexan had a 52.5% responder rate and lorazepam 40.5% responder rate (40% vs. 27% remission rate, respectively) Therapeutic efficacy of the study med was moderate or very good for 32 (80%) patients treated with silexan and 19 (51.3%) patients treated with lorazepam. Both also improved sleep duration and latency (ability to fall asleep)	+ -Tight control of silexan quality and purity. -1-week washout of other drugs and those with HAM-A scores that dropped >25% were excluded. -No serious adverse events occurred. -Silexan: 9/11 adverse effects were GI disturbance. -Lorazepam: 1 pt. had nausea and 6 from fatigue (a known SE)	- -No mention how often Silexan or lorazepam were taken by the participants. -Silexan is proprietary **LOW QUALITY** Due to variable stated above. Additionally, research bias may be present due to the fact that the auther has served as a consultant for the Silexan-sponsoring company	-Reduction in HAM-A score also extended to the last measurement (8 weeks – 2 weeks after completion) -Researchers concluded that Silexan 80mg is generally safe and is at least as effective and comparable to larazepam 0.5mg. -Safety was also assessed to be generally safe compared to total
Toda, M. (2011) Evaluation of Effects of	RCT	N=21 healthy female university	Stress markers (salivary cortisol),	N=7 lavender aroma N=7 peppermint	VAS r/t perceived level of stress immediately at	Peppermint: -Sig lower perception of stress in all	+ -Tight variable control of aroma	– -Small sample size for each group (n=7)	-Peppermint may be clinically useful for

Lavender and Peppermint Aromatherapy Using Sensitive Salivary Endocrinological Stress Markers (cross-referenced in peppermint table)		students (age 21-27)	subjective stress level	aroma N=7 control (odorless jojoba)	5 minutes, and 10 minutes after administration	three instances. -Stat. sig decrease in salivary cortisol immediately after inhalation. Lavender: -Stress decreased gradually over 10 minutes. No stat. sig. change in cortisol levels but there was a tendency toward an increase in cortisol after inhalation. -Control: No stat. sig. stress decrease -There were no stat. sig. differences in subjective stress among all three groups at any sampling point.	administration and salivary sampling	without crossover -All female **LOW QUALITY** due to single study small sample size	relieving mental stress -Regarding lavender, the researchers conjecture that the distress experienced with lavender may be due to increasing parasympathetic activity and its sleep-inducing effects (drowsiness) or may have been due to the sleep quality of the "poor sleepers" in the group, (the body resisting drowsiness)
Kazemzadeh, R. (2016). Effect of lavender aromatherapy on menopause hot flushing: A crossover randomized clinical trial	RCT (crossover)	N=100 Women between ages 45-55 who had hot flushing complaints Hospital in Iran	Menopause hot flushing	n=100 in lavender group n=100 in placebo group (diluted milk) Women were administered lavender or placebo aromatherapy inhalation	Self-report of # of times each woman had a hot flushing episode per week	Occurrence of hot flushing decreased sig. in the lavender group compared to placebo (avg 21x/week before intervention for lavender, avg 10x/week after lavender. - Control had avg. 20x/week before	+ -4-week washout period between groups - Specific parameters noted for what the women were to categorize as a "hot flush"	- -Possible variation in personal symptoms may have made hot flush definition more subjective than intended **MODERATE QUALITY**	The noticeable difference may likely be related to an alteration in stress levels, therefore effecting menopausal symptoms.

				2x/week for 12 weeks. (4-week washout period between crossover)		and 19x/week after).			

Citation	Design/ Method	Sample/ Setting	Uses Studied	Interventions	Instruments	Study Findings	Preliminary Quality of Evidence (High/Moderate/ Low/Very Low) & Rationale		Importance and/or Additional Considerations
Heshmati, A. (2017). The effect of peppermint (Mentha piperita) capsules on the severity of primary dysmenorrhea	RCT (double blind, placebo-controlled)	N= 102 female students ages 18-25 with moderate-severe dysmenorrhea. College dormitory in Iran	Dysmenorrhea	N=46 in Peppermint capsule group N=44 in placebo group (starch capsules) (attrition n=12 total r/t unwillingness to continue participation) Peppermint group received three 330mg peppermint capsules/day for first 3 days of menstrual cycle.	VAS scores during period -Cycle length -Painkillers taken -If painkillers are taken, they were to write down their pain level before taking the painkiller then record the type and amount of painkiller taken.	Peppermint group had a statistically significant lower mean pain scores in both the 1st and 2nd cycles compared to placebo. -No stat. sig. difference in pain duration.	+ Double-blinding -Tested two menstrual cycles -No stat. diff. in demographics -No reported side effects	− Patients were permitted to take painkillers (poss. confounding factor) -Painkillers were permitted, however there is no no specific information is given on limits. **LOW QUALITY**	Double-blinding is not usually possible with EO studies, so this study shows great promise for future investigation of internal peppermint for this specific pain relief (peppermint: antispasmotic activity on smooth muscles. Mentha component: effects kappa opiod receptors
Cash, B. (2016). A Novel Delivery System of Peppermint Oil Is an Effective Therapy for Irritable Bowel Syndrome Symptoms	RCT (double-blind, placebo-controlled)	N= 72 patients who fulfilled Rome III criteria for IBS-M (mixed) or IBS-D (diarrhea type) Carried out	IBS Symptoms	N= 35 in peppermint group N=35 in control group Each group took either 180mg peppermint oil or placebo capsules TID for 4 weeks.	Patients completed a daily diary of BMs and IBS symptoms 2 weeks before randomization as well as during tx. -TISS score at baseline, 24h, and 28d. (TISS = abd.	-24h: Patients in PO group experienced a stat sig reduction from baseline compared to placebo in 2 of the 8 IBS sx evaluated (abdominal pain/discomfort and mean	+ -3-week prohibited medication washout (prohibited medications listed and reasonable) -Weekly check-ins with HC provider to	− -75% participants in this study were female **MODERATE QUALITY**	- “Subjects receiving PO experienced a significant decrease in the number of severe and unbearable symptoms at 28 days compared to those receiving placebo (66.8 vs. 34.9 %, respectively, P =

		in "four geographically diverse study sites in the USA" – enrolled by healthcare practitioners		-Capsules designed to be released in small intenstine	Pain/discomfort, bloating, distension, pain at evacuation, BM urgency, constipation, diarrhea, passage of mucus or gas, sense of incomplete evacuation)	intensity of BM urgency) -28d: PO group experienced stat. sig reduction in mean sx scores for abd pain/discomfort, abd. Bloating/distension, and pain at evacuation.	assess safety and program adherence.		0.0282)." -Suggests possible clinical significance for those with IBS-M or D.
Sites, D.S. (2014) Controlled breathing with or without peppermint aromatherapy for postoperative nausea and/or vomiting symptom relief: a randomized controlled trial	RCT	N= 42 laporoscopic post-operative patients in a nonprofit magnet hospital in the southeastern U.S.	PONV	N= 16 receiving controlled breathing with sham vial without peppermint. N=26 received peppermint and controlled breathing	-DOS Score (descriptive ordinal scale) for nausea symptoms 0-10 . -Intervention efficiacy described as "no antiemetic required" -Score of 0 on PONV DOS at 10 minutes equals full effectiveness.	No stat sig difference between the placebo group and PO group, however, the total % of people with PONV after PO intervention was less compared to placebo. -Those who received PO asked to continue the therapy in the hospital and at home.	+ -All nurses trained in controlled breathing and the technique was standardized amongst them. -Sham vial without peppermint used for placebo	− -Large study attrition and time constraints (17 months), so the amount of patients was lower than desired (hoped for 130 to attain 0.8 power) -Lower control number than treatment **VERY LOW QUALITY**	-Many exclusions occurred in this study due to numerous factors including deviating from protocol, lack of CRNA availability, and nonexistence of PONV. -Controlled breathing is an appropriate first line intervention for PONV and peppermint holds promise – more studes should be done.
Mann, N.S. (2012). Peppermint Oil in Irritable Bowel Syndrome: Systematic Evaluation of 1634 Cases	Systematic Evaluation with Meta-Analysis	1634 Cases of IBS	IBS Abdominal pain - Abdominal distention -Bowel Frequency -Flatulence	N=1634 cases searched on PubMed. No search limitations.	Qualitative Meta-analysis (QMA)	Peppermint oil: 79% of cases showed abdominal pain relief. - 83% of cases showed abdominal distention relief.	+ Very large sample size	− -Some cases lack specifics on demographics -Lacks specifics on challenges with pooling	- This analysis shows evidence that PO does indeed help with these IBS symptoms. Even though dosage and frequency data were not

with Meta-Analysis						-73% of cases showed reduction in bowel frequency and flatulence -20% of cases showed adverse SE.		data **MODERATE QUALITY**	pooled, this qualitative evaluation may be valuable to support further research on PO's safety and -Most common SE reported: Heartburn, perianal burning, blurred vision, N/V, dizziness, and renal stones
Hines, S. (2012). Aromatherapy for treatment of postoperative nausea and vomiting	Cochrane Review	N= 2 RCTs that investigated PO for nausea (Anderson, 2004, and Tate, 1997)	PONV	Anderson: n=33. Compared isopropyl alcohol, peppermint oil, and saline inhalation Tate: n=18. Compared peppermint oil inhalation, peppermint essence inhalation, and placebo in a PACU	-VAS -Request for anti-emetics.	Anderson: Alcohol: 45% requested anti-emetics. PO: 60% requested anti-emetics Saline: 50% required anti-emetics Tate: unclear results	+	− The two studies could not be compared due to differing drug administration times and measurement units. **VERY LOW QUALITY**	-Since this review, more studies have been done on PO and n/v -Historically, The effect of PO may be due to analgesic, anti-emetic, and/or antispasmodic properties
Toda, M. (2011) Evaluation of Effects of Lavender and Peppermint Aromatherapy Using Sensitive Salivary	RCT	N=21 healthy female university students (age 21-27)	Stress markers (salivary cortisol), subjective stress level	N=7 lavender aroma N=7 peppermint aroma N=7 control (odorless jojoba)	VAS r/t perceived level of stress immediately at 5 minutes, and 10 minutes after administration	Peppermint: -Sig lower perception of stress in all three instances. -Stat. sig decrease in salivary cortisol immediately after inhalation.	+ -Tight variable control of aroma administration and salivary sampling	− -Small sample size for each group (n=7) without crossover -All female **LOW QUALITY**	-Peppermint may be clinically useful for relieving mental stress -Regarding lavender, the researchers conjecture that the distress

Endocrinological Stress Markers (cross-referenced in lavender table)						Lavender: -Stress decreased gradually over 10 minutes. No stat. sig. change in cortisol levels but there was a tendency toward an increase in cortisol after inhalation. -Control: No stat. sig. stress decrease -There were no stat. sig. differences in subjective stress among all three groups at any sampling point.		due to single study small sample size	experienced with lavender may be due to increasing parasympathetic activity and its sleep-inducing effects (drowsiness) or may have been due to the sleep quality of the "poor sleepers" in the group, (the body resisting drowsiness)
Ruepert, L. (2011) Bulking agents, antispasmodics and antidepressants for the treatment of irritable bowel syndrome	Cochrane Review and meta-analysis	N= 5 RCTs that studied peppermint and IBS Capanni, Czalbert, Cappello, Leck, Liu	IBS symptoms	N= 269 patients between Capanni, Cappello, & Czalbert studies N=225 between Cappani & Leck	IBS Symptom scores	-Statistically significant benefit present for peppermint oil in improvement of IBS symptom score. -Capanni & Lech found a statistically significant improvement in global assessment with peppermint	+ Large N for measures studied	− -Capanni: Dosage of peppermint not clear - Unclear heterogenicity for the five studies **MODERATE QUALITY**	-Peppermint oil was considered under the "antispasmodic" umbrella for this review due to its known effect on smooth muscles
Wu, J. (2010). Complementary and	Expert opinion	n/a Dr. Wu is a MD and	Peppermit likely acts as a smooth muscle relaxant. "The major advantage of peppermint oil is its safety profile. Common side effects include heartburn and a perianal burning sensation, though they are generally mild and readily avoidable if patients use						Expert summary on this topic. Very small

alternative medicine modalities for the treatment of irritable bowel syndrome: facts or myths?		Professor in the department of Medicine and Therapeutics and the Instutute of Digestive Diseases in Hong Kong	enteric-coated or pH-dependent capsules" – p. 707 -Peppermint may be more tolerable due to the absence of anticholinergic SE.						mention of PO.
Ford et al. (2008)	Systematic Review with Meta-Analysis	N=4 RCTs, 392 patients total Lech, Liu, Capanni & Cappello	IBS symptoms	PO compared to placebo	Multiple instruents used	"Fifty two of 197 (26%) patients randomised to peppermint oil had persistent symptoms compared with 127 of 195 (65%) receiving placebo (relative risk 0.43, 0.32 to 0.59)" -Test for overall effect: z=5.39, P< 0.001	+ Detailed meta-analysis with CI's, test for heterogenicity, relative risk, and test for overall effect.	- **MODERATE QUALITY**	These four studies were also reviewed in the review by Ruepert and both these reviews corroborate one another that PO is more effective than placebo for IBS sx.

EUCALYPTUS

Citation	Design/ Method	Sample/ Setting	Uses Studied	Interventions	Instruments	Study Findings	Preliminary Quality of Evidence (High/Moderate/ Low/Very Low) & Rationale		Importance and/or Additional Considerations
							+	−	
Kim et al. (2014). The effect of 1,8-cineole inhalation on preoperative anxiety: A randomized clinical trial	RCT	N=62 voluntary participants Setting: A Korean University Hospital	Anxiety (pre-operative)	N=15 in control (almond oil) N=15 in limonene N=16 in 1,8-cineole, N=16 in eucalputus Participants inhaled the substance for 5 minutes and underwent a nerve block for surgery 20 minutes later	Anxiety-VAS, STAI POMS (profile of mood states), BP, Pulse	-Eucalyptus, limonene, 1,8-cineole, and almond oil significantly decreased pre-op anxiety on all three scales. -A-VAS: 1,8-cineole had stat. sig. reduction in pain compared to control. -Eucualptus also showed stat. sig less anxiety compared to control ($p<0.001$) -No stat. sig difference between pain, BP, and pulse between groups	-All participants were not taking any antidepressants or anxiolytics -Three tests were used and compared	-No detailed description on randomization. -Small sample sizes when broken up into four groups. **LOW QUALITY** due to sample size and unclear randomization	-61% of Eucalyptus oil is comprised of 1,8-cineole and is the major active constituent. It is thought to inhibit the activity of acetyl-cholinesterase. - Eucalyptus inhalation may be useful to relieve pre-operative anxiety.

Jun et al. (2013). Effect of eucalyptus oil inhalation on pain and inflammatory responses after total knee replacement: A randomized clinical trial	RCT	N=52 patients diagnosed with osteoarthritis who undersent TKR. Korean Univeristy Hospital	Pain Inflammatory response (after total knee replacement - TKR)	N=25 in eucalyptus group N=27 in control group -Participants inhaled either eucalypus or almond oil on a gauze pad placed beneath the nose for 30 minutes per day on 3 consecutive days beginning the 3rd day after surgery.	P-VAS (pain) Bloos pressure Heart Rate C-reactive protein concentration White blood cell count	-Heart rate, CRP, and WBC count did not differ significantly between groups. -Pain and diastolic blood pressure had a stat. sig. decrease after inhalation for all three days for those in the eucalyptus group compared to control	+ Randomization explained. -All patients had surgery from the same physician. -Gas chrom. done to verify oil content.	− -All patients had oxycodone, fentanyl, NSAIDs, and antibiotics as well however the variation which they took these medications is not stated. -Did not explain how many in each group had a single or double knee replacement **VERY LOW QUALITY** due to lack of clarity on single/double knee and consideration of pharm. pain relief utilization	There is no direct evidence that eucalyptus oil affected inflammatory markers in these individuals, however it may be a useful nursing intervention for pain after a total knee replacement.
Warnke, P. (2006). Antibacterial essential oils in malodorous cancer patients: clinical observations	Case studies	Three main case studies presented, all of which had necrotic malodorous ulcers	Inflammation Would Healing Malodor	N/A	N/A	All three case studies showed photographic evidence that a eucalyptus oil application reduced inflammation, eliminated	+ Followed patients at least three weeks.	− Case studies **VERY LOW QUALITY**	-Re-epithelization also occurred but they are unable to account for this effect. They postulate it may be r/t

in 30 patients		related to cancer tumors. Photographs included. These three are a sampling from 30 patients who experienced similar results.				malodor, and decreased pain associated with the ulcers.			antibacterial qualities of eucalyptus. -Even though these are case studies, this may be a worthwhile treatment if other treatments are refused or non-feasible.
Sherry, E. (2004). Successful use of an inhalational phytochemical to treat pulmonary tuberculosis: A case report	Case study	1 28-yo Fijian woman	Tuberculosis	Clinical symptoms and microbiological TB markers	Pt. had been unwell for 12 months. Labs: Hgb 7.0, ESR 125. Sputum positive for mycobacterium tuberculosis and chest x-ray was consistent with this diagnosis. -Inhaled eucalyptus globulous oil 3x/day for cough while waiting to begin DOTS treatment. -10 days after beginning eucalyptus inhalation, she reported reduced malaise, improved appetite, and absent cough. No temps. ESR 110. Sputum cultures were negative however chest x-ray remained unchanged.		+	− -Case study -Possibility of unknown confounding factors **VERY LOW QUALITY** r/t case study status	This may be the first documented case of eucalyptus inhalation to treat pulmonary TB.
Sadlon (2010). Immune-modifying and antimicrobial effects of eucalyptus oil and simple inhalation devices	Review Summary	Asthma: 10 patients with bronchial ashma had a 23.7% increase in FEV1 and a 26.1% decrease in airway restriction after three days of cineole inhalation and continued four days after treatment. A 12-week trial by Juergens (n=32) found the patients were able to decrease their oral glucocorticoid dose and rescue inhaler use and maintained lung function capacity four times longer than those who did not inhale eucalyptus. Rhinosunusitis: One study (n=150) showed efficiacy of 200mg oral eucalyptus reducing headache, facial tenderness, malaise, coryza, and nasal secretions by over 80% after seven days. COPD: 200mg oral cineole was given to 242 COPD patients three times/day for six months. Exacerbations were significantly decreased in frequency compared to placebo (0.4 vs. 0.9) as well as severity and duration of exacerbations. Dyspnea scores improved, but not significantly more than placebo.							

Citation	Design/ Method	Sample/ Setting	Uses Studied	Interventions	Instruments	Study Findings	Preliminary Quality of Evidence (High/Moderate/ Low/Very Low) & Rationale		Importance and/or Additional Considerations
Cho, Ys (2017). Comparison of three cooling methods for burn patients: a randomized clinical trial	RCT (treating physician blinded)	N=96 burn patients in a Koren hospital (within 3h of accident and burn covering less than 5% of their body surface area)	Pain from burns Skin temperature	N= 30 Burnshield (TTO) dressing applied. N= 31 burn cool spray applied every 5 minutes. N= 33 (Tap water cooling was done for 20 minutes in shower)	P-VAS Skin temperature	-All three reduced VAS pain score after 20 minutes. -Tap water group showed sig higher VAS pain scores from the beginning than the other two groups -No sig. diff. in pain between use of burn cool spray and Burnshield. -Skin temp: Burnshield dressing application did not decrease skin temp as effectively as water or burn cool spray	+ -Patients randomized – Inclusion and exclusion criteria specific -Extensive statistical analysis	– -Three different application methods (dressing with TTO, running water, and spray) may confound results of TTO effect. -90% had superficial burns so it is difficult to determine the effect on more severe burns **LOW QUALITY**	-Included this due to the components of “Burnshield” as 96% water, tea tree oil, and emulsifiers, so comparable to using a TTO dilution -Aside: healing time with burnshield was 2d shorter than with other patients ($p < 0.101$ so not stat. sig. but of interest) -
Santamaria (2014). Antimicrobial effect of Melaleuca alternifolia dental gel in	RCT with crossover	N=34 volunteers with fixed orthodontic appliances (no caries, periodontal disease, or	Dental biofilm (plaque) and oral bacteria.	N=17 using melaleuca gel N=17 using Colgate total -Each group used either melaleuca or colgate for 7	-Plaque index (clinical biofilm) -Bacteria count (saliva samples) -measured before	-Melaleuca gel was more effective in decreasing dental biofilm and bacteria colonies (stat. sig achieved)	+ Crossover design - Composition of melaleuca gel listed	– -Relatively small sample size -poss. of confounding factor present to make the	-Biofilm alteration is a concern in orthodontics and melaleuca gel may decrease the likelihood of increased bacteria and predisposition

orthodontic patients		infiltrated restorations)		days, then had a 15-day rest wher the returned to their "normal" brushing, then they repeated the intervention with switched groups.	intervention, after day 7, then before and after the 2nd rouch (crossover)	compared to commercial brand Colgate toothpaste.	(5% melaleuca)	TTO into a tooth gel. LOW QUALITY r/t sample size	to periodontal disease. -People did not like the taste and first sensation of the melaleuca gel
Lee et al. (2014). A randomized controlled trial of topical tea tree preparation for MRSA colonized wounds	RCT (single-blind)	N= 32 patients in non-government nursing homes with stage II or above MRSE-colonized wounds. Hong Kong	MRSA colonization and wound healing	N=16 who received 10% topical TTO preparation N=16 in control group who received routine saline guaze dressing. -4-weeks of treatment	MRSA bacterial count Wound healing condition at weekly intervals	-TTO group: MRSA completely eradicated in 14 (87.5%) of the 16 patients. -TTO group: all wounds with previous delayed healing (>6 weeks) were healed within 28 days w/o adverse reaction -Stat. sig. less MRSA colonization in TTO group for each week (1-4)	+ Effect size from previous pilot study had been determine d at 0.46 -TTO compositi on displayed -Inclusion/ exclusion criteria listed.	– -No more than 105 MRSA bacteria per gm of wound tissue was an exclusion criteria. (unknown effect on severe MRSA infections) -no notable limitations, though this study should be repeated. – MODERATE QUALITY	-Tea Tree oil shows great promise as a treatment for MRSA-colonized wounds
Kwon et al. (2014). Comparison of clinical and histological effects between lactobacillus-fermented Chamaecyparis obtusa and tea tree	RCT Double-blind Split-face	N=34 patients with mild-moderate acne South Korea.	Acne	Each patient (n=34) had each side of their face randomly assigned the LFCO or TTO preparations and were instructed to apply them twice per day for 8 weeks	-LEEDS revised grading scale (for acne) -Count of inflammatory and non-inflammatory lesions. -Sebum levels -Measured pre-intervention,	-Lesions reduced in both groups -LFCO had a 65.3% decrease in lesions -TTO had a 38.2% decrease in lesions -LFCO had a decrease in sebum prodution	+ -8-week duration -Double-blinding explained (identical color and odor to cream)	– -No control group present, so "vehicle effect" cannot be excluded. **LOW QUALITY** r/t lack of control	-A few patients experienced erythema on TTO side, but this was not stat. sig -TTO does not seem to work as well as LFCO, however this study does not show if it may have had an impact r/t a control group, such as

oil for the treatment of acne: an eight-week double-blind randomized controlled split-face study					and at weeks 1, 2, 4, and 8.				soap and water.
Gnatta et al. (2013). Comparison of hand hygiene antimicrobial efficacy: Melaleuca alternifolia essential oil versus triclosan	Double-blind Crossover	N=15 volunteers	Antimicrobial effect Hand hygiene	Soap with 0.3% TTO Soap with 0.5% triclosan Each group washed hands, artificially contaminated hands, then washed with their assigned intervention.	-E-coli contamination	-Soft Soap plus 0.3% TTO had no stat. sig. advantage over regular soap or soap with triclosan.	+ -Limited to 18-55 yo (skin microbiota changes after age 60) -Extensive analysis of soap components -Extensive data analysis	− **LOW QUALITY** due to small sample size	The authors discussed that there is no agreed upon concentration of TTO to achieve antimicrobial efficacy
Chin et al. (2013). The Effect of Tea Tree Oil (Melaleuca alternifolia) on Wound Healing Using a Dressing Model	Quasi-experimental study	N= 10 participants diagnosed with abscessed wounds containing staph aureus.	Wound healing	N=4 Used "matched participants," the preferred method with this small of a sample. (one experimental and one "control" participant for each pair) N=6 additional participants who received TTO	Wound size Erythema Induration	-1st matched pair: TTO participant had "no sign of abscess" after 24h compared to 15 days of the matched participant, -2nd matched pair: TTO participant received no abx and was healing well after 3	+ -3-month time frame -Oil was analyzed -Patch testing done to r/o reactions	− -Very small sample size -Wounds assessed by different nurses (though the researcher worked closely with the clinic nursing staff) **VERY LOW QUALITY**	This study replicates in humans an in vitro study conducted by Edwards-Jones on a dressing model over petri dishes in 2004. -Although this is quasi-experimental and very low quality due to the design, the empirical results are promising for

				treatment (fumes)		days. Decrease in 1 cm size after 6 days compared to 19 days of the control participant having little improvement. -6 additional patients received treatment and 5/6 showed an average healing time of 4.4 days.			future research on humans and the results correlate with previous in vitro studies.
Blackwood et al. (2013). Tea tree oil (5%) body wash versus standard care (Johnson's Baby Softwash) to prevent colonization with methicillin-resistant Staphylococcus aureus in critically ill adults: a randomized controlled trial	RCT	N= 391 ICU patients in two ICUs in Northern Ireland	MRSA prevention in critical care patients (primary outcome was new MRSA colonization during ICU stay)	N= 5% TTO-enriched body wash group N= standard body wash preparation (JBS) Patients given at least one bed bath/day Intervention termination criteria: adverse effect, discharge from the ICU, death, or MRSA colonization.	Sequentail Organ Failure Assessment score (SOFA), Therapeutic intervention scoring system (TISS), ICU LOS, ICU mortality	-10% developed new MRSA colonization (39 patients) -No patients developed MRSA bacteremia -3 significant prognostic factors for MRSA colonization: SOFA score at baseline, ICU days, and # of device changes (but not which body wash they used) -TTO group had sig. longer length of stay, # of devices in situ, and longer duration of	+ -Wide variety of instruments and statistics	− -Planned sample size was 1,080 patients, then it was found they would need 2024 patients to detect a 40% reduction in MRSA colonization (this was not feasible and the sample size reduced) -Sig greater amount of men in the JBS group. **LOW QUALITY**	-The study suggested future studies consider using TTO nasal cream as well, since this was the primary infection site. They also recommended possibly leaving the TTO on the skin as an alternative to using it and washing it off. -Unable to recommend TTO body wash for MRSA prevention, however no adverse effects were found.

						ventilation. -TTO group had sig. higher percentage of patients nursed adjacent to another patient with MRSA and used a larger amount of body wash			
Wound Healing and Management Node Group (2013). Evidence summary: Wound management: tea tree oil	Evidence Summary (Joanna Brigg's EBP Institute)	<u>Healing promotion</u>: -Small RCT (n=10) found TTO was more effecting at promotion of healing than a saline dressing. -One uncontrolled trial (n=12) found TTO was used as a wound cleansing solution and 8 participants had wound size reduction. -15 case studies showed similar results of TTO helping heal diabetic, post-amputation, non-healing, or pressure ulcer wounds. <u>Wound infection management</u>: -Small RCT (n=10) found TTO dressing did not have a significant effect on MRSA bacteria count compared to saline dressing (undefined wound types). -An uncontrolled trial (n=12) found that a wound cleansing solution did not eradicate MRSA infection in 12 mixed-etiology wounds. -In vitro: TTO may have effects on other bacteria (staph aureus, E. coli, Candida albicans…) <u>Irritation and allergic response:</u> -Two studies (n=528) showed patch testing showing a non-to-mild irritation of TTO preparations (from 10%-100% concentration) - Lit review of 10 RCTs showed mild skin irritation when applied to wounds, but only significantly in one trial. Most case studies did not show any adverse effects. <u>BEST PRACTICE RECOMMENDATIONS</u> • "There is some evidence that TTO could be used to promote wound healing. (Grade B) • There is some evidence that TTO could be used effectively as a topical antibacterial in wound management. (Grade B)"							"There is some evidence that TTO could be used to promote wound healing. (Grade B) • There is some evidence that TTO could be used effectively as a topical antibacterial in wound management. (Grade B)"
Koo et al. (2012). Ocular surface discomfort and Demodex: effect of tea tree oil	Prospective randomized study	N= 335 patients with ocular surface discomfort (Dryness, pruritis, ocular pain, or visual	Ocular discomfort	N= 54 demodex free patients (no treatment) N= 141 demodex pts with TTO eyelid scrub N=140 demodex pts with eyelid	-OSDI: Ocular Surface Disease Index (self-report of ocular discomfort on a scale of 0-100)	-TTO group: average number of Demodex and the OSDI scores were significantly decreased (overall as well as in the	+ -Large sample size -over the course of 27 months - Examiner blinded -demodex-	− Compliance was an issue. -Would have been useful to see how the 54 patients without	"Some studies indicate that Demodex is a nonpathogenic parasite. However, other reports that Demodex is an etiologic factor in chronic blepharitis,

eyelid scrub in Demodex blepharitis		disturbance) Department of Opthamology of a hospital in Korea		scrub without TTO Pts instructed to scrub eyelid twice daily with scrub for 3-5 minutes with cotton tip and solution. (TTO: 10% solution in carrier oil)	-Demodex count	moderate and good compliance groups). 23.6% of TTO pts eradicated demodex. -Control group: Demodex decreased slightly but not stat. sig. Only 7% of patients were demodex free. -Both OSDI score and Demodex counts were stat. sig. reduced in the TTO group compared to control.	free patients excluded -patients with demodex included and randomized -Measured patient compliance	demodex infection would have responded to the treatment **MODERATE QUALITY**	con- junctival inflammation, and meibomian gland dysfunction." TTO may be a good treatment for ocular symptoms r/t demodex parasite
Edmondson et al (2011). Uncontrolled, open-label, pilot study of tea tree (Melaleuca alternifolia) oil solution in the decolonisation of methicillin-resistant Staphylococcus aureus positive	Uncontrolled case series (pilot study)	N=11 participants	MRSA (can TTO decolonize MRSA from acute and chronic wounds?) Wound Healing	3.3% TTO solution wash applied to wounds – residual allowed to stay on wounds before dressing. Assessed before intervention, then every two weeks. Wound swabs taken before intervention, at 4 weeks, and 12 weeks.	-MRSA swab and microscopy -General assessment of wound size and state	-All patients were still positive for MRSA post-study -8/12 had smaller wounds before they finished/withdrew from the study than when the study began.	+ 12 week enrollment/follow-up -specific inclusion/exclusion crieteria -Pts. Not on antibiotic treatment	− Uncontrolled case study -No mention how often wounds were washed with TTO. -No mention what assessments entailed -Only 2 patients completed 12 weeks of the study (very high	-Data was still collected for those who withdrew from the study early r/t antibiotic commencement or other means. -The authors conjecture the possibility of higher concentrations of TTO left on the wound for longer periods of time to possibly yield a different effect.

wounds and its influence on wound healing								attrition) **VERY LOW QUALITY**	
Flaxman, D (2005). Is tea tree oil effective at eradicating MRSA colonization: a review (Structured abstract)	Mini-Review	2 studies reviewed (Caelli et al, 2000; Dryden et al, 2004)	MRSA	Caelli: N=30 patients with MRSA colonization (treatment and control group). TTO ointment to nares and TTO body wash for minimum of 3 days but a range of 1-34d. Outcome: did not eradicate after 2 and 4d post-treatment at MRSA positive sites Dryden: N=236 patients RCT. 10% TTO to nares and lesions. 5% TTO body wash. 110 in treatment group and 114 in control group. Swabbed again at 2 and 14 days post-treatment and MRSA was eradicated in nares ($p<0.001$). Overall clearance was only significantly better compared to control for nasal MRSA and not overall MRSA colonization in other sites.			+ -More studies found but were excluded for various reasons such as in vitro status. -Listed reasons for inclusion/exclusion	− -Many studies excluded, one study very small, so not a large "review." -Both studies assessed multiple types of wounds (this may be a positive) **LOW QUALITY**	"Neither study demonstrated overall statistically significant benefits for the use of tea tree preparations to eradicate MRSA colonization compared to usual treatments" – p. 126

ROSEMARY

Citation	Design/ Method	Sample/ Setting	Uses Studied	Interventions	Instruments	Study Findings	Preliminary Quality of Evidence (High/Moderate/ Low/Very Low) & Rationale		Importance and/or Additional Considerations
Laccourreye, O. (2017). Benefits, pitfalls and risks of phytotherapy in clinical practice in otorhinolaryngology	Review (of plant derivatives for ENT purposes)	N/A	Rhinosinusitis	N/A	N/A	Rosemary has been used to treat rhinosinusitis (r/t anti-inflammatory action) - "Finally, gingivitis and dental plaque reacted comparably to mouth-wash based on chlorhexidine or an association of ginger, rosemary and calendula" – p. 97	+	− Very general description of many plant derivatives for multiple ENT problems **VERY LOW QUALITY**	-Cited articles containing rosemary were similar general reviews -"Extracts of various herbs, notably echinacea, eucalyptus, petasites hybridus, pelargonium sidoides, rosemary, spirulina and thyme, show superiority over placebo for rhinosinusitis and allergic rhinitis, as does gingko biloba for selected vertigo" – p. 95
Panahi, Y (2015). Rosemary oil vs minoxidil 2% for the treatment of androgenetic alopecia: a randomized	RCT	N=100 patients with androgenetic alopecia (AGA)	Alopecia	N=50 rosemary oil N=50 minoxidil -Methods unknown	"Standardized professional microphotographic assessment" taken initially then at 3 and 6 months -Assessed itching, greasiness,	-No sig. change at 3 months in either group. -Both groups had an increase in hair count at 6-months however the difference was not stat. sig. between the two	+ -6 months of treatment -large sample size	− [ABSTRACT ONLY]	Unable to assess quality due to iinability to locate article

comparative trial					and dandruff	groups. -Rosemary group had sig. less scalp itching.			
Koteles, F. (2014). Role of expectations and pleasantness of essential oils in their acute effects	Randomized experimental study (double blind, crossover)	N=33 volunteers attending a summer camp for people interested in CAM.	Pleasantness of EO Expectancies of EO (Placebo Effect)	Each participant experienced Rosemary, eucalyptus, and lavender. - Inhaled each oil for three minutes then vital signs were taken 1-minute after the three-minute inhalation. 5 minutes rest time was given between oils.	Subjective: Alertness (7-point likert scale), perception of odor, Heart rate, Blood pressure Objective: HR, BP	-Lavender: significant decrease in Systolic BP. -Eucalyptus: significant increase in alertness was found. It also had a sig. higher stimulating effect than rosemary or lavender. -Perceived pleasantness and expectations had no impact on physical variables. -Expectancy of rosemary oil was a significant predictor for an increase in alertness. The same is true for a decrease with lavender.	+ Exclusion criteria included those with anosmia, resp. disease, or medications that can affect alertness.	− -Small study Short-term, low dosage effects are the only things measured. -Unable to exclude possible crossover effect. **LOW QUALITY**	Hypothesis was "expectations have a greater impact on the assessed cognitive and physiological variables than pleasantness of EOs" – p. 331 Eucalyptus oil was the only oil to produce significant change in alertness independent of expectation.
Fernandez, L.F. (2014). Effectiveness of Rosmarinus officinalis essential oil	RCT: Prospective study	N=32 patients diagnosed with hypotension	Blood Pressure Internal use	N=32 for 3 phases: 1. 12 week pre-treatment where patients received placebo (olive oil)	Blood pressure (carried out at the same pharmacy by the pharmacist	-Increase in SBP and DBP during intervention phase ($p < 0.0001$). There was a rapid increase during	+ -Rosemary oil components analyzed. -Monitored patients	− Convenience sample **LOW QUALITY** More studies	Exploration of a pharmaceutical use for rosemary oil. Rosemary may be a safe and effective method of

as antihypotensive agent in primary hypotensive patients and its influence on health-related quality of life		Spain		2: 44 weeks of 1mL q8h dropped on a sugar lump (for flavor) 3: 12 weeks post-treatment with placebo	for all participants)	the first week then a plateau for the remainder of the intervention followed by a rapid decrease in phase 3 (post-treatment) back to baseline -Max increase 21.76% to 3.7% on low end -Corr. data to improved quality of life during intervention.	regularly -The same routine was followed for BP procedure for all pts. -Extensive statistical methodology described and shown in article	should be done to confirm this effect.	increasing systolic & diastolic BP and health-related quality of life. Strong results to study this further.
Mirsadraei, M. (2013). Effects of rosemary and platanus extracts on asthmatic subjects resistant to traditional treatments	Active comparator study	N=40 asthmatic patients on at least 4 asthma drugs and still had uncontrolled asthma.	Asthma symptoms	N=10 in rosemary group N= 10 in Platanus group N=10 in placebo 1 N=10 in placebo 2	Clinical findings, Spirometry, Exhaled nitric oxide, asthma control test (ACT). Measured before treatment and after (1 month)	-6 subjects had SE (2 rosemary, 4 platanus). -Significant improvement in pt. satisfaction with Rosemary compared to Platanus. -Sig improvement in cough, sputum production, chest pain, and wheezing in rosemary group. -Significant improvement in FEV1 in Platanus group but not in rosemary.	+ N/A (not enough information)	− [ABSTRACT] -small sample size	Unable to grade quality due to abstract status. “Conclusion: Rosemary and Platanus extract showed promising result in resistant asthma. Further studies about most effective gradient of these herbal medicines are recommended.”
Pengelly,	RCT	N=28 older	Cognitition	4 separate doses	Cognitive	Dose-specific	+	−	-Measured acute

A. (2012). Short-term study on the effects of rosemary on cognitive function in an elderly population	(placebo-controlled, double-blinded, crossover)	adults (mean age 78)	in elderly Internal use Medicinal food	of rosemary: 750mg, 1,500 mg, 3,000 mg, and 6,000 mg - Powdered rosemary added to tomato juice. (placebo=no rosemary, just juice) -7-day washout between doses	Drug Research computerized assessment (CDR); Mood (VAS) & alertness.	results: -750 mg: significant improvement in memory speed, but quality of working memory was sig. impaired. Sig. increase in alertness. -1,500 mg: continuity of attention sig. impaired compared to placebo. -6,000 mg: significant impairment in memory speed from baseline (non-sig from 750mg dose, however). Sig. decrease in alertness.	-Rosemary components evaluated -Extra steps taken to blind all parties (placebo pill was given with all juices) -7-day washout period between	8 men, 20 women (sex-specific results?) -Short-term study -Methods not completely explained. -May have other confounders from patients, including fluid intake status (this was not recorded, but was mentioned as a limitation). LOW QUALITY	effects -Would be interesting to repeat on younger patients. Lower-dosage rosemary may benefit from further testing and appears to be safe for internal short-term use.
McCaffrey, R., (2009). The effects of lavender and rosemary essential oils on test-taking anxiety among graduate nursing students.	Quasi-experimental design	N=40 nursing students Repeated measures (same group, three separate tests on three different instances)	Anxiety (test-taking)	Independent variables: Rosemary EO, Lavender EO.	TAS (test anxiety score – 10 item self-report of perceived stress) score of students, BP, pulse Each variable was taken before and after testing 1. TAS Score 2. Blood	-Control: no change in any of the three variables. -Lavender: Significant differences in pre and post TAS scores and pulses. Showed anxiety reduction post-test compared to	+ General consensus among participants regarding effect of lavender vs. rosemary (internal reliability).	- -Isolated sample -Actual tests the students were taking may have elicited different stress levels r/t exam content/time in semester/per	The researcher surveyed the participants and found that the lavender was almost “too” relaxing and they had to “fight” to be alert, whereas the rosemary had an effect of increased clarity.

					Pressure 3. Pulse	the control. (p=0.003 and .000). -Rosemary test: Significant differences in pre and post TAS scores and pulses. Both scores showed an anxiety reduction post-test compared to the control (P=.01 and .033)		formance on previous exams. **VERY LOW QUALITY** Due to possibility of multiple confounding factors	
Hongratanaworakit, T. (2009). Simultaneous aromatherapy massage with rosemary oil on humans	RCT	N=35 volunteers	Autonomic Stimulation	N=20 in control group and N=15 in rosemary group Each group self-massaged 1 mL of rosemary or placebo (sweet almond oil) into their abdomen for 5 minutes.	Blood pressre (SBP and DBP), Pulse, Respiratory Rate (RR), Skin temperature, "mental and emotional condition" via VAS scales of relaxation, vigor, calmness, attentiveness, mood, and alertness. -2 trials done of the same treatment to the same group	-RR decreased in control group and sig. increased in rosemary group ($p<0.05$) -Both groups had an increase in DBP but the rosemary group had a sig. larger increase compared to control. -Rosemary group felt more attentive at the end of the 2nd trial compared to control (control was less attentive) (sig. $p< 0.05$)	+ -Breathing masks given to participants to assist in blinding to aroma -Abdomen covered with plastic wrap to minimize evaporation. -controlled experimental environment	− -Did not report all specific data and p-values (only relevant ones) -No mention of "washout" time between two trials. -No mention of oil purity confirmation **LOW QUALITY**	"Since blood pressure is determined by the activity of the sympathetic branch of the ANS, an increase of blood pressure shows an increase of sympathetic tone, i.e., an increase of autonomic arousal" – p. 378
Burnett,	RCT	N=73	Anxiety	N=25 in control	Heart rate,	-HR decreased	+	−	-Researchers

Km (2004). Scent and mood state following an anxiety-provoking task		undergraduate students		group N= 25 in rosemary group, N=23 in lavender group. Each group received three drops of their oil or water (for control group). Participants received the drops on their left wrist then asked to complete a difficult crossword puzzle in 10 minutes	Bloood pressure, termperature (fingertip) POMS for mood state	in all three groups with the largest drop in the lavender group. -Temperature increased for all three groups (lavender had the largest increase) -Rosemary was assoc. with higher tension-anxiety scores on POMS. -Lavender group assoc. with higher vigor-activity scores than rosemary (this is contrary to hypothesis) -Range of scent pleasantness scores for both rosemary and lavender	-Physical metrics observed. -moderate-large study -Controlled environment -Measured "pleasantness" of each aroma in an attempt to analyze emotional response as a covariate.	No mention of oil testing for purity or components **VERY LOW QUALITY** due to possibility of accommodation to stress before measuring stress markers (or activity was not stressful enough)	conjectured that it is possible the crossword puzzle was not stressful enough or 10 minutes was long enough for the participants to acclimate to the stressor since all groups had decreased heat rate and increased temperature. -Researchers conjecture Rosemary has the risk of over-stimulation.
Moss et al. (2003). Aromas of rosemary and lavender essential oils differentially affect cognition and mood in healthy	RCT – single blinding	N=145 volunteers	Cognition	N=48 in rosemary group N=48 in lavender group N=48 in control group Four drops of oil were placed on a diffuser pad and put below testing cubicles for 5 minutes	CDR computerized assessment system for cognitive performance. -Bond-Lader VAS for mood measurement	-<u>Memory speed</u>: control had sig. quicker responses than both oils -<u>Working memory:</u> rosemary and control sig. greater than lavender. - <u>Attention speed</u>: Control	+ Measured many cognitive factors and cross-referenced these measures.	– -No independent oil component verification **MODERATE QUALITY**	Despite subjective alertness in rosemary group, actual performance did not improve (however working memore did improve). May be related to increased arousal used for memory recall. Mood states and

adults				before testing.		sig. quicker than lavender Attention accuracy: no sig. diff. Alertness: Rosemary had sig. increase in alertness compared to lav. & control. Contentedness: Rosemary had sig. increased contentedness compared to control. Lav. Produced sig. decrease in contentedness compared to control (however still had higher degree of contentedness than control) Calmness: no sig diffs.			actual performance do not necessarily correlate (hedonic effect?)

PATCHOULI

Citation	Design/ Method	Sample/ Setting	Uses Studied	Interventions	Instruments	Study Findings	Preliminary Quality of Evidence (High/Moderate/ Low/Very Low) & Rationale		Importance and/or Additional Considerations
							+	−	
Trongtokit, Y. (2005). Comparative repellency of 38 essential oils against mosquito bites	Controlled Clinical Trial	N=3 volunteers (38 essential oils were tested in this study)	Insect repellency (against Ae. aegypti mosquitoes)	Each volunteer had 1 mL of essential oil placed on a specified location on the arm (undiluted, 10% concentration, and 50% concentration.)	Time to first mosquito bite measured. Repellency "failure" defined as two bites or more.	Patchouli was among four oils that provided 2 hours of repellency at the highest concentrations. -Patchouli had 60 minutes of repellency at 50% concentration and 0 minutes at 10% concentration.	-Tight control of conditions (in lab) -US EPA recommended this mosquito species as one that can most likely give general information about all mosquitoes. -Mosquitoes behaved similarly and predictively on all three humans.	-Small study -Study states there is not necessarily historical use of this as a mosquito repellent. **LOW QUALITY** due to small sample size, but promising for future research.	-Repellency generally increased with increased concentration. -Patchouli performed equally well to citronella oil, a known mosquito repellent.

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Matthews et al. (2015). Interventions for nausea and vomiting in early pregnancy	Cochrane Review	N= 2 studies containing single therapy lemon oil Yavari Kia, Safajou, Shahnazi, and Nazemiyeh (2014) Keating and Chez (2002)	Nausea/vomiting during early pregnancy	Keating (2002): Double-blind placebo-controlled RCT. N=26 (14 in lemon group, 12 in placebo). Lemon oil mixed with honey was placebo compared to the intervention of ginger syrup. Ginger syrup group had an improvement on the nausea scale and less vomiting. Yavari (2004): RCT, n=100 (50/50 placebo and lemon). Instructed to place 2 drops lemon oil on cotton and take 3 slow breaths, repeating in 5 minutes if necessary. Placebo non-scented oil. PUQE scores for lemon group were reduced compared to placebo.			Keating: **LOW QUALITY** Yavari: **LOW QUALITY**		
Johnson, C. (2014). Effect of Aromatherapy on Cognitive Test Anxiety Among Nursing Students	Quantitative study with randomization and pre-test and post-test design	N=39 undergraduate nursing students at a private nursing school.	Anxiety	N=18 in control group, N=21 in lemon oil group	CTAS – Cognitive Test Anxiety Survey	-Students in the lemon oil group had significantly lower CTAS scores post-intervention compared to pre-intervention. -There was no stat. sig. difference between the CTAS scores between groups pre- and post-intervetion.	+ **VERY LOW QUALITY**	− -35 female, 4 male – the author mentions this did not have an effect on the outcome but does not describe the method to arrive at this conclusion. -CTAS given 24 hours after the exam (this may have been too long to aaccurately	There are several essential oils that are said to reduce anxiety, but lemon is a low-cost option.

								assess anxiety)	
Goepfert, M. (2017). Aroma oil therapy in palliative care: a pilot study with physiological parameters in conscious as well as unconscious patients	RCT (ABSTRACT ONLY)	N=30 conscious and unconscious patients	Physiological parameters of EO exposure	N=10 in control, n=15 conscious palliative patients, N=5 unconscious patients	HR, Oxygen Saturation, Blood pressure, Respiratory rate,	Healthy persons: Significant increase in RR, HR, and diastolic blood pressure for lemon. Sig. decrease in RR in lavender group. -"Conscious and unconscious patients reacted with a significant increase in all measured parameters to lemon oil and with a significant decrease in all parameters except for oxygen saturation to lavender oil"	+ Comparing non-emotional physical parameters with essentially blinding to subject in unconscious group.	− (ABSTRACT) Unable to assess quality	-This study is interesting due to the fact that the unconscious person is essentially blinded to the emotional response. -All physical reactions were very short-lived (only during intervention) -"Significant physiological reactions were measured after simulation with aroma oils in all three groups in this study. Healthy probands showed different reactions than palliative patients irrespective to their conscious state."
Sun (2007). D-limonene: safety and clinical applications	Evidence Review	Gallstone Dissolution: n=200+ "In patients with gallstone surgery, infusion of 20 mL d-limonene every other day dissolved gallstones overlooked during surgery." Complete or partial dissolution of gallstones occurred in 141/200 patients (48% had complete dissolution) GERD: n=32 in two studies. Oral use of d-limonene has been effective at relieving heartburn and GERD (up to 89% achieving complete relief by day 14 of treatment). Anticancer: n=4 case studies "Evidence from a phase I clinical trial shows a partial response in a patient with breast cancer and stable disease for more than six months in three patients with colorectal cancer."							

Citation	Design/ Method	Sample/ Setting	Uses Studied	Interventions	Instruments	Study Findings	Preliminary Quality of Evidence (High/Moderate/ Low/Very Low) & Rationale		Importance and/or Additional Considerations
Shirazi (2017). The Effect of Topical Rosa damascena (Rose) Oil on Pregnancy-Related Low Back Pain	RCT (placebo and non-treatment control controlled)	N=120 women with pregnancy-related low back pain. Iranian healthcare facility	Pregnancy-related low back pain.	N=40 in rose oil group, N=40 in placebo group (almond oil), N=40 in control group (no intervention) -Women in the oil groups were to apply 7 drops of oil for 100 cm^2 to painful part of skin without massage twice daily for 4 weeks.	Pain-VAS Roland-Morris Disability Questionnaire	-Rose oil had a significant VAS reduction compared to both control and placebo. -Significant pain decreases in the rose oil and carrier oil groups -Control group had a significant increase in Pain-VAS. -Placebo and Rose oil groups had a significantly lower RMDQ score than control.	+ - Oils applied without massage. -Description of rose oil preparation and analysis -No adverse effects occurred	− -Short duration (4 weeks) -Long-term effects of the oil not evaluated **MODERATE QUALITY**	Lifestyle modification and "topical herbal oils" including Rose oil is a traditional Persian medicine recommendation for pain and fatigue in pregnancy
Uysal (2016). Investigating the effect of rose essential oil in patients with primary dysmenorrhea	RCT	N=100 patients with primary dysmenorrhea Hospital emergency room.	Dysmenorrhea	N=50 in control group (75 mg. diclofenac and saline diffuser) N= 50 in rose oil group (75 mg. diclofenac and rose oil diffisuion). -Patients were either given 75 mg diclofenac or	VAS, RR, BP, MAP, and HR. Recorded at baseline, 10 minutes post-treatment, and 30 minutes post-treatment.	The 30 minute VAS value showed the VAS average for the aromatherapy group has significantly lower compared to the control group	+ - Rose oil fragrance was controlled to have ample time for prevention of placebo group smelling it. - Control group had	− -Study has rose oil as an adjuvant and not primary treatment. -Uncontrolled environment (emergency room) -Unknown whether it was the rose	Included this study even though the participants also had dicofenac, since the diclofenac was consistent between the two groups. "The present study suggests that aromatherapy

				75 mg diclofenac IM or the same plus 2% rose oil aromatherapy.			saline diffusing in their room to add to placebo/control variables.	oil that had an effect or if it had something to do with the effects on the brain through smelling something nice (olfactory and limbic system) **LOW QUALITY**	with rose essential oil, which is a non-pharmacologic treatment method, as an adjuvant to conventional treatment methods may be beneficial for pain relief in individuals with primary dysmenorrhea." – p. 1
Kheirkhah (2014). Comparing the effects of aromathera py with rose oils and warm foot bath on anxiety in the first stage of labor in nulliparous women k	RCT	N=120 primigravida women in the 1st stage of labor at a hospital in Iran	Anxiety during labor	N= 36 patients in footbath and 1% rose oil N=36 patients in footbath group N=36 patients in routine care group (control) Done before the beginning phase, at the beginning of the active phase (4 cm dilation) and beginning of transition phase (8 cm dilation).	A-VAS (anxiety) measured immediatel y before and after each interventio n	-All three groups had stat. sig less anxiety after first intervention. -Rose oil group had stat. sig less anxiety than both groups in both the first and second intervention. Additionally, the anxiety score continued to drop in the rose oil group from 4cm-8cm dilation, which was not the case in the placebo or control groups.	+ - Randomizati on explained -Placebo and control groups present	– -Unknown whether the results show anything about rose oil in particular or aromatherapy in general. **LOW QUALITY** due to inability to distinguish rose oil from aromatherapy in general.	-Foot bath is used by some midwives as a way to increase comfort, reduce pain, and is thought to reduce sympathetic activity. - Other studies have shown similar results with lavender aromatherapy
Igarashi (2014). Effects of olfactory stimulation with rose and orange	RCT (crossover design)	N=20 Female university students.	Emotional and physiologica l olfactory response to rose or orange.	Either rose, orange, or room air were injected into an "odor bag" and placed on the subjects' chest, approx.	-Oxy-hemoglobin concentrati on in the prefrontal cortex measured	-Significant decrease in oxy-Hb concentration in right prefrontal cortex with both oils compared to control (no sig.	+ -Tight control of experimental conditions. -Detailed physiologica	– -All female (could there be a physiological or emotional difference if	Both rose and orange oil produced physiological and psychological relaxation. This study gives a

oil on prefrontal cortex activity				10 cm under the nose, with a flow rate of 3 liters/min for 90 seconds	with infrared "TRS system" -Subjective evaluation of emotional impact (comfortable/uncomfortable, relaxed/awakening, and natural/artificial)	difference in left, though the oils are lower than the control). - Emotion: "slightly" to "moderately" comfortable, relaxed, natural with rose or orange oil but indifferent or slightly comfortable with control. Orange oil produced the highes feelings of comfort, relaxation, and natural, followed by rose.	l data provided.	male?) - Unknown if the oils themselves or the aromatherapy aspect is creating the outcomes **MODERATE QUALITY**	physiological support data for this conclusion. -

FRANKINCENSE

Citation	Design/ Method	Sample/ Setting	Uses Studied	Interventions	Instruments	Study Findings	Preliminary Quality of Evidence (High/Moderate/ Low/Very Low) & Rationale		Importance and/or Additional Considerations
Majdinasab, N. (2017). Effect of Boswellia serrata on cognitive impairment in multiple sclerosis patients	RCT (double-blind, placebo-controlled)	N=60 patients with MS with subjective cognitive complaints	Cognition (in MS patients)	N=30 in Frank. Group (BS) who received 450 mg powdered BS (filler was lactose and starch) BID for 2 months. N=30 in placebo group who received a capsule with only lactose and starch.	MACFIMS (minimum assessment of cognitive function in MS) testing done before treatment and at 2 months.	-The BS group had significantly higher CVLTII-TL and BVMTR-TL scores at 60 days compared to placebo. -This means that there were significant improvements in auditory/verbal and visual/spatial memory in MS patients who took the BS compared to placebo. -No noticeable effects on auditory and visual processing speed, verbal fluency, spatial processing and executive function.	+ Double-blinding	− -2 months of treatment is relatively short-term -Small sample size **MODERATE QUALITY**	According to the researchers, there is likely a dose-dependent effect and recommend more studies for longer periods of time and higher dosages.
Prabhavathi, K. (2014). A randomized, double blind, placebo	RCT (double-blind, placebo-controlled, cross over	N=12 "healthy volunteers"	Pain	Each participant was exposed to the mechanical pain model (progressive pressures applied to the	-Force exerted when participants first experienced pain	-Pain threshold: mean pain threshold force and time with BS were sig. increased at 2h and 3h compared to placebo.	+ -participants were pre-screened to be as homogenous as possible	− -Small sample size and all male **LOW QUALITY**	The BS groups had a sig. higher pain threshold and pain tolerance compared to placebo as well as

controlled, cross over study to evaluate the analgesic activity of Boswellia serrata in healthy volunteers using mechanical pain model	study)			nail bed) and given either 250 mg of BS or indentical-appearing placebo capsules. 2 week washout between the two drugs then the experiment was repeated.	(threshold) - Force exerted when they could no longer tolerate the pain (tolerance). - Recordings taken at baseline, 1 hr, 2hrs, and 3 hrs after drug administration.	-Mean threshold force of BS also sig. at 3h compared to baseline. -Pain tolerance: Sig. increase in mean pain tolerance force for BS after 1 hr, 2h, and 3h. Mean pain tolerance sig. increased at 2h compared to placebo.	with laboratory values/BMI/ gender (male), etc. -Tight control of participant activity before testing	due to small sample size	compared to baseline threshold and tolerance. -No side effects noted suggest probable safety and tolerability.
Khosravi Samani (2011). The effect of frankincense in the treatment of moderate plaque-induced gingivitis: a double blind randomized clinical trial	RCT (double-blind, placebo-controlled)	N=75 (high school female patients with moderate plaque-induced gingivitis)	Gingivitis, plaque	N=15 BS extract (group 1) N= 14 BS powder (group 2) N= 15 no med (group 3) N= 10 extract and SRP (scaling and root planning)(group 4) N= 10 powder and SRP (group 5) N= 10 only SRP (group 6) Extract and powder were both constituted in a gum base and participants	Gingival index, Plaque index, Bleeding index, Probing pocket depth	-Group C (pooled SRP and BS therapy) showed the best overall improvement in all four outcomes. Next were group A (only BS therapy) and D (only SRP) -Periodontal health status: medications with our without SRP were effective (SRP itself had no "remarkable effect") -Extract had a slightly higher superiority to powder, but this was not significant.	+ -Extensive statistical analyses -Measured many variables between groups to compare and minimize confounding factors	− -Possibility for patient non-adherance at home -Short duration **MODERATE QUALITY**	-Results in favor of treatment of chronic plaque induced gingivitis with BS are most likely due to an anti-inflammatory effect. - Interesting that BS without SRP outperformed SRP by itself.

				instructed to chew it three times/day for 14 days.					
Kirste, S. (2011). Boswellia serrata acts on cerebral edema in patients irradiated for brain tumors: a prospective, randomized, placebo-controlled, double-blind pilot trial	Prospective, randomized, placebo-controlled, double-blind pilot trial	N=44 patints with malignant cerebral tumors (primary or secondary)	Cerebral edema	N= 22 in BS 4200 mg/day N=22 in placebo group	-Cerebral edema volume (measured with MRI) -Toxicity, cognitive function, quality of life, and need for antiedematous medication. -BS blood serum levels -Measured before therapy, after therapy, and at 4week f/u.	- BS group: 60% of patients had a decrease of edema to less than 25% of baseline value or had no edema at all (compared to 26% achieving this in the placebo group). -The BS group had a larger percentage of those who had either a large or slight decrease of edema after therapy and at follow-up. -The patient with the highest BS serum levels had one of the largest reductions of edema.	+ - Pharmacist consultation(to set dose) -need for additional medication considered in analysis.	− -Missing information regarding length of treatment and time between intervention and follow-up. -No sig. difference between dexamethasone use, though the placebo group had an average higher use of this. **LOW QUALITY**	-This preparation of BS is sold as a dietary supplement in Germany (H15) and is reported to have no adverse effects. -It is possible that there may be a relation to tumor volume reduction and cerebral edema -The authors suggest a phase 3 trial should be done to further determine dexamethasone dose and antitumor effect.
Abdel-Tawab, M. (2011). Boswellia serrata: an overall assessment of in vitro, preclinical, pharmacokinetic and clinical data	Evidence Summary	<u>RA:</u> One trial by Sander, Herborn, and Rau (1998): N=37. Double-blind placebo controlled pilot study, N=37. Measured BS preparation in addition to previous therapy and NSAIDS. No measurable efficacy of BS preparation and no effect on pain. NSAID doses smaller in BS group, but not significantly. <u>OA:</u> Kimmatkar, Thawani, Hingorani, and Khiyani (2003): N=30. 8 week randomized double-blind, placebo-controlled crossover that found 999mg BS/day sig. improved pain, flexion, and walking distance compared to placebo. Sontakke et al. (2007) N=66. 6 mo randomized open label equivalence study. Sig diff in WOMAC score (pain, stiffness, diff. perf. Daily activity) vs. baseline after 2 months of 999mg BS/day therapy and 1 month following d/c. Compared to valdecoxib, the BS groups had sig lower scores even after 7 months. Sengupta et al. (2008): N=75. 90d randomized double-blind placebo-controlled. Compared BS to placebo. Found higher dose BS (250mg vs. 100mg) sig. improved pain 7d after beginning treatment.								RA study too old and too little information.

		Asthma: Gupta et al. (1998): Explorative clinical trial. N=80. BS group had a significant improvement in overall asthma control (FEV1, FVC, and PEFR) compared to placebo.	

Citation	Design/ Method	Sample/ Setting	Uses Studied	Interventions	Instruments	Study Findings	Preliminary Quality of Evidence (High/Moderate/ Low/Very Low) & Rationale		Importance and/or Additional Considerations
Sharifi (2017). Topical use of Matricaria recutita L (Chamomile) Oil in the Treatment of Monosymptomatic Enuresis in Children	Randomized placebo-controlled trial with parallel design.	N=80 patients with enuresis (nocturnal or daytime)	Enuresis (incontinence) in children	N=40 in chamomile group N=40 in placebo group (almond oil) Parents put 6 drops of their oil on the suprapubic area once per night.	-Frequency of enuresis -Adverse events Measured at baseline, 2, 4, and 6 weeks.	Frequency of enuresis significantly lower in the chamomile group compared to placebo at 2 weeks, 4 weeks, and 6 weeks.	+ -8-week duration -Double-blind	− -Local chamomile production from school of pharmacy (can this be duplicated?) -Recurrence rate not considered. **MODERATE QUALITY**	-Chamomile has historically been used as a treatment for enuresis in children in traditional Persian medicine for "warming up the bladder" -May have spasmolytic and anticholiergic activity. -Unknown whether systemic effect or aroma created the outcomes.
Hashempur, Mh (2017). Efficacy of topical chamomile oil for mild and moderate carpal tunnel syndrome: a	RCT	N= 77 patients with mild-moderate carpal tunnel syndrome	Carpal tunnel symptoms in mild-mod carpal tunnel	N= 39 in chamomile group (1% chamomile) N=38 in placebo group. Patients put 5 drops of the oil on the palmar area of	-Boston Carpal Tunnel Questionnaire (BQ) – Persian version. -BQ includes Functional status score, symptom severity score.	-Symptom severity in chamomile group had significant improvement compared to placebo group. They also had significant increases in functionality.	+ -Oil analyzed with gas chromatography -specific inclusion/exclusion, -randomization explained -massage	− -relatively short-term study. -No follow-up data. -Sesame oil used as carrier oil, which is said to have anti-inflammator	The authors mention the anti-oxidant, anti-inflammatory, and analgesic properties of chamomile oil and consider the anti-inflammatory and anti-

randomized double-blind placebo-controlled clinical trial				the wrist every morning and every evening for four weeks. Massaging was prohibited on this part of the wrist		-Dynamometry revealed a significant improvement in chamomile group.	prohibited on treated part of wrist.	y, antioxidant, and anesthetic activity, so possible counfinding factor **LOW QUALITY**	oxidative processes to be the main factor for this improvement.
Shoara (2015). Efficacy and safety of topical Matricaria chamomilla L. (chamomile) oil for knee osteoarthritis: A randomized controlled clinical trial	RCT (three-arm, blinded, randomized placebo-controlled trial using parallel design)	N=84 patients	Pain related to Osteoarthritis of the knee	N=28 in chamomile group N=28 in placebo (paraffin) group N=28 in diclofenac group Patients applied their medication (chamomile, paraffin, or diclofenac gel) to the affected knee three times/day for three weeks.	-APAP need (# of tablets needed total over 3 weeks) -WOMAC questionnaire	-Chamomile group had sig. less need for apap compared with both the placebo and diclofenac groups. -No significance between groups for pain, physical function, and stiffness (WOMAC), however all three groups had a significant decrease in these measures individually.	+ -Specific inclusion/exclusion criteria including needing to use greater than 2g APAP/day or other analgesics -Massaging of knee was not permitted.	− -Study not blinded to aroma -Sesame oil was used as a carrier (may have anti-inflammatory effects and possibly chondroprotective effects) -short-term effects - Most patients female (84%) **LOW QUALITY**	Chamomile may decrease the need for analgesics for those with OA as well as improve physical function and stiffness.
Hashempur (2015). A pilot randomized double-	Pilot randomized double-blind placebo-	N=23 patients	Carpal tunnel symptoms in severe carpal tunnel	N= 12 in chamomile group N=11 in placebo group	Electromyography instrument for electrodiagnosis	-Significant improvement in symptoms in chamomile group compared	+ Tight inclusion/exclusion criteria	− -pilot study -small sample size -short-term	Researchers conjecture anti-inflammatory reasons for these outcomes.

blind placebo-controlled trial on topical chamomile (Matricaria chamomilla L.) oil for severe carpal tunnel syndrome	controlled trial			Patients put 5 drops of the oil on the palmar area of the wrist every morning and every evening for four weeks. Massaging was prohibited on this part of the wrist	-Boston Carpal Tunnel Questionnaire (BQ)	with placebo. -No significant differences in electordiagnostic parameters (e.g. nerve function)		-Sesame oil used may confound results **LOW QUALITY**	

APPENDIX C

EVIDENCE USE PROFILES

Lavender

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate/ Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)
Pain Relief	9 studies: 6 RCTs 1 RCT with double-blinding 1 Semi-experimental trial 1 open crossover trial (Seyed-Rasooli, Nasiri, Hasanzadeh, Akcan, Irmak, Ghods Kaviani, Sheikhan, Kim)	746	Unable to blind, Some studies also received pain medication (Irmak, Sheikhan)	7 low, 1 moderate, 1 very low = Low Quality	Studies using lavender for pain relief include both those who use topical lavender or inhaled lavender, or both. Most studies used VAS pain scale and some also measured physical parameters such as heart rate and blood pressure. Topical: Statistically significant reduction of pain in 4 studies Inhalation: Statistically significant reduction of pain in 4 studies, including a study that measured vital signs in infants undergoing a heel stick. Compared to cold therapy, lavender did not significantly change pain experience vs. control or cold therapy alone - Hasanzedah Lavender inhalation does not appear to have a significant effect on vital signs or mental stress levels in hospitalized post-CABG patients. – Bikmoradi	Although most studies are of low quality in design or execution, use of lavender oil via topical application or inhalation showed statistically significant short-term pain reduction on its own and compared to placebo. This was true for mild-moderate acute pain, chronic pain, and labor pain. The mechanism is not clear, however

					Labor Pain: Use of lavender during labor may assist in decreased perception of pain and increased level of contentment (but does not necessarily have an effect on labor outcome) – Kaviani	there is a possibility that lavender application and/or inhalation can temporarily reduce mild-to-moderate pain. STRONG
Anxiety	7 studies: 6 RCTs 1 RCT with double-blinding (Karadag, Seyed-Rasooli, Hasanzadeh, Bikmoradi,Seol, Kim, Woelk*, Toda)	363	Lavender type not specified (Karadag), unable to blind in most studies	6 low, 1 very low = Low Quality	All studies studied lavender inhalation for anxiety. Subjective anxiety was reduced significantly in 4 studies. 1 study (Hasanzadeh) showed a decrease in anxiety related to pain when combined with cold therapy. Cortisol levels were monitored in one study (Toda) and were not affected by the participant's subjective report of anxiety reduction. Lavender inhalation did not significantly reduce anxiety in post-CABG patients or during an invasive bladder procedure (Bikmoradi & Seol) *Oral use and double blinded study by Woelk: Researchers concluded that Silexan 80mg is generally safe and is at least as effective and comparable to lorazepam 0.5mg.	A general trend exists that lavender inhalation produces a decrease in anxiety in both controlled experiments and anxiety related to mild-moderate pain, though there was not a strong effect on anxiety related to post-CABG patients or during an invasive bladder procedure There is one study available that concluded an internal preparation

					-Safety was also assessed to be generally safe - Woelk	of lavender was at least as effective as lorazepam taken long-term (Woelk). WEAK
Sleep Quality	3 RCTs 1 Randomized Controlled Pilot Study (Karadag, Lillehei, Lytle, Liu) 1 systematic review (Lillehei)	256 (10 studies in Lillehei review, no pooled n= avail)	Lavender type not specified (Karadag), unable to blind, multiple study problems in Lillehei.	2 low, 3 very low = Very Low Quality	Lavender improved subjective feelings of restful sleep in 4 studies and helped participants fall asleep more easily in one study. (Lillehei) One study conjectured lavender may have a longer-term effect on sleep quality (Lillehei), and another was unable to find parasympathetic activity pointing toward long-term sleep quality improvement (Liu) One systematic review by Lillehei: Further supports lavender may assist with sleep quality for some individuals	There is moderate evidence that lavender may assist in reducing time to fall asleep and subjective perception of sleep quality. STRONG (In part due to inclusion of a systematic review supporting this conclusion)
Fatigue	1 RCT (Bagheri-Nesami)	60	Only in hemodialysis patients and many confounding factors in study	Very Low Quality	Fatigue was studied in patients with chronic fatigue undergoing hemodialysis over 4 weeks. No difference in fatigue levels between lavender treatment group and control group during the trial or in follow-up.	There is no evidence that lavender therapy helps improve fatigue symptoms NO CONCLUSION
RLS	1 RCT	70	No placebo	Low Quality	Lavender massage may be helpful in alleviating RLS symptoms in	According to one

	(Hashemi)		group -possibility of confounding factor of massage		hemodialysis patients. This may also be r/t anxiety, which was not measured in this study.	study, lavender may alleviate RLS symptoms in some individuals NO CONCLUSION (confounding factor of massage)
Dysmenorrhea	1 RCT 1 Randomized Experimental Trial (Raisi, Matsumoto)	113	Author bias (created dysmenorrhea questionnaire – Raisi) Sampling bias	Low-Very Low Quality	Lavender inhalation may relieve the severity of primary dysmenorrhea symptoms in women, including pain and short-term mood symptoms. Menstrual flow intensity is typically correlated to pain, however the participants in one trial by Raisi had a reduction of pain without any noticeable change in menstrual flow.	Lavender may temporarily reduce pain and mood symptoms related to primary dysmenorrhea. WEAK
Dementia	1 Cochrane Review on Dementia (Forrester)	4 studies related to Lavender	High risk of reporting bias in reviewed studies	Very Low Quality	"There is plenty of non-randomized evidence of both benefit and harm for aromatherapy for dementia. The seven randomized trials included in this review show equivocal evidence for the benefits of aromatherapy, and further evidence for its effectiveness is needed."	There is conflicting evidence regarding the use of lavender to improve cognitive and behavioral dementia symptoms. More studies are needed. NO CONCLUSION
Menopause Hot Flushin	1 RCT (Kazemzadeh)	100	Possibility of non-compliance with	Moderate Quality	Women ages 45-55 inhaled lavender for 20 minutes at a time 2x/week and the occurrence of hot flushes	Lavender inhalation may have a positive effect on reduction of menopause-

g			recording hot flushes within guideline definitions.		dropped dramatically in this group compared to placebo (by over half, on average)	related hot flushes WEAK

Peppermint

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate/ Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)
Dysmenorrhea	1 RCT (double-blinded) (Heshmati*)	102	Patients were permitted to take painkillers but exact doses were not recorded	Low Quality	Internal use: 330 mg. peppermint capsules were used for two menstrual cycles and the group that received Peppermint had statistically significant lower mean pain scores in both the 1st and 2nd cycles compared to placebo.	Peppermint taken internally may reduce menstruation-related pain, however more studies are needed NO CONCLUSION Due to lack of explanation of allowable

						painkillers.
IBS Symptoms	1 RCT, (double-blinded) (Cash*) 3 systematic reviews with meta-analysis (Mann, Ruepert, Ford)	2,200	Inconsistency in dosage and frequency of treatment.	3 moderate = Moderate Quality	- IBS-M or D: "Subjects receiving PO experienced a significant decrease in the number of severe and unbearable symptoms at 28 days compared to those receiving placebo – Cash - IBS Symptoms: 79% of cases showed abdominal pain relief. - 83% of cases showed abdominal distention relief. -73% of cases showed reduction in bowel frequency and flatulence -20% of cases showed adverse SE, most commonly heartburn - Mann Statistically significant benefit present for peppermint oil in improvement of IBS symptom score and global assessment - Ruepert -Systematic review by Ford also reviewed the studies reviewed by Ruepert and they came to the same conclusions "Fifty two of 197 (26%) patients randomized to peppermint oil had persistent symptoms compared with 127 of 195 (65%) receiving placebo	There is not an established dose and frequency, but there are numerous studies and cases that suggest that peppermint oil, when taken internally, can significantly improve IBS symptoms such as pain relief, abdominal distention and bowel frequency/flatulence. The most common side effect is heartburn. STRONG
Nausea /Vomiting	3 RCTs (Sites, Anderson, Tate)	93	Large attrition and effect power was not obtained (Sites),	3 very low = Very Low Quality	Peppermint was used to treat post-operative nausea and vomiting and results were mixed between studies. No statistically significant difference between the placebo and peppermint groups, however, the total percentage of people with PONV after peppermint intervention was less compared to placebo. Even still, those who received	Peppermint is commonly used to treat nausea and may be helpful for some individuals but little evidence exists to support the

			missing information from Anderson and Tate studies.		peppermint asked to continue the therapy in the hospital and at home.– Sites Alcohol inhalation: 45% requested anti-emetics. PO inhalation : 60% requested anti-emetics Saline inhalation: 50% required anti-emetics - Anderson	idea of peppermint inhalation as an anti-nausea agent. WEAK
Stress	1 RCT (Toda)	21	Very small sample	Low Quality	Compared Peppermint, lavender and control. Peppermint: Significantly lower perception of stress in all trials in this study. There was also decrease in salivary cortisol immediately after inhalation.	Peppermint oil may improve short-term stress perception WEAK

Eucalyptus

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate/ Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)
Anxiety	1 RCT (Kim)	62	Small sample for	Low Quality	Eucalyptus inhalation decreased anxiety in the pre-	Eucalyptus may have a short-term

			each sample group (only 15 in treatment group)		operative setting compared to not using eucalyptus	effect reducing anxiety before surgery WEAK
Pain	1 RCT (Jun)	52	Study confounded with pharmacol ogical pain treatment	Very Low Quality	Pain and diastolic blood pressure significantly decreased with eucalyptus inhalation compared with not inhaling eucalyptus for first 3 days post total-knee replacement.	Eucalyptus inhalation may have an analgesic effect however it is impossible to determine if the effect is due to the oil specifically or due to the general anxiolytic effects of aromatherapy inhalation. NO CONCLUSION
Inflam mation	1 RCT (Jun) 1 Case study collection (Warnke)	55	Jun study very short-term	2 very low = Very Low Quality	Heart rate, CRP, and WBC count did not differ significantly between groups, therefore the researchers found no link between systemic inflammation markers and eucalyptus inhalation. – Jun. All three case studies in Warnke showed photographic evidence that a eucalyptus oil application reduced inflammation, eliminated malodor, and decreased pain associated with three large cancer-related ulcers that were previously non-healing. - Warnke	Eucalyptus inhalation does not appear to have a systemic anti-inflammatory effect. Although it may have a positive effect on inflammation and wound healing in some people with

						chronic wounds, more evidence needs to be gathered before recommending this therapy. NO CONCLUSION
Tuberculosis	1 Case Study (Sherry)	1	Case study, uncontrolled, and retrospective analysis	Very Low Quality	One woman with tuberculosis inhaled eucalyptus 3x/day for her cough. After 10 days she reported a significant improvement in symptoms and her previously positive sputum culture returned negative despite no change in her chest x-ray.	NO CONCLUSION
Asthma	1 review (2 studies reviewed) (Sadlon)	42	Review article; some missing information	Low Quality	Eucalyptus inhalation resulted in a 23.7% increase in FEV1 and a 26.1% decrease in airway restriction after three days of cineole inhalation and continued four days after treatment. Another trial found those who inhaled eucalyptus were able to reduce glucocorticoid dose and rescue inhaler use.	Eucalyptus inhalation treatment may have a positive effect on asthma symptoms, including an increase in FEV1, a decrease in airway restriction, and possibly a reduction in need for asthma medications. WEAK

Rhinosinusitis	1 review (1 study reviewed) (Sadlon*)	150	Review article; some missing information	Low Quality	200mg oral eucalyptus reduced headache, facial tenderness, malaise, nasal congestion and nasal secretions by over 80% after seven days.	Oral eucalyptus oil may help reduce symptoms associated with rhinosinusitis (common cold) by over 80% by day 7. WEAK
COPD	1 review (1 study reviewed) (Sadlon*)	242	Review article; some missing information	Low Quality	200mg oral cineole given three times/day for six months resulted in a significant decrease in number, severity, and duration of exacerbations compared to placebo (0.4 vs. 0.9). Dyspnea scores improved, but not significantly more than placebo.	Oral eucalyptus oil (600 mg/day) may decrease the frequency, severity, and duration of COPD exacerbations WEAK

Tea Tree

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate/ Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)

Burns	1 RCT (Cho)	96	Study had inconsistent application methods between study groups	Low Quality	Pain was reduced in TTO group after 20 minutes compared to both another commercial treatment and running water, though the difference was not significant. TTO had no significant effect on skin temperature.	Very weak evidence for using TTO for burn pain and cooling NO CONCLUSION
Dental Plaque	1 RCT (Santamaria)	34	Small sample size	Low Quality	Tooth gel with TTO was more significantly more effective in decreasing dental biofilm and bacteria colonies compared to commercial brand Colgate toothpaste.	Tea tree oil used in toothpaste may decrease the number of harmful bacteria in dental biofilm and reduce the risk of periodontal disease. WEAK
MRSA & Wound Healing	2 RCTs (Lee, Blackwood) 1 Uncontrolled case series (Edmondson) 2	749	Multiple application techniques and unclear and inconsistent TTO concentrations	1 moderate, 1 low, 2 very low = Low Quality	TTO group: MRSA completely eradicated in 14 (87.5%) of the 16 patients. -TTO group: all wounds with previous delayed healing (>6 weeks) were healed within 28 days w/o adverse reaction – Lee TTO-infused body wash did not prevent MRSA colonization for ICU patients (10/391 became colonized with MRSA in nares). - Blackwood -Small RCT (n=10) found TTO dressing did not have a significant effect on MRSA bacteria count compared to saline	Treatment of MRSA with TTO has mixed results in human studies, from complete eradication to no difference in MRSA count after treatment, however there is wide variability in application

	Reviews: (Wound Healing, Flaxman)				dressing (undefined wound types). -An uncontrolled trial (n=12) found that a wound cleansing solution did not eradicate MRSA infection in 12 mixed-etiology wounds. – Wound Healing and Management Node Group All 11 patients were still positive for MRSA post-study and 8/12 had smaller wounds before they finished/withdrew from the study than when the study began. – Edmondson "Neither study demonstrated overall statistically significant benefits for the use of tea tree preparations to eradicate MRSA colonization" - Flaxman	techniques and study characteristics. TTO had generally few adverse reactions. UNCERTAIN
Acne	1 RCT (double blind, split-face) (Kwon)	34	No control group, so vehicle effect cannot be excluded	Low Quality	Study compared TTO vs. an alternative acne wash containing lactobacillus. Both treatments reduced acne, however TTO had only a 38.2% decrease after 8 weeks while the alternative wash decreased lesions by 65.3%	Unable to make a conclusion due to small sample size and comparison to specific acne wash without a control group. NO CONCLUSION
Antimicrobial Effect and Wound Healing (non-	1 RCT (Gnatta) 1 Quasi-experimental study (Chin)	35	Limited to ages 18-55 in Gnatta. Inconsistency in wound assessment	Low-Very Low Quality	Soft Soap plus 0.3% TTO did not decrease e-coli during handwashing significantly better than regular soap or soap with triclosan. – Gnatta Those who received TTO	There is conflicting evidence for efficacy of TTO for wound healing and as an antimicrobial agent, however cases exist that suggest TTO

MRSA)	1 Review (Wound Healing and Management Node Group)		in Chin		treatment for wounds healed faster on average than those who did not receive TTO. – Chin "There is some evidence that TTO could be used to promote wound healing. (Grade B) • There is some evidence that TTO could be used effectively as a topical antibacterial in wound management. (Grade B)" - Wound Healing and Management Node Group	may have expedited wound healing time compared to no treatment and may be used as a topical antibacterial. WEAK
Ocular Discomfort	1 Prospective Randomized Study (Koo)	335	Compliance with treatment, not a controlled study	Moderate Quality	People with symptoms of eye discomfort who were also positive for the parasite Demodex were treated with either a TTO eyelid scrub or an eyelid scrub without TTO. The Overall Ocular Surface Disease Index scores and demodex counts were significantly reduced in the TTO group.	TTO may be a good treatment for ocular symptoms r/t demodex parasite, which may be an etiologic factor in some eye infections such as blepharitis, conjunctival inflammation, and meibomian gland dysfunction. WEAK

Rosemary

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate/ Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)
Alopecia	1 RCT (Panahi)	100	Data pulled from abstract, unable to locate full article	Very Low Quality	Study compared application of rosemary oil to application of minoxidil. Both treatments increased hair count at 6 months but there was not a significant difference between the two treatment groups. The group that applied rosemary oil had fewer complaints of scalp itching than the minoxidil group.	NO CONCLUSION
Blood Pressure	2 RCTs (1 double-blind) (Fernandez*, Hongratanaworakit)	67	Convenience sample, no control group (Fernandez) Lack of	2 low = Low Quality	Rosemary was taken internally by 32 volunteers with low blood pressure for 44 weeks, in which time both systolic and diastolic blood pressures increased from 3.7-21.76% throughout the entire group. After treatment ended BPs	Ingested and inhaled rosemary may be a safe and effective method of increasing systolic & diastolic BP and health-related quality of life. WEAK

			specific statistical values for all measures (Hongratanaworakit)		returned to baseline hypotensive state. These volunteers also reported an improved quality of life during the rosemary intervention. Rosemary inhalation and topical self-massage application produced an increase in respiratory rate, diastolic blood pressure, and feelings of attentiveness compared to control. This suggests a possible link to an increase in autonomic arousal (Hongratanaworakit)	
Asthma	1 Active Comparison Study	40	Data pulled from abstract, unable to locate full article.	Very Low Quality	Rosemary inhalation was compared to platanus inhalation and placebo in persons with at least 4 asthma drugs and uncontrolled asthma. The group who inhaled rosemary had significant improvement in cough, sputum production, chest pain, and wheezing. FEV1 improved in both groups, however platanus more so than rosemary.	Unable to make a conclusion due to insufficient evidence NO CONCLUSION

Cognition	2 RCTs (Pengelly*, Moss)	173	Elderly population may confound data in Pengelley trial so it is not transferrable to younger adults.	1 low, 1 moderate = low/moderate	Rosemary was given internally to elderly residents in a nursing home in four doses ranging from 750mg-6,000mg/day. It was found that the residents had significant improvement in memory speed and alertness with 750mg rosemary, however the quality of working memory was impaired. 6,000mg dose had the most deleterious effect on cognition – Pengelly Rosemary inhalation improved alertness during a cognitive task, however did not significantly improve speed or accuracy during the task. - Moss	Low-dose oral intake of rosemary oil may assist the elderly in alertness and memory speed. Rosemary inhalation may improve the subjective sense of alertness, but does not appear to have an effect on actual performance of a cognitive task. WEAK
Anxiety	1 RCT (Burnett), 1 Quasi-experimental study (McCaffrey)	113	Poor study designs	2 very low = Very Low Quality	Students inhaled rosemary and lavender during a stressful cognitive task. One study reported the students who inhaled rosemary had reduced anxiety and increased clarity (McCaffrey), however the study by Burnett noted a	Rosemary may have an effect on increasing alertness, however it also may increase feelings of anxiety and tension in some individuals. WEAK

					higher tension-anxiety scores with rosemary compared to lavender.	

Patchouli

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate/ Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)
Insect Repellent	1 Controlled Clinical Trial	3	Small experiment	Low Quality	60 minutes of complete mosquito repellency achieved at 50% concentration applied on a human arm, which is comparable to citronella, a known mosquito repellent. No protection was noted at 10% concentration (Trongtokit)	Patchouli may have mosquito-repellency properties that are concentration dependent. WEAK

Lemon

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate/ Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)
Nausea/ Vomiting	2 RCTs (Keating & Yavari, in review by Goepfert)	126	Missing information regarding these studies	2 low = Low Quality	Lemon oil did not improve nausea as effectively as ginger syrup (Keating) Lemon oil inhalation reduced nausea scores compared to no intervention (Yavari, n=100)	Lemon oil inhalation may help relieve mild nausea WEAK
Anxiety	1 RCT (Johnson)	39	High possibility of sampling error due to timing of questionnaire	Very Low Quality	Lemon oil inhalation during an exam reduced anxiety scores in nursing students 24 hours after taking an exam, however not significantly more than not inhaling lemon oil.	NO CONCLUSION
Gallstones	2 studies (in evidence review by Sun)	200+	Evidence review; missing individual study	Low Quality	D-limonene infusion resulted in complete or partial dissolution of gallstones in two clinical trials. Complete or partial dissolution of	Oral d-limonene may be used as a treatment to assist in dissolution of gallstones

			information.		gallstones occurred in 141/200 patients (48% had complete dissolution).	WEAK
GERD	2 studies (in evidence review by Sun)	32	Evidence review; missing individual study information.	Low Quality	Oral use of d-limonene has been effective at relieving heartburn and GERD (up to 89% achieving complete relief by day 14 of treatment).	Oral d-limonene may help relieve GERD symptoms WEAK
Anticancer	4 case studies (in evidence review by Sun)	4	Evidence review; missing individual study information.	Very Low Quality	"Evidence from a phase I clinical trial shows a partial response in a patient with breast cancer and stable disease for more than six months in three patients with colorectal cancer."	Several cases exist that suggest d-limonene may have antitumoral effects when taken orally. VERY WEAK

Rose

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate /Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)
Low Back Pain	1 RCT (Shirazi)	120	Participant complianc	Moderate Quality	Pregnant women with low back pain who applied rose oil to their backs over a four-	Topical rose oil to the low back may have an analgesic

(pregnancy-related)			e at home with treatment		week period achieved a significant reduction in pain compared to not applying rose oil.	effect for pregnancy-related low back pain. WEAK
Dysmenorrhea	1 RCT (Uysal)	100	Study confounded by use of pain medication, Uncontrolled environment (ER)	Low Quality	Women admitted to the emergency room for dysmenorrhea who inhaled rose oil in addition to 75 mg of diclofenac had significantly less pain after 30 than women who had diclofenac alone.	Unable to make a conclusion for pain relief due to high likelihood of confounding pain medication and the possibility of an anxiolytic response as the primary factor in the reduced pain scores. NO CONCLUSION
Anxiety	1 RCT (Kheirkhah)	120	Study specifically on labor-related anxiety.	Low Quality	During early labor, rose oil aromatherapy via foot bath reduced the mothers' anxiety significantly and continued to do so throughout active labor compared to a foot bath without rose oil.	Using rose oil aromatherapy alongside a foot bath may reduce labor-related anxiety. WEAK

Frankincense

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate /Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)
Cognition in persons with Multiple Sclerosis	1 RCT (Majdin asab*)	60	Small sample and relatively short-term study for long-term condition.	Moderate Quality	Significant improvements were noted in auditory/verbal and visual/spatial memory in MS patients who took Frankincense compared to placebo. -No noticeable effects on auditory and visual processing speed, verbal fluency, spatial processing and executive function.	Frankincense taken internally may have a positive effect on memory for people with MS, however evidence is very weak and more studies should be done. WEAK
Pain	1 RCT (Prabha vathi*)	12		Low Quality	The participants who took 250 mg. frankincense capsules had a significantly higher pain threshold and pain tolerance not only compared to baseline, but also compared to placebo.	Frankincense taken internally may have an prophylactic analgesic effect. WEAK
Gingivitis / Dental	1 RCT (Khosra	75	Possibility of	Moderate Quality	Frankincense re-constituted in a gum base facilitated	Topical frankincense may have a positive

Plaque	vi)		compliance issue with home treatment.		improvement in reduction of plaque and improvement in periodontal health when participants chewed the gum for two weeks. The best results were a combination of BS gum and scaling/root planing (SRP) treatment, however BS alone also outperformed SRP alone.	effect on plaque reduction and gingivitis, either used alone or with SRP treatment. WEAK
Cerebral edema	1 RCT (Kirste*)	44	Missing information from study (treatment length)	Low Quality	Participants with brain tumors and cerebral edema had a larger decrease in cerebral edema while taking 4200 mg frankincense compared to those who did not take frankincense.	Internal use of frankincense may have an effect of reducing cerebral edema in those with brain tumors, however the results of this study are unable to confirm causation. NO CONCLUSION
Osteoarthritis	2 RCTs (*Kimmatkar, *Sengupta) 1 randomized	171	Limited information available from this study – information from 2011	Low Quality	All three studies show evidence of significant improvement of OA after taking from 250-999mg frankincense per day for a range of 7 days – 7 months. Flexion, pain, walking distance, WOMAC scores all	WEAK

	open label equivalence study (*Sontakke)		evidence summary by Abdel-Tawab.		improved with frankincense as a stand-alone therapy (including compared to valdecoxib (Sontakke))	

Chamomile

	Quality Assessment					Summary
Use	Number of studies	Total Pooled N=	Limitations & Biases	Overall quality of evidence (avg. from evidence table) High/Moderate /Low/Very Low	Summary of Findings	Preliminary Conclusion & Strength (Strong/Weak/No Conclusion)
Incontinence	1 RCT (Sharifi)	80	Oil produced independently from local pharmacy (duplicatable?), unknown long-term effect.	Moderate Quality	Compared to placebo, topical application of chamomile oil to the suprapubic area once per night resulted in a significantly lower frequency of enuresis in children as early as 2 weeks	There is some evidence that chamomile may be used as a short-term treatment for day or nighttime incontinence in children, however more evidence is needed. WEAK
Carpal	1 RCT	100	No follow-	2 low quality	Mild-Moderate: 4 weeks of	Topical application of

Tunnel Syndrome	(Hashempur, 2017) 1 Randomized Pilot Study (Hashempur, 2015)		up information, sesame oil used as diluent, which may confound results.	= Low Quality	topical application of chamomile oil to the wrist significantly improved carpal tunnel symptom scores (particularly in functionality and nerve function) compared to placebo. Moderate-severe: The same application of chamomile oil significantly improved symptoms compared to placebo, but did not show a significant difference in nerve function.	chamomile oil may have a positive effect on overall carpal tunnel syndrome symptoms, including pain and functionality, particularly in mild-moderate carpal tunnel syndrome. WEAK
Osteoarthritis	1 RCT (Shoara)	84	Ssesame oil used as diluent, which may confound results.	Low Quality	Chamomile oil was compared to placebo and diclofenac for OA of the knee and the group who applied chamomile oil had significantly less need for acetaminophen than either group. All three groups also improved knee functionality, however there were no significant differences between the groups.	Topical Chamomile may decrease the need for analgesics for those with OA as well as improve physical function and stiffness. WEAK