
Aromatherapy and Essential Oils: A Map of the Evidence

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program is comprised of four ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program and Cochrane Collaboration. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, and interface with stakeholders. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee comprised of health system leadership and researchers. The program solicits nominations for review topics several times a year via the [program website](#).

Comments on this evidence report are welcome and can be sent to Nicole Floyd, Deputy Director, ESP Coordinating Center at Nicole.Floyd@va.gov.

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This topic was developed in response to a nomination by the Office of Patient Centered Care and Cultural Transformation (OPCC&CT) to guide the use of aromatherapy and essential oils in the VHA. The scope was further developed with input from the topic nominators (*ie*, Operational Partners), the ESP Coordinating Center, the review team, and the technical expert panel (TEP).

In designing the study questions and methodology at the outset of this report, the ESP consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

The authors gratefully acknowledge Robin Paynter, MLIS, and the following individuals for their contributions to this project:

Operational Partners

Operational partners are system-level stakeholders who have requested the report to inform decision-making. They recommend Technical Expert Panel (TEP) participants; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on draft report; and provide consultation on strategies for dissemination of the report to field and relevant groups.

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Technical Expert Panel (TEP)

To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members are listed below:

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Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center and the ESP Center work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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ABSTRACT

Background: The purpose of this review is to provide the Veterans Health Administration (VHA) with a broad overview of the effectiveness of aromatherapy and essential oils (EOs), and the health conditions for which these interventions have been examined.

Data Sources and Study Selection: We searched multiple databases through February 2019 for systematic reviews (SRs) of aromatherapy and EOs for health conditions. Using pre-specified inclusion criteria, all abstracts and full-text articles were dual-screened for inclusion. When there were several qualified reviews for the same health condition, we selected a single review based on its recency, methods, scope, and applicability.

Data Abstraction: From each review, we abstracted the focus of the SR, the number of controlled trials included, combined number of participants, duration of trials, condition treated, and relevant findings from controlled trials. We abstracted separate data for each of 5 outcome categories: psychological outcomes, nausea/vomiting, pain and other physical outcomes, sleep outcomes, and global health outcomes.

Data Synthesis: For each review and outcome category we assigned values representing the effectiveness level of the intervention and confidence in the evidence and used these values to generate evidence maps. Additionally, we provide a narrative synthesis of the findings.

Results: We included 26 SRs representing the most recent and comprehensive evidence available. There is moderate-confidence evidence that aromatherapy is beneficial for pain in dysmenorrhea. Aromatherapy is potentially effective for pain in labor/childbirth; blood pressure reduction in hypertension; stress, depression, and sleep in hemodialysis patients; stress in healthy adults; anxiety in perioperative patients; and sleep quality in various populations, with low to moderate confidence in the evidence. For EOs applied topically, there is moderate confidence in the potentially positive effect of tea tree oil for tinea pedis. There is insufficient evidence of efficacy for all other conditions examined.

EVIDENCE REPORT

INTRODUCTION

The Veterans Health Administration (VHA) is seeking to increase the use of effective new practices and approaches in health care as part of its current transformation to a more patient-centered healthcare model that focuses on the Veterans' goals and priorities for their health. The use of various low-risk complementary and alternative health interventions has been increasing both within and outside of the VHA.

Essential oils (EOs) are part of a tradition of herbal medicine dating back thousands of years.² EOs are volatile oils that contain the “essence” of an aromatic plant’s fragrance. Conventional methods for extracting EOs include steam or water distillation from raw plant material,³ or cold-press extraction from citrus peel.⁴ The therapeutic inhalation of EOs is thought to have physiological and/or psychological benefits.⁵ Aromatherapy using EO is thought to mediate emotional responses by affecting the neuroendocrine system and autonomic nervous systems.⁶ In addition to the inhalation of EOs, there are various topical applications that are purported to be beneficial apart from their aromatic qualities, for instance as antiseptics. The chemical components of EOs have been shown to inhibit microbial and fungal growth.^{7,8}

EO aromatherapy is being used increasingly in hospitals and other healthcare settings.^{9,10} For instance, aromatherapy has been used to help manage the behavioral and psychological symptoms of dementia, such as restlessness and aggression, and to improve sleep.¹¹

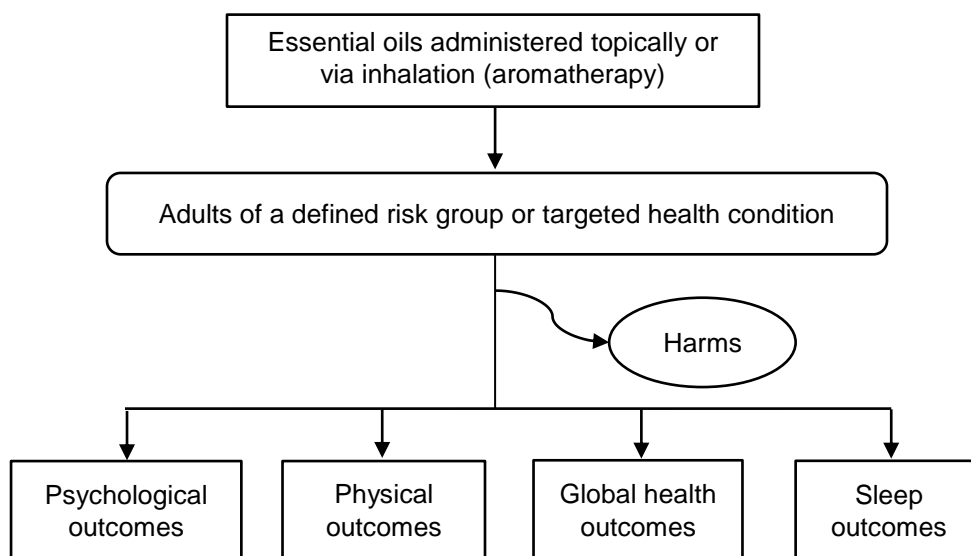
Despite their increasing use, little is known about the benefits and risks associated with the use of EOs. The purpose of this report is to provide a broad overview, using evidence maps, of the health conditions and target populations for which EO interventions have been studied. Evidence maps are a relatively new form of evidence synthesis, and their purpose is to identify research gaps and future research needs, rather than to conduct comprehensive, in-depth analyses or form conclusions about a focused research question. Although standardized definitions and methodology are still being established, an evidence map generally includes a systematic search of a broad field of research and a visual representation of the body of literature.¹² This report and evidence map characterize the current knowledge about the effectiveness of inhaled and topical EOs and will inform decision-making about these modalities in the VHA.

METHODS

TOPIC DEVELOPMENT

This topic was nominated by Dr. Peter Glassman, Chair of the Medical Advisory Panel, Pharmacy Benefits Management Service, in conjunction with Dr. Benjamin Kligler, National Director for the Integrative Health Coordinating Center, Patient-Centered Care & Cultural Transformation (OPCC&CT). The scope was refined through a process that included a preliminary review of published peer-reviewed literature and consultations with our operational partners and a panel of technical experts. The research question for this evidence map was: What evidence is available that examines the effectiveness of aromatherapy or essential oils for health-related indications? Our approach to the research question is shown below in Figure 1.

Figure 1. Analytic framework



SEARCH STRATEGY

We conducted a comprehensive search for systematic reviews (SRs) and meta-analyses of EO interventions. We consulted with a research librarian to develop the search strategy, and a second research librarian peer-reviewed the search strategy using the instrument for Peer Review of Search Strategies.¹³ The search of electronic databases queried Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE, Ovid PsycINFO, CINAHL, Epistomonikos, and Ovid EBM Reviews Cochrane Database of Systematic Reviews (CDSR, DARE, HTA, and Cochrane CENTRAL), and included all available years of publication from database inception (1946 for Ovid MEDLINE®) through February 2019; Appendix A provides the search strategies for each database. We further examined the bibliographies of relevant publications, searched the PROSPERO registry for

completed systematic reviews, and consulted subject matter experts for potentially relevant studies.

STUDY SELECTION

We applied pre-specified selection criteria (Appendix B) to assess the titles and abstracts yielded by the literature search. We used Abstrackr,¹⁴ an online tool for screening citations, and retrieved potentially relevant articles for review at the full-text level. Two investigators independently assessed all abstracts and full-text articles for inclusion and resolved disagreements through discussion and consensus.

We selected SRs and meta-analyses that included randomized controlled trials (RCTs) of clinical aromatherapy or topically applied essential oils for specific health indications, risk populations, or targeted settings such as healthcare waiting spaces.

We excluded reviews examining only children or adolescents. If an eligible SR included both pediatric and adult populations, we abstracted data from only the trials in adults.

We classified aromatherapy-massage (EO-massage) as an inhaled modality, and only included data from trials that included a massage-only control group. We similarly included data from 1 trial of aromatherapy combined with acupressure that included an acupressure-only control group. We excluded data from trials that did not control for concurrent interventions.

We excluded data from interventions in which oral or mucous membranes made direct contact with EOs, such as mouth rinses, vaginal applications, or orally ingested EO formulations. Table 1 specifies the criteria for population, interventions, comparators, outcomes, timing, and setting (PICOTS).

Table 1. PICOTS

Key Question	<p>What evidence is available on the effectiveness of aromatherapy or essential oils for health-related conditions?</p> <ul style="list-style-type: none"> ▪ In which health conditions/target populations have they been studied? ▪ Which formulations have been studied? ▪ What is the effect of the intervention in each health condition studied? 4 effect categories: <ul style="list-style-type: none"> • No effect • Unclear • Potential positive • Positive ▪ What is the level of confidence in the evidence for that effect? 4 confidence levels: <ul style="list-style-type: none"> • Insufficient • Low • Moderate • High
Population	Adults (18+) receiving an EO intervention for a targeted health condition or risk group.
Interventions	<i>Include:</i> Essential oil preparations that are inhaled or topically applied; massage with EO is included as an inhaled modality.

	<i>Exclude:</i> Essential oil preparations that are ingested, consumed, or absorbed through oral and mucosal membranes. Also exclude preparations where essential oils are combined with another drug or active ingredient.
Comparators	No limits for comparators of inhaled-only EO interventions. For EO-massage interventions, include only data from trials that had a massage-only comparator arm (eg, using an inert/carrier oil).
Outcomes	<ul style="list-style-type: none"> ▪ Psychological symptoms ▪ Physical outcomes ▪ Global outcomes (measures of quality of life or function, such as activities of daily living, mobility, social functioning, and employment) ▪ Harms
Timing	Any duration of treatment and follow-up
Study design	Systematic reviews and meta-analyses that include randomized controlled trials. Non-systematic reviews, reviews of reviews, and primary studies are excluded.
Setting	No limits

Potentially eligible SRs met all the following quality criteria: 1) clearly reported their search strategy and inclusion criteria; 2) performed a comprehensive search of at least 2 electronic databases; and 3) assessed the included studies for potential risk of bias and reported the findings.¹⁵

We identified the distinct health conditions and target populations that were examined by the potentially eligible SRs. When there were several qualified SRs of an intervention for the same health condition, we selected a single review to represent the evidence for that health condition or population, based on recentness, methodological quality, scope, and applicability.

DATA ABSTRACTION

From each SR selected for the evidence map, we abstracted the following data: targeted health condition or population of the SR, intervention modalities and comparators used among eligible trials, number of RCTs and CCTs, sample size, and findings. Data were abstracted by 1 investigator and confirmed by at least 1 additional reviewer.

Some of the SRs selected for the evidence map examined a range of complementary therapies for a targeted health condition or included trials of EO interventions that we excluded from our scope, such as orally ingested formulations, or trials comparing EO-massage versus usual care. We abstracted data from trials that met our PICOTS criteria (Table 1).

We abstracted outcome data in 6 categories: psychological symptoms, nausea/vomiting, pain and other physical outcomes, global outcomes (specifically measures of functional status or quality of life), sleep quality, and adverse effects. If the effect sizes or P-values for the primary trials were not reported in the SR, we relied on the qualitative summary of findings provided by the SR authors.

QUALITY ASSESSMENT

To qualify for inclusion in our evidence map, SRs were required to assess the methodological quality of RCTs using a standardized instrument, among other criteria.¹⁵ We took the

adjudications made by the primary SR authors at face value and used their quality assessments to rate the overall body of evidence.

DATA SYNTHESIS

We used the vector graphics in Microsoft Excel (2016) to generate scatter plots based on categorical values representing levels of effect and confidence in the evidence. The rows in the scatter plots present each of 26 health conditions/target populations. Each bubble represents the summary of findings for 1 of 5 outcome categories (psychological, nausea/vomiting, pain or other physical outcomes, global, and sleep). Because harms were infrequently reported, they are not represented in the evidence maps.

Two reviewers independently assessed the effectiveness of the interventions and confidence levels, based on data from eligible trials as reported in the systematic reviews. We resolved disagreements through discussion or by consulting a third reviewer until we reached consensus.

We classified the effect of the intervention for each targeted health condition and outcome as follows:

- *No effect*: a preponderance of null or negative findings.
- *Unclear*: the systematic review reported mixed findings for a single outcome, or mixed findings across multiple outcomes within the same category, with no preponderance of either benefit or negative effects.
- *Potential positive effect*: multiple outcomes within the same category (physical, psychological, global health, or sleep) with at least 1 clear finding of benefit; or mixed findings for a single outcome with a preponderance of evidence of a positive effect among RCTs.
- *Positive effect*: numerous studies or a large sample showing a positive effect.

For a modality to be classified as having a positive effect required consistent, statistically significant effects from well-conducted trials. When there were mixed findings for a single outcome that included both positive and null findings, we classified the overall effect as either unclear or potentially positive, depending on the preponderance of findings particularly among RCTs. If the findings across a group of studies were truly mixed to the extent that there was no preponderance of evidence in 1 direction or another, or if there were methodological limitations in the included trials, we classified it as unclear/insufficient. However, if there were a clear signal for benefit on at least 1 outcome in a category, we classified the overall body of evidence as having a potential positive effect.

We provide a narrative synthesis of findings according to treatment modality and outcome. Some SRs of inhaled EOs focused on a specific outcome such as nausea or sleep quality. Other SRs examined a specific health condition and reported multiple outcomes. We therefore compiled the findings for similar outcomes, grouping together psychological outcomes, nausea/vomiting, pain and other physical signs/symptoms, global outcomes, sleep quality, and adverse effects.

RATING THE BODY OF EVIDENCE

For each conclusion on the effect of an intervention (*ie*, no effect, unclear, potential positive, or positive effect) we characterized the level of confidence in the body of evidence specific to that outcome category and health-related condition. We calculated a rough estimate of confidence based on the number of participants in the included trials; the number of studies; the quality of the included trials, and the overall risk of bias; whether there were serious inconsistencies in the findings; and any limitations in the applicability of the evidence (Appendix C). Table 2 outlines the criteria we used for scoring.

Table 2. Domains for assessing level of confidence

Domain; range of points	Description
Sample size; 1 to 3	1: N ≤ 100 2: N = 100-500 3: N = 500+
Number of studies; -1 or 0	0: More than 1 study -1: Only 1 study
Consistency; -1 or 0	0: No major flaw -1: Serious inconsistency
Directness; -1 or 0	0: No major flaw -1: Limited applicability
Overall ROB/study quality; -1 or 0	0: Unclear or low ROB (good quality) -1: High ROB (poor quality)

ROB = Risk of bias

We used the sum of points from each domain to classify the level of confidence into 4 categories as follows:

- (3 points) *High*: Consistent findings from at least 2 studies with a large combined sample size and low risk of bias.
- (2 points) *Moderate*: Evidence comes from a single large study with no major flaws, or from 2+ studies with limitations in sample size, study quality, applicability, or consistency of findings.
- (1 point) *Low*: Small combined sample size, or major deficiencies in the body of evidence.
- (≤ 0 points) *Insufficient*: The body of evidence consists of only 1 small study or has unacceptable deficiencies.

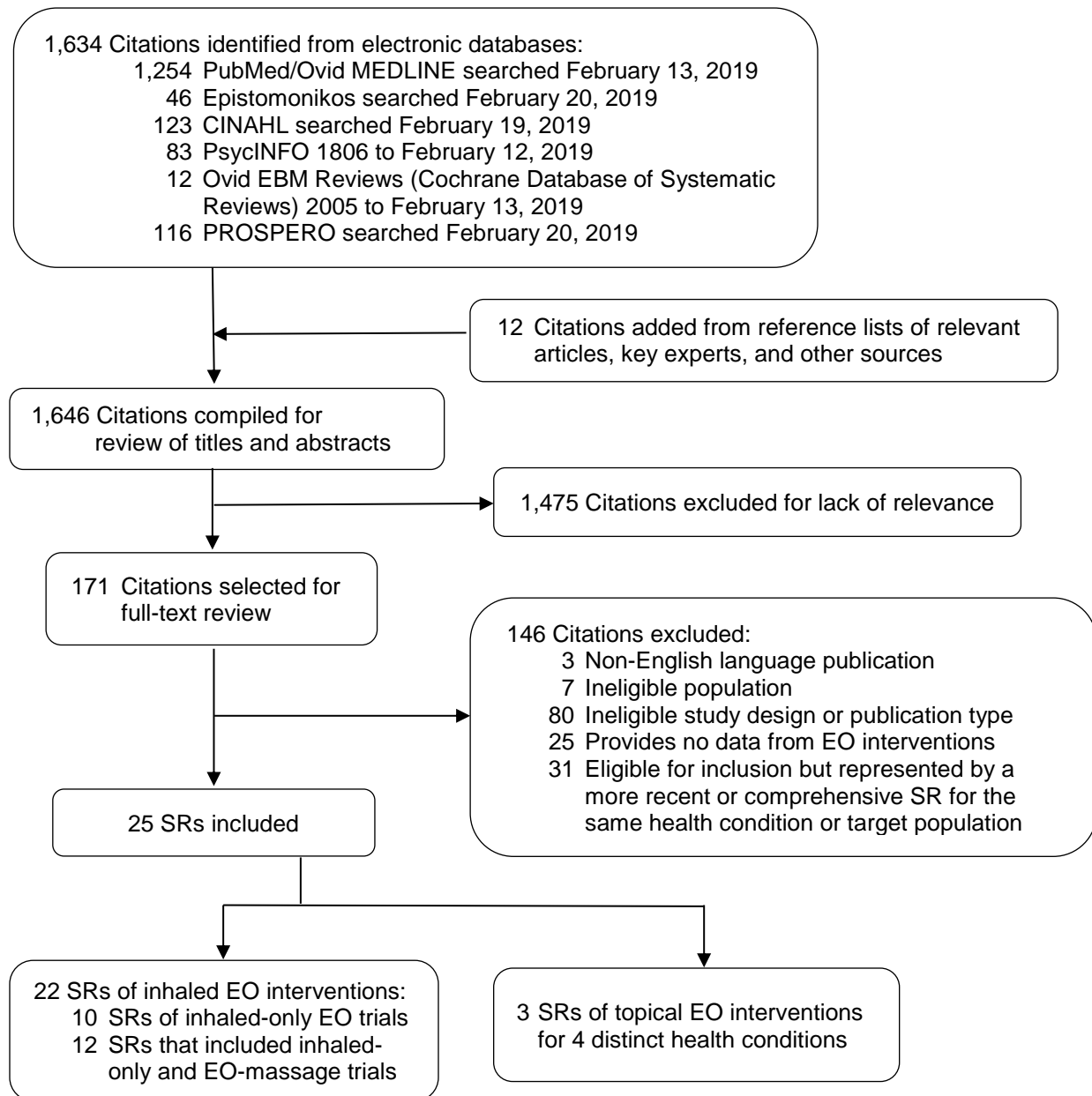
For the evidence maps, we grouped together studies with either unclear effect or insufficient level of confidence into a combined category of unclear/insufficient evidence.

RESULTS

LITERATURE FLOW

Our search of electronic databases, bibliographies, and other sources resulted in a total of 1,646 citations. After reviewing titles and abstracts, we included 171 for further screening at the full-text level. Of these, 56 SRs met our inclusion criteria. After reviewing all eligible SRs, we selected 25 SRs representing the most recent and comprehensive evidence available on each health-related condition and/or population (Figure 2).

Figure 2: Literature Flow Chart



Abbreviations: EO = essential oil; SR= systematic review

KEY QUESTION: What evidence is available that examines the effectiveness of aromatherapy or essential oils for health-related indications?

Twenty-six health-related conditions/target populations were examined by the 25 SRs selected for the evidence map. Twenty-two SRs provide evidence on inhaled EO interventions,¹⁶⁻³⁷ which encompass aromatherapy combined with massage (EO-massage) as well as inhaled-only aromatherapy. Three SRs provide evidence on topical EO interventions.³⁸⁻⁴⁰ One SR of topical EOs for various fungal infections included both tinea pedis and onychomycosis, and we present the findings for these health conditions separately.

Figure 3 shows the number of trials for each health condition according to treatment modality. Evidence from 171 eligible trials is represented among the 25 SRs. Hemodialysis, perioperative patients, dysmenorrhea, labor/childbirth, sleep, anxiety, and depression were the most widely studied conditions/populations. Aromatherapy interventions were most often delivered via inhalation, though the method of application varied widely. Inhaled EO studies used a range of administration methods: the EO could be released to the air by diffusion or vaporization, applied to cotton and attached to the subject's clothing, inhaled directly from a vessel, applied to the inside of a ventilation mask, or added to the lotion/oil used during massage – all of these were commonly described as aromatherapy. SRs of aromatherapy frequently included trials of aromatherapy-massage (Figure 3), which may involve direct dermal exposure through the addition of EO to massage lotion/oil or may be limited to inhalation only if the EO is diffused in the room during massage. In many cases the SR referred to the intervention simply as “aromatherapy-massage” without specifying whether the exposure was administered via massage oil or diffuser. When details of the methods of the EO-massage trials were provided, dermal contact was the most commonly described exposure method.

Table 3 specifies the outcomes reported for each health condition/target population. The results for these outcomes are presented in Figure 4, a map of the evidence for inhaled EO interventions in 22 health conditions. There is evidence that inhaled EOs are beneficial for pain in dysmenorrhea,²³ and the level of confidence in the evidence is moderate. Inhaled EOs have potential benefit for physical symptoms during labor/childbirth²⁶ (moderate confidence) and for patients with hypertension²⁵ (low confidence). Two SRs provided low-confidence evidence of a potential positive effects on sleep quality.^{24,35} There is moderate-confidence evidence that aromatherapy has no effect on anxiety in palliative care.¹⁸ The effects of inhaled EOs are unclear for nausea/vomiting, and for all other conditions studied.

Figure 5 presents an evidence map for the effects of topical EO interventions for 4 health conditions. There is evidence of potential effectiveness in the use of topical tea tree oil for tinea pedis,⁴⁰ and the level of confidence in the evidence is moderate. The effectiveness of topical EOs is unclear for onychomycosis, acne, and episiotomy wound healing.

Table 3. Populations, health conditions, and/or symptoms addressed in systematic reviews of essential oil interventions

Label used in figures	Comments about study samples	Outcome category	Targeted symptom or measured outcome
Acne ³⁸	1 trial in patients with mild to moderate facial acne vulgaris	Physical	Skin lesion count, acne severity
Anxiety, healthcare waiting spaces ¹⁷	Samples included patients awaiting dental or surgical procedures	Psychological	Anxiety
Anxiety, palliative care ¹⁸	Participants included patients rather than caregivers	Psychological	Anxiety
Anxiety, various populations ¹⁹	Samples included patients with clinical anxiety, other health conditions or settings (eg, cancer, perioperative, ICU, colonoscopy), or healthy volunteers	Psychological	Anxiety
Complications, hemodialysis ²⁴	---	Psychological Physical Global Sleep	Anxiety; depression; stress Fatigue, pruritis QOL Sleep quality
Depressive symptoms, various populations ²²	Only 1 of 8 eligible studies targeted patients with depression or anxiety. The others enrolled healthy volunteers or those with various health conditions (eg, cancer, pregnancy, postpartum, mothers of children with ADHD)	Psychological	Depressive symptoms measured by various scales
Dysmenorrhea ²³	---	Physical	Pain
Nausea/vomiting, postoperative ²⁶	Studies of patients undergoing a variety of surgical procedures	Nausea/vomiting	Nausea severity
Nausea/vomiting, early pregnancy ²⁸	---	Psychological Nausea/vomiting	Satisfaction with treatment Nausea and vomiting severity; vomiting intensity
Onychomycosis ⁴⁰	---	Physical	Conversion to negative culture; resolution of symptoms
Pain, hemiplegic shoulder pain after stroke ²⁹	---	Physical	Pain
Pain, postoperative ³⁰	Samples included various surgical procedures	Physical	Pain
Perioperative symptoms, various surgery types ³¹	Samples included various surgical procedures	Psychological Physical Nausea/Vomiting	Anxiety Pain Nausea/Vomiting
Physical symptoms, labor/childbirth ²⁶	---	Physical	Pain, duration of labor, emergency C-section, spontaneous membrane

Label used in figures	Comments about study samples	Outcome category	Targeted symptom or measured outcome
			rupture, and spontaneous labor onset
Psychological symptoms, women aged 45+ ³²	Peri- and post-menopausal women	Psychological	Anxiety; depression
SBP/DBP, hypertension ²⁵	Patients with hypertension or pre-hypertension	Physical	SBP, DBP
Sexual symptoms, women aged 45+ ³³	Peri- and post-menopausal women	Psychological	Sexual desire; vaginal dryness during intercourse, avoiding intimacy
Sleep, critical care/ICU ³⁴	---	Sleep	Sleep quality
Sleep, various populations ³⁵	Samples included mostly healthy volunteers, and some patients with insomnia or ischemic heart disease	Sleep	Sleep quality
Stress, healthy adults ³⁶	---	Psychological	Stress
Stress, nurses ³⁷	---	Psychological	Work-related stress
Symptom relief, burn patients ²⁰	---	Psychological Physical Sleep	Anxiety Pain Sleep quality
Symptom relief, cancer ²¹	Samples included patients with various forms of cancer	Psychological Physical Global	Anxiety Pain, mobility, tiredness, and various other physical symptoms (from RSCL) QOL; functioning
Tinea pedis ⁴⁰	'---	Physical	Conversion to negative culture; resolution of symptoms
Various symptoms, dementia ¹⁶	'---	Psychological Global	Behavioral and psychological symptoms of dementia (BPSD); cognitive function; agitation; resistance to taking medication; relationship with caregiver ADL; QOL
Wound healing, episiotomy ³⁹	'---	Physical	Redness; edema; ecchymosis; discharge; approximation; exudation; dyspareunia

Abbreviations: ADL = activities of daily living; BPSD = Behavioral and psychological symptoms of dementia; DBP = diastolic blood pressure; EO = essential oil; QOL = quality of life; RSCL = Rotterdam Symptom Checklist; SBP = systolic blood pressure; SR = systematic review

Note: All studies in a review may not have addressed each population or condition

Figure 3. Number of trials of essential oil interventions for targeted health conditions/populations, by treatment modality

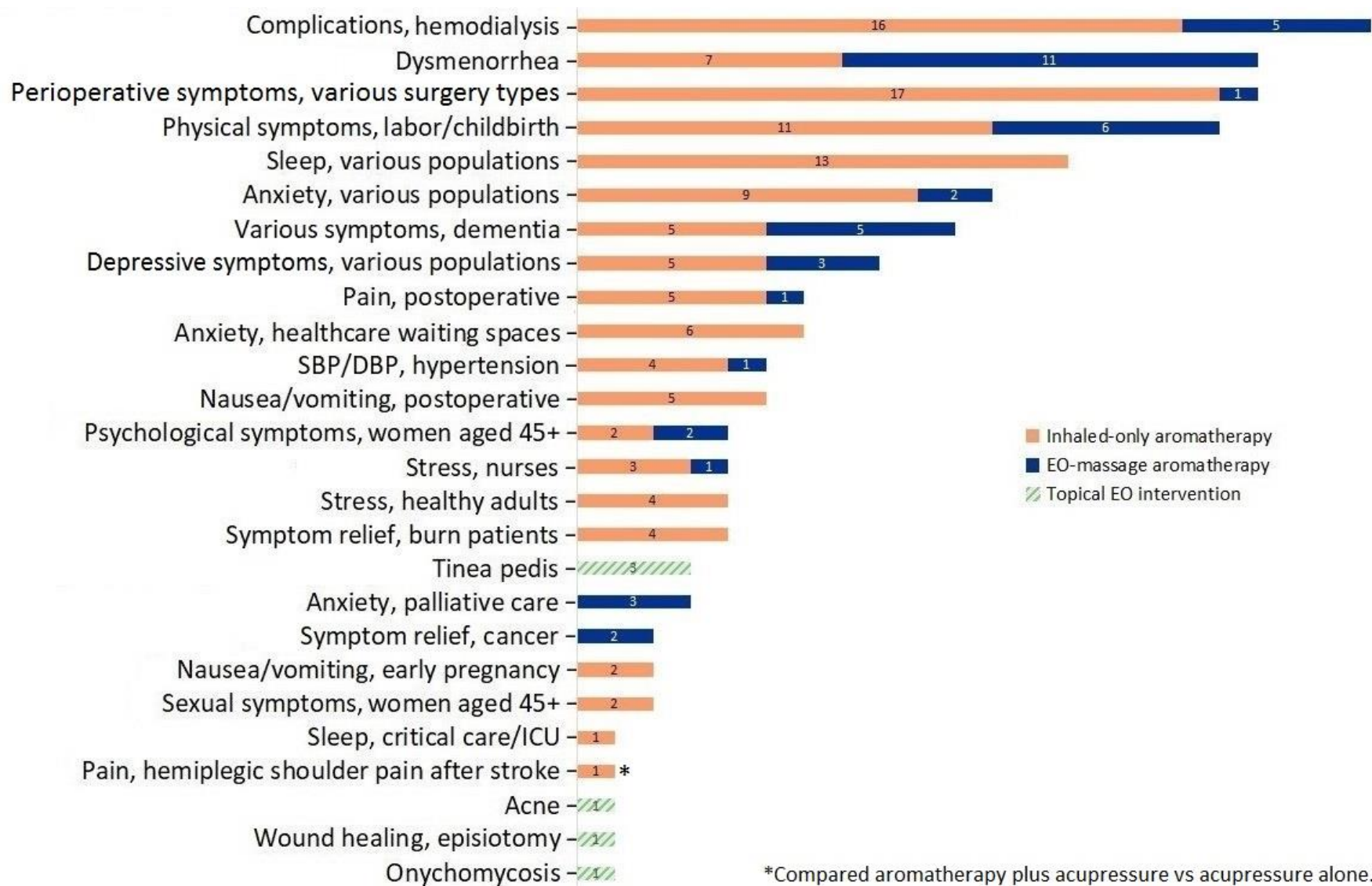
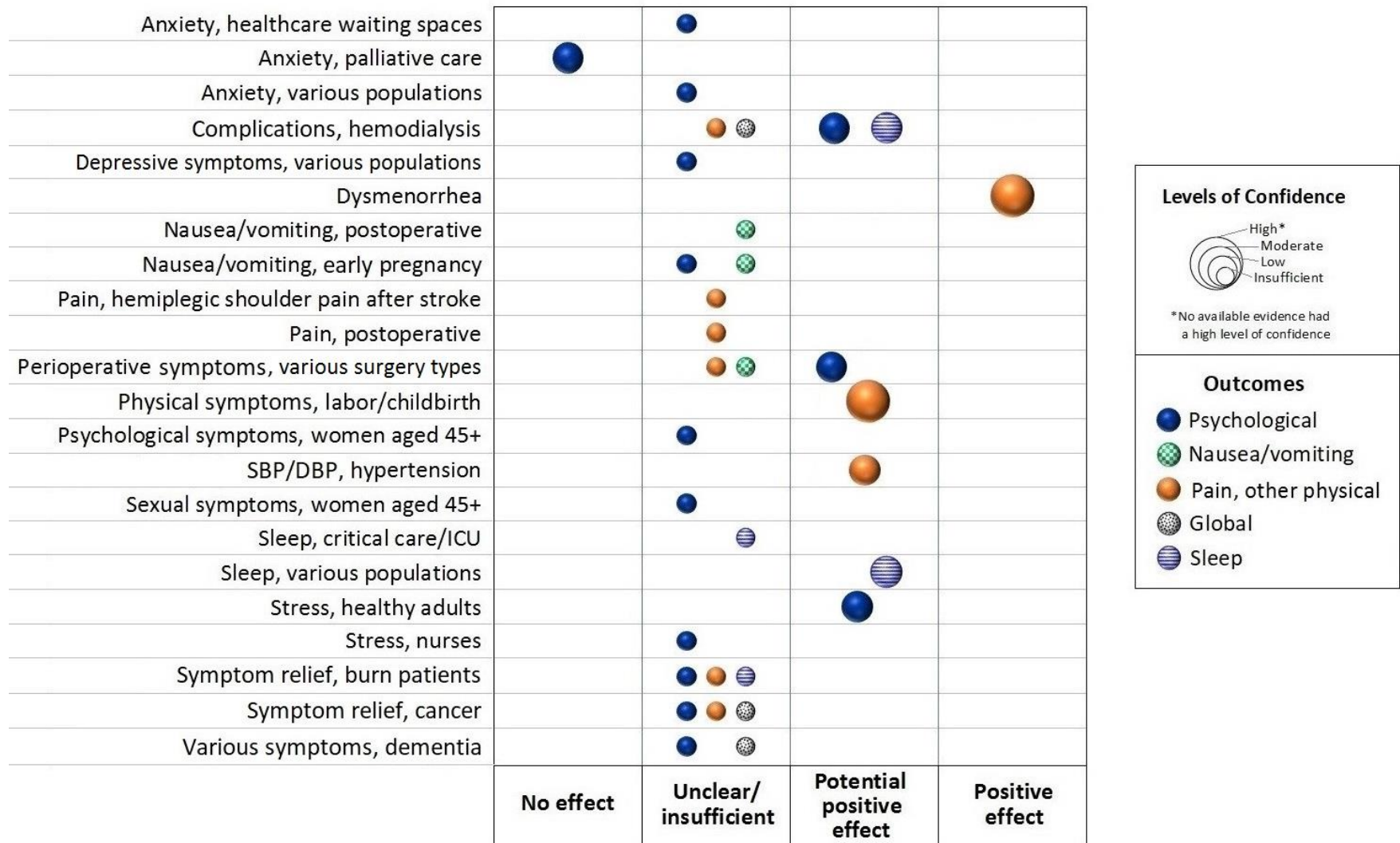


Figure 4. Map of the evidence from systematic reviews of inhaled essential oils for targeted health conditions/populations



Inhaled EO interventions - Psychological outcomes

Seven SRs examined the effects of inhaled EOs on anxiety and reported mixed findings. Table 4 provides a summary of the findings. An SR of hemodialysis patients found potential positive effects on anxiety, depression, and stress,²⁴ and an SR of perioperative patients found a potential positive effect on reducing anxiety.³¹ The level of confidence in these findings was low. A meta-analysis of 3 RCTs found no effect on anxiety in palliative care (low confidence).¹⁸ Evidence of effectiveness for anxiety was unclear for waiting room settings,¹⁷ burn patients,²⁰ cancer,²¹ hemodialysis,²⁴ women aged 45+,³² and in an SR of various populations.¹⁹

Of 3 SRs that examined stress, 2 found evidence of a potential positive effect (low confidence) in healthy adults³⁶ and hemodialysis patients.²⁴ Evidence of effect was unclear in an SR of occupational stress among nurses.³⁷

The effects of inhaled EO interventions on depression, behavioral problems in dementia, and other psychological outcomes were also unclear (Table 4).

Table 4. Psychological health outcomes in systematic reviews of inhaled essential oil interventions

Health condition, population N trials (N pts) EO modality	Findings	Overall effect	Level of confidence
Anxiety, healthcare waiting spaces ¹⁷ 5 RCTs (N=793) 1 CCT (N=72) Inhaled	<u>Anxiety in health care waiting rooms (5 RCTs, N=793; 1 CCT N=72):</u> Mixed findings. <u>2 low-ROB RCTs of dental patients (N=219 and N=340):</u> reduction in anxiety in 1, no difference in the other. <u>3 unclear-ROB RCTs of pts awaiting surgical procedures (N=234):</u> significant reduction with aromatherapy, although 1 RCT included the effect of a soothing nature DVD. Effect sizes and p-values NR. <u>1 CCT of pts awaiting surgery (N=72):</u> STAI score 11.0(±2.2) points lower with AT after waiting period, P-value NR.	Unclear	Insufficient
Anxiety, palliative care ¹⁸ 3 RCTs (N=160) of EO-massage	<u>Anxiety (3 high-ROB RCTs; N=160):</u> No difference; Anxiety by STAI (MD= -2.60 [95% CI: -7.82 to 2.63], P = 0.33). Heterogeneity NS ($\chi^2=2.31$, P=0.31, I ² =13%).	No effect	Low
Anxiety, various populations ¹⁹ 11 RCTs (N=1,076) Inhaled only: 9 RCTs EO-massage: 2 RCTs Lavender	<u>Anxiety (9 high-ROB RCTs, N=964):</u> 3 RCTs favored Tx (P ≤ 0.05 reported), 6 RCTs found no effect. Effect sizes and P-values NR. <u>Stress (3 high-ROB RCTs, N=152):</u> Significant reduction in 1 RCT (N=42, P < 0.01), 2 RCTs found no effect. Effect sizes NR.	Unclear	Insufficient
Symptom relief, burn patients ²⁰ 4 RCTs (N=248) Inhaled Lavender and/or rose	<u>Anxiety (2 high-ROB RCTs; N=110):</u> Mixed findings. 1 RCT (N=60) found significant benefit: STAI -0.93 [95% CI -1.46 to - 0.39], P=0.0007 1 RCT (N=60) found no effect: STAI -0.46 [95% CI -0.97 to 0.05]	Unclear	Insufficient
Symptom relief, cancer ²¹ 2 RCTs (N=139) of EO-massage	<u>Anxiety immediately following massage (2 high-ROB RCTs, N=139):</u> Mixed effects. 1 RCT (N=52) found significantly greater reduction in massage-only control. 1 RCT (N=87) found benefit in both T and C. Effect sizes NR; differences between groups NR. <u>Anxiety longer-term (2 high-ROB RCTs, N=139):</u> Mixed findings. 1 RCT (N=52) found no differences between groups. 1 RCT (N=87) found improvement on RSCL subscales: psychological (P < 0.01), severe psychological (P < 0.01); no significant change in anxiety with massage-only. Effect sizes NR; differences between groups NR.	Unclear	Insufficient

Health condition, population N trials (N pts) EO modality	Findings	Overall effect	Level of confidence
Various symptoms, dementia ¹⁶ 10 RCTs (N=363) 8 Inhaled-only 2 Massage-EO	<p><u>BPSD</u>: 2 unclear-ROB RCTs (N=91) found greater reduction in BPSD in Tx group, effect sizes NR. 1 RCT reported P<0.01; P-value NR in 1 RCT.</p> <p><u>Cognitive function (1 high-ROB RCT, N=28)</u>: Significant improvement in Tx group. Effect size and P-value NR.</p> <p><u>Agitation</u>: Mixed findings. 2 RCTs found significant reduction: 1 low-ROB RCT (N=72) effect size and P-value NR; 1 unclear-ROB RCT (N=70) significant reduction on agitation and other symptoms (P < 0.01)</p> <p>2 RCTS found no difference: 1 low-ROB RCT (N=114) and 1 high-ROB RCT (N=7). Effect size and P-values NR.</p> <p><u>Resistance to taking medication (1 high-ROB RCT, N=13)</u>: No difference. Effect size and P-value NR.</p> <p><u>Relationship with caregiver (1 high-ROB RCT, N=16)</u>: Positive improvement. Effect size and P-value NR.</p>	Unclear	Insufficient
Depressive symptoms, various populations ²² 8 RCTs (N=858) Inhaled only: 5 RCTs EO-massage: 3 RCTs	<p><u>Improvement in depressive symptoms (8 RCTS; N = 858)</u>: <u>EO inhaled only (5 RCTs, N=694)</u>: Mixed findings. In 1 high-ROB RCT of 40 healthy volunteers: change in TMD score -1.28 ± 2.6 vs 0.5 ± 2.2 (P<0.05). In 1 high-ROB RCT of 28 postpartum women: mean difference in EPDS scores at end point was -3.981 (P = NS).</p> <p>1 Unclear RCT in 13 pregnant women and 2 Low-ROB RCTs (313 cancer pts receiving radiotherapy and 320 pregnant women) found no stat. sig. differences.</p> <p><u>EO massage (3 RCTs, N=164)</u>: Mixed findings. 1 high-ROB RCT in 32 pts with depression and/or anxiety found benefit: baseline/endpoint MADRS scores: 30/18.1 vs 19.8/21.1 (P<0.05).</p> <p>1 low-ROB RCT in 42 cancer pts and 1 high-ROB RCT in 90 women aged 45-60 found no stat. sig differences.</p>	Unclear	Insufficient
Complications, hemodialysis ²⁴ 15 RCTs (N=865) 7 CCTs (N=332) Inhaled only: 14 RCTs and 2 CCTs EO-massage: 1 RCT and 5 CCTs	<p>Mixed findings with preponderance of benefit. Effect sizes and P-values NR.</p> <p><u>Anxiety (6 unclear-ROB RCTs; N=335)</u>: 5 RCTs favor tx; 1 found no effect.</p> <p><u>Depression (3 unclear-ROB RCTs; N=192)</u>: All 3 favor tx; 1 RCT found significant positive effect on depression but no effect on anxiety.</p> <p><u>Stress (2 unclear-ROB RCTs; N=120)</u>: Both favor tx.</p>	Potential positive	Low
Early pregnancy ²⁸ 1 unclear-ROB RCT, N=100 Inhaled-only; Lemon oil	<p><u>Satisfaction with treatment</u>: No difference. MD = 1.47 (95% CI: 0.91 to 2.37), P = 0.11</p>	Unclear	Insufficient



Health condition, population N trials (N pts) EO modality	Findings	Overall effect	Level of confidence
Perioperative symptoms, various surgical procedures ³¹ 14 RCTs (N=1,571) 4 CCTs (N=342) Inhaled-only except for 1 RCT (Massage-EO)	<u>Anxiety reduction, various surgery types: 4 RCTs (N=336)</u> Mixed findings with potential positive effects. 1 low-ROB RCTs (N=109) found significant difference in STAI: -3 vs -2 (P = 0.02). 1 low-ROB RCT (N=60) found no sig. differences in STAI at any timepoint (12.6 vs 42.73 after intervention; 41.33 vs 41.56 at 3d post-op). 1 high-ROB RCT (N=87) found reduction in STAI (48 to 37) with lavender-sandalwood (P=0.03 vs placebo 43 to 39) but not with orange-peppermint (43 to 37). 1 CCT of 72 cardiac and general surgery pts found significant improvement: STAI -12.4 vs -2.4 (P < 0.01).	Potential positive	Low
Psychological symptoms, women aged 45+ ³² 4 RCTs (N=296) Inhaled : 2 RCTs EO-massage: 2 RCTs	<u>Short-term effect on psychological symptoms (anxiety and depression; 4 high-ROB RCTs, N=296):</u> Multiple dissimilar rating scales for outcomes were reported in MA, therefore effect was rated unclear.	Unclear	Insufficient
Sexual symptoms, women aged 45+ ³³ 2 RCTs (N=181) Inhaled only	<u>Sexual desire (1 high-ROB RCT; N=100):</u> significantly improved with lavender. Effect size and P-value NR. <u>MENQOL - sexual domain (1 unclear-ROB RCT, N=81):</u> Significant improvement with neroli oil. Effect size and P-value NR.	Unclear	Insufficient
Stress, healthy adults ³⁶ 4 RCTs (N=123) of inhaled only	<u>Subjective stress level (MA of 3 RCTs, 2-high ROB, 1 unclear-ROB, N = 80):</u> Favors treatment. SMD = -0.96 (95% CI: -1.44 to -0.48), Z = 3.93, P < 0.0001; heterogeneity: I ² = 0%, P = 0.58. Another high-ROB RCT (N=30) not included in MA found no difference.	Potential positive	Low
Stress, nurses ³⁷ 1 RCT (N=32) of EO-massage 3 CCTs (N=195) of inhaled only	<u>Work-related stress 1 high-ROB RCT (N=32), 3 CCTs (N=195):</u> 1 6-wk RCT found significant interaction between time and group (P < 0.05). 1 CCT (N=110) found reduction on days 3-4 of 4-day trial. 1 CCT (N=14) found mixed results. Effect sizes and P-values NR in the CCTs. 1 CCT (N=71) found no effect on workplace stress.	Unclear	Insufficient

Abbreviations: BPSD = Behavioral and Psychological Symptoms of Dementia; CCT = clinical controlled trial; EO = essential oil; EPDS = Edinburgh Postnatal Depression Scale; MA = meta-analysis; MADRS = Montgomery-Åsberg Depression Rating Scale; MD = mean difference; MENQOL = Menopause-specific Quality of Life Questionnaire; NR = not reported; NS = not significant; P = p-value; PBO = placebo; pts = participants; RCT = randomized controlled trial; ROB = risk of bias; RR = risk ratio; RSCL = Rotterdam Symptom Checklist; SMD = standard mean difference; STAI = State-Trait Anxiety Inventory; TMD = Total Mood Disturbance; tx = treatment.

Inhaled EO interventions – Nausea/vomiting

Three SRs provided data on the effects of inhaled EOs on nausea/vomiting (see Table 5 for a summary of findings). SRs in perioperative³¹ and postoperative²⁷ patients reported mixed findings. An SR of aromatherapy during pregnancy also reported mixed findings. The overall effectiveness for nausea/vomiting was unclear in all 3 reviews.

Table 5. Effects of inhaled EO interventions on nausea/vomiting

Target population N trials (N pts) EO modality	Findings on nausea/vomiting	Overall effect	Level of confidence
Perioperative symptoms, various surgical procedures ³¹ 6 high-ROB RCTs, N=901; 1 CCT, N=60 Inhaled-only	Various EOs and measures used among trials; peppermint oil used most commonly. Mixed findings: 4 RCTs and 1 CCT reported statistically significant positive effects. 2 RCTs reported null effects. Unclear effect reported in 1 CCT.	Unclear	Insufficient
Postoperative ²⁷ 4 high-ROB RCTs (N=115) Inhaled-only	MA of 4 RCTs of peppermint oil, Nausea severity at 5 minutes post-initial treatment: no difference; SMD = -0.18 (95% CI: -0.86 to 0.49). Significant heterogeneity: I ² = 66% (P = 0.03)	Unclear	Insufficient
Early pregnancy ²⁸ 2 RCTs (N=160) Inhaled-only	Mixed effects: 1 unclear-ROB RCT (N=100) of lemon oil: PUQE score on day 3 of intervention: no effect, mean difference -0.46 (95% CI: -1.27 to 0.35), P=0.27 PUQE scores from baseline to day 3 of intervention: Significant improvement; mean difference -1.50 (95% CI -2.41 to -0.59), P=0.0012 1 high-ROB RCT (N=60) of mint oil: Severity of nausea on day 4: no effect: mean difference -0.88 (95% CI: -1.93 to 0.17), P=0.099 Vomiting intensity on day 4: no effect, mean difference -0.32 (95% CI: -1.45 to 0.81), P=0.58	Unclear	Insufficient

Abbreviations: CCT = clinical controlled trial; EO = essential oil; MA = meta-analysis; NR = not reported; NS = not significant; P = p-value; PBO = placebo; pts = participants; PUQE = Pregnancy-Unique Quantification of Emesis/Nausea; RCT = randomized controlled trial; ROB = risk of bias; SMD = standard mean difference.

Inhaled EO interventions – Pain and other physical signs/symptoms

Seven SRs reported pain outcomes in trials of inhaled EO interventions. Table 6 provides a summary of the findings. An SR of dysmenorrhea found statistically significant effects on pain reduction in a meta-analysis of 7 RCTs of inhaled-only EO (SMD = -1.02, 95% CI -1.59 to -0.44) and in a meta-analysis of 11 RCTs of EO-massage (SMD = -0.87, 95% CI -1.14 to -0.60), although there was significant heterogeneity in both analyses.²³ The overall effect was positive and the level of confidence was moderate, in part due to the large number of trials (17) and combined sample size (N=1,534).

There was evidence of a potential positive effect on labor pain,²⁶ and the level of confidence was moderate.

Inhaled EO was associated with reduced systolic and diastolic blood pressure in patients with hypertension, based on evidence from a small high-ROB RCT and 4 CCTs.²⁵ Given limitations in the study methods, we rated the evidence of effectiveness for hypertension as potential positive, with a low level of confidence.

Table 6. Effects of inhaled EO interventions on pain and other physical signs/symptoms

Health condition, population N trials (N pts) EO modality	Findings	Overall effect	Level of confidence
Symptom relief, burn patients ²⁰ 4 RCTs (N=248) Inhaled lavender and/or rose	<u>Pain (2 high-ROB RCTs; N=110):</u> significant effect in both. 1 RCT (N=50) effect estimate: -1.22 [95% CI -1.83 to -0.61], P<0.0001; 1 RCT (N=60) effect estimate: -0.67 [95% CI -1.19 to -0.14], P=0.01. SR authors note heterogeneity in study characteristics, evidence insufficient for concluding effectiveness.	Unclear	Insufficient
Symptom relief, cancer ²¹ 2 RCTs (N=139) of EO-massage	<u>Pain, mobility, tiredness (1 high-ROB RCT; N=52):</u> No difference between groups. <u>Physical symptoms (1 high-ROB RCT; N=87):</u> Within tx group improvement on physical (P < 0.05) and severe physical symptoms (P < 0.001) on RSCL subscales. Effect sizes NR; differences between groups NR.	Unclear	Insufficient
Dysmenorrhea ²³ 17 RCTs (N=1,534) Inhaled only: 7 RCTs EO-massage: 11 RCTs (1 RCT of both inhaled EO-massage)	<u>Pain in RCTs of Inhaled EO (7 RCTs, 2 low-ROB, 5 unclear-ROB, N = 817):</u> SMD -1.02 (95% CI: -1.59 to -0.44), significant heterogeneity I ² = 95% (P<0.0001) <u>Pain in RCTs of EO Massage (11 RCTs, 1 low-ROB, 10 unclear-ROB, N = 791):</u> SMD -0.87 (95% CI: -1.14 to -0.60), significant heterogeneity I ² = 70% (P = 0.0001)	Positive	Moderate
Complications, hemodialysis ²⁴ Fatigue: 4 RCTs (N=201) Inhaled-only Pruritus: 4 CCTs (N=163) EO-massage	<u>Fatigue (2 low-ROB and 2 unclear-ROB RCTs; N=201):</u> Mixed findings. Lavender had a positive effect on fatigue reducing fatigue in 2 RCTs (1 low-ROB, 1 unclear-ROB. 2 other RCTs (1 low-ROB, 1 unclear-ROB) found lavender had no effect. Effect sizes and P-values NR. <u>Pruritus: 4 CCTs (N=163):</u> reported a positive effect on reducing pruritus. Effect sizes and P-values NR. No data from RCTs.	Unclear	Insufficient
SBP/DBP, hypertension ²⁵ 1 RCT (N=30), 4 CCTs (N=170) Inhaled only: 1 RCT and 3 CCTs EO-massage: 1 CCT	<u>SBP (1 high-ROB RCT, N=30; 4 CCTs, N=170):</u> significant decrease P < 0.00001 in RCT; 2 CCTs (N=103) found significant decrease; 2 CCTs (N=67) no data. <u>DBP (1 high-ROB RCT, N=30; 4 CCTs, N=170):</u> Significant decrease in 1 RCT, P < 0.00001; 2 CCTs (N=103) found significant decrease, 2 CCTs (N=67) no data.	Potential positive	Low

Health condition, population N trials (N pts) EO modality	Findings	Overall effect	Level of confidence
Physical symptoms, labor/childbirth ²⁶ 17 RCTs (N=1,926) Inhaled only: 11 RCTs EO-massage: 6 RCTs	<p><u>Pain:</u> <i>Pain score in trials with dilation info</i> (6 RCTs, 1 high-, 5 unclear-ROB; N=656 baseline; 652 post): baseline ND (MD=0.09[-0.12 to 0.30]; Z=0.86 [P=0.39]); post-intervention significant reduction (MD=-0.82 [-1.55 to -0.09]; Z=2.21 [P=0.03]) <i>Pain score in trials without dilation info</i> (4 RCTs, 2 high-, 2 unclear-ROB; N=364): baseline ND (MD=-0.09 [-0.37 to -0.19]; Z=0.62 [P=0.53]); post-intervention significant reduction (MD=-2.01 [-3.63 to -0.39]; Z=2.43 [P=0.02]) <u>Duration of labor:</u> <i>Total First-stage labor duration</i> (4 RCTs, 2 high-, 2 unclear-ROB; N=737): No difference (MD=-0.62 [-1.70 to 0.47]; Z=1.11 [P=0.27]) <i>Active First-stage labor duration</i> (6 RCTs, 1 low-, 5 unclear-ROB; N=531): Significantly shorter (MD=-0.69[-1.02 to -0.36]; Z=4.08 [P<.0001]) <i>Second stage labor duration</i> (10 RCTs, 3 high-, 7 unclear-ROB; N=1,246): No difference (MD=-3.92[-8.42 to 0.58]; Z=1.71 [P=0.09]) <i>Third stage labor duration</i> (4 RCTs, 1 high-, 3 unclear-ROB; N=228): Significantly shorter (MD=-3.32[-6.26 to -0.38]; Z=2.21 [P=0.03]) <u>Other outcomes:</u> <i>Incidence of emergency C-section</i> (6 RCTs, 1-high-, 1-low, 4 unclear-ROB; N=988): No difference (RR=0.78 [0.48 to 1.26]; Z=1.01 [P=0.31]) <i>Incidence of spontaneous membrane rupture</i> (2 RCTS, 1 high-, 1unclear-ROB; N=573): No difference (RR=1.00 [0.64 to 1.56]; Z=0.01 [P=0.99]) <i>Incidence of spontaneous labor onset</i> (2 RCTS, 1 high-, 1unclear-ROB; N=573): No difference (RR=0.99 [0.89 to 1.10]; Z=0.19 [P=0.85])</p>	Potential positive	Moderate
Pain, hemiplegic shoulder pain after stroke ²⁹ 1 RCT (N=30) Inhaled + acupressure (vs acupressure)	<p><u>Pain:</u> 1 unclear-ROB RCT, N = 30 of aromatherapy plus acupressure vs acupressure control (20 min 2x daily for 14 days) Positive effect on mean (3 days) pain score: -1.936 (95% CI: -2.788 to -1.085)</p>	Unclear	Insufficient
Pain, postoperative ³⁰ 6 RCTs (N=474) Inhaled only: 5 RCTs EO-massage: 1 RCTs	<p><u>Pain</u> (6 RCTs; N=474): 2 RCTs (1 high-,1 unclear-ROB; N=104), found no difference. 4 RCTs (2 high-, 2 unclear-ROB; N=373) found greater decrease with AT. Effect size and P-value NR.</p>	Unclear	Insufficient
Perioperative symptoms, various surgical procedures ³¹ 14 RCTs (N=1,571) 4 CCTs (N=342) Inhaled-only except for 1 RCT (Massage-EO)	<p><u>Pain (various surgery types; 5 RCTs, N=414; 1 CCT, N=40):</u> Mixed findings. 4 high-ROB RCTs (N=354) reported significant benefit on various pain measures (10-pt VAS or NAS most commonly) at time points from 5 min to 16 h post-op. 1 low-ROB RCT (N=60, vitrectomy) reported similar reductions on day 1 between massage-EO (eucalyptus-lemon oil) vs neutral oil: FPS score for shoulder -1.1 vs -0.8, neck -0.85 vs -0.8, back -0.75 vs -0.6. P-values NR. No sig diff in NAS reduction in 1 CCT of 40 cardiac surgery pts: 5.6 to 5.0 after lavender inhalation, P = NS.</p>	Unclear	Insufficient

Abbreviations: AT = aromatherapy; CCT = clinical controlled trial; DBP = diastolic blood pressure; EO = essential oil; FPS = Faces Pain Scale; h = hours; MA = meta-analysis; NAS = numerical analog scale; NR = not reported; NS = not significant; P = p-value; PBO = placebo; pts = participants; RCT = randomized controlled trial; ROB = risk of bias; RSCL = Rotterdam Symptom Checklist; SBP = systolic blood pressure; SMD = standard mean difference; SR = systematic review; tx = treatment; VAS = visual analog scale.

Inhaled EO interventions – Sleep quality

The effects of inhaled EOs on sleep quality were reported in 4 SRs. Table 7 provides a summary of the findings. Potential positive effects were reported in 2 SRs. Evidence of effectiveness in 2 other SRs was unclear.

An SR of inhaled EO in hemodialysis patients provided evidence from 4 trials that suggested a potential positive effect on sleep quality,²⁴ though the confidence in the evidence was low. Another SR examined the use of aromatherapy for sleep promotion in a variety of populations that included patients with a health condition as well as healthy volunteers.³⁵ Among the 9 trials identified, 6 reported statistically significant improvements in sleep quality. The preponderance of benefit suggests a potential positive effect, although methodological limitations in the trials rendered the level of confidence low.

An SR of non-pharmacological interventions for sleep promotion in critical care patients identified 1 RCT (N=25) of aromatherapy, and found no evidence of benefit.³⁴ Because the evidence is based on only 1 small trial, the level of confidence in this finding is unclear/insufficient. An SR of aromatherapy for symptom relief in burn patients provided data from an RCT comparing lavender with music therapy, which also provided unclear evidence of effectiveness.²⁰

Table 7. Sleep quality in systematic reviews of inhaled essential oil interventions

Population N trials (N pts)	Intervention characteristics	Findings	Summary of effect	Level of confidence
Burn patients ²⁰ 1 unclear-ROB RCT (N=48)	7 drops of 10% lavender vs music therapy for 20 min, 3 nights	Lavender vs music therapy, sleep quality VAS: 0.48 [95% CI -1.05 to 0.09]	Unclear	Insufficient
Hemodialysis ²⁴ 2 low-ROB and 1 unclear-ROB RCTs (N=182) 1 CCT (N=53)	Lavender or orange EO applied near patient (eg, to patient's collar; cotton ball 6-8 inches from pillow; or gauze bandage 2 inches from nose). Variation in exposure: 1 RCT during hemodialysis; 1 RCT and 1 CCT throughout the night; 1 RCT not specified	Preponderance of benefit; heterogeneity in timing and methods of EO exposure. Effect sizes and P-values NR.	Potential positive	Low
Critical care/ICU ³⁴ 1 high-ROB RCT (N=25)	1 drop of lavender oil vs 1 drop distilled water applied to pillowcase for 1 night each; 15 hours washout between	No between-group differences in RCSQ sleep scores: mean 59.84 (2.91) vs 63.28 (2.48), P-value NS.	Unclear	Insufficient

Various populations ³⁵ 9 unclear/high-ROB RCTs (N=265) 4 CCTs (N=58)	Various methods and durations, such as Aromastream device used continuously through the night in 1 RCT; vial held 3 inches from nose for 3 minutes in another RCT. Lavender oil used most frequently.	Mixed findings with preponderance of benefit. 1 RCT of peppermint, 1 RCT of jasmine, and 4 RCTs of lavender, found statistically significant results for improved sleep quality. Effect sizes NR.	Potential positive	Low
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Abbreviations: AT = aromatherapy; CCT = clinical controlled trial; EO = essential oil; NR = not reported; NS = not significant; P = p-value; PBO = placebo; pts = participants; RCSQ = Richards-Campbell Sleep Questionnaire; RCT = randomized controlled trial; ROB = risk of bias; VAS = visual analog scale.

Inhaled EO interventions – Global outcomes

Global outcomes were seldom reported among the SRs of inhaled EO interventions. Three SRs provided data on global outcomes from 3 RCTs and 2 CCTs. Table 8 presents a summary of the findings. The effects of inhaled EO on global outcomes were unclear in patients with cancer,²¹ dementia,¹⁶ and hemodialysis.²⁴ The evidence is insufficient for drawing conclusions.

Table 8. Global outcomes reported in systematic reviews of inhaled EO interventions

Health condition N trials (N pts) EO modality	Findings	Overall effect	Level of confidence
Cancer ²¹ 2 RCTs (N=139) of EO-massage	<u>Function</u> (1 high-ROB RCT; N=52): Within tx group effect (P<0.03), but no significant differences between groups. <u>QOL</u> (1 high-ROB RCT; N=87): Tx group improved on RSCL subscales (P < 0.001); no significant changes for massage-only control. Effect sizes NR.	Unclear	Insufficient
Dementia ¹⁶ 1 low-ROB RCT(N=114) of EO-massage 1 CCT (N=7) of inhaled-only	<u>ADL</u> : Mixed findings. No difference in 1 low-ROB RCT (N=114) of 10% Melissa oil massaged into hands and upper arms 1-2 min 2x daily for 12 weeks. Benefit found in 1 CCT (N=7), EO applied every 3 hrs. to sachet pinned to shirt collar, 2 weeks each of lavender and thyme. 6 Pts required less assistance with ADL tasks. Effect size and P-values NR. <u>QOL</u> : (1 low-ROB RCT, N=114) Favors Tx (P < 0.05). Effect size NR.	Unclear	Insufficient
Hemodialysis ²⁴ 1 CCT (N=80) Inhaled-EO	1 CCT (N=80) used wet wipes scented with chicory essence, applied to patients' hands and faces 3x per day. Significant positive effect on SF-36 QOL. Effect sizes and P-values NR. No data from RCTs.	Unclear	Insufficient

Abbreviations: ADL= activities of daily living; CCT = clinical controlled trial; EO = essential oil; hrs. = hours; RSCL = Rotterdam Symptom Checklist; QOL = quality of life; NR = not reported; NS = not significant; P = p-value; RCT = randomized controlled trial; ROB = risk of bias; Tx = treatment.

Inhaled EO interventions – Adverse effects

The occurrence or absence of adverse effects of inhaled EO interventions was reported in only 2 SRs. An SR of anxiety among various populations¹⁹ reported that no adverse effects occurred in an RCT of 122 intensive care unit (ICU) patients administered EO-massage with lavender versus carrier oil for 30 minutes, or in an RCT of 340 patients awaiting a dental appointment who were exposed to lavender oil using a candle burner. An SR of aromatherapy for dementia¹⁶ reported adverse effects from 2 trials of EO-massage: In an RCT of 114 patients, 2 patients treated with massage using Melissa oil had unspecified serious adverse events; and 1 small RCT (N=7) reported the occurrence of allergic reactions from EO-massage (number of patients not specified), and 1 participant reported drowsiness.

Topical EO interventions

Three SRs of topical EO interventions provided evidence on acne,³⁸ fungal infections,⁴⁰ and wound healing in episiotomy.³⁹ Figure 5 and Table 9 present the findings on effectiveness and harms.

The SR of fungal infections,⁴⁰ reported mixed findings with a preponderance of benefit in 3 trials of topical EOs for treating tinea pedis. The overall evidence suggested a potential positive effect, and the level of confidence was moderate. The same SR included a trial of tea tree oil versus clotrimazole for onychomycosis, the findings of which were inconclusive.

Significantly positive findings for acne³⁸ and wound healing in episiotomy³⁹ were reported, but because in each case the evidence was based on a single trial (N<100), the level of confidence was insufficient. The overall effect was therefore rated unclear for these health conditions.

Figure 5. Map of the evidence from systematic reviews of topically applied essential oils for targeted health conditions

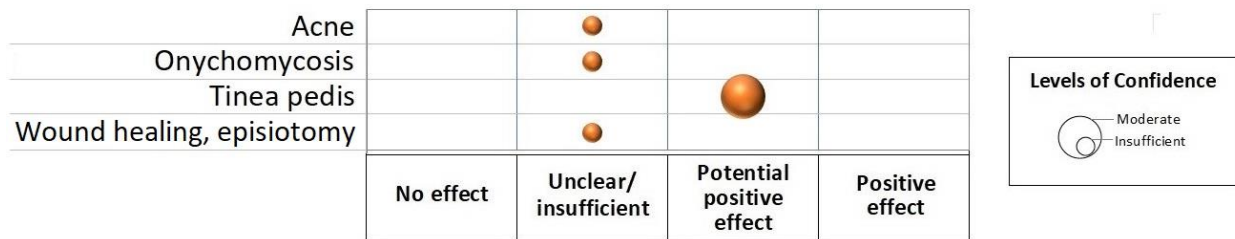


Table 9. Findings from systematic reviews of topical essential oil interventions

Health condition N trials (N pts) EO if specified	Findings	Overall effect	Level of confidence
Acne ³⁸ 1 unclear-ROB RCT (N=60) Tea tree oil, 5%	<u>Total skin lesion counts at 45 days:</u> Favors TTO, mean difference -7.53 (95% CI: -10.40 to -4.66) <u>Change of acne severity score at 45 days:</u> Favors TTO, mean difference -5.75 (95% CI -9.51 to -1.99)	Unclear	Insufficient
	<u>Harms, TTO vs placebo:</u> Minimal pruritus occurred in 3/30 (10%) vs 2/30 (6.7%). Mild burning sensation on the skin area where the oil was applied: 1/30 (3.3%) vs 2/30 (6.7%). Minimal scaling 1/30 (3.3%) vs 0 (0%)	Unclear	Insufficient
Wound healing, episiotomy ³⁹ 1 unclear-ROB RCT (N=60) Lavender/ thymol (2%)	REEDA healing scale 7 days after episiotomy: significant improvement (P = 0.013); also, significant reductions in hyperemia (P = 0.027); edema (P = 0.027); exudation (P = 0.016); dyspareunia: 2.7 ±1.5 vs 5.3 ±2.7 (P < 0.001). No significant effect on ecchymosis; border approximation (effect size and P-values NR).	Unclear	Insufficient
	<u>Harms:</u> systematically reviewed, none reported.	Unclear	Insufficient
Onychomycosis ⁴⁰ 1 low-ROB RCT (N=117) Tea tree oil	100% TTO vs 1% clotrimazole (2x daily for 6 months), no placebo arm. <u>Conversion to negative culture:</u> 18% vs 11%. <u>Full or partial resolution of symptoms:</u> 60 vs 61%, declining to 56 vs 55% 3 months later. Topical clotrimazole has low effectiveness in practice. Therefore, overall effect is unclear.	Unclear	Insufficient
	<u>Harms:</u> occurred in 5 vs 3 patients (TTO vs clotrimazole, total N=117, randomized per group NR).	Unclear	Insufficient
Tinea pedis ⁴⁰ 2 RCTs of tea tree oil: 1 low-ROB (N=158) 1 unclear-ROB (N=121) 1 CCT (N=70) of bitter orange oil (OBO)	<u>Conversion to negative culture (2 RCTs of TTO, N=279):</u> Mixed findings. Significantly higher cure rates at both 25% and 50% TTO 2x daily for 4 wks. vs placebo in 1 low-ROB RCT (N=158); no difference between 10% TTO 2x daily for 4 wks. vs placebo in 1 unclear-ROB RCT (N=121). <u>Clinical assessment (2 RCTs of TTO, N=279):</u> TTO superior to placebo in improvement of symptoms in 1 low-ROB and 1 unclear-ROB RCT. <u>1 CCT (N=70) of OBO:</u> 3 arms of different OBO preparations produced more rapid cure rates vs. imidazole; after 2 wks. 93% were cured using 100% OBO, 80% cured using 25% OBO, and 50% using 20% OBO; vs 0% cured using placebo (P-values NR).	Potential positive	Moderate
	<u>Harms:</u> 1 unclear-ROB RCT (N=121) reported that no adverse effects occurred in the TTO group.	Unclear	Insufficient

Abbreviations: CCT = non-randomized controlled clinical trial, NR = not reported, OBO = bitter orange oil, REEDA = Redness, Edema, Ecchymosis, Discharge, Approximation; RCT = randomized controlled trial, ROB = risk of bias, TTO = tea tree oil.

SUMMARY AND DISCUSSION

These evidence maps provide a broad overview of the evidence on clinical aromatherapy and topical EO interventions. We systematically searched the literature for SRs and meta-analyses of these interventions, and we included 25 SRs examining these interventions across a variety of targeted health-related conditions and populations. We compiled evidence maps to illustrate the reported effects of each intervention in the populations studied.

The only condition for which we found a preponderance of evidence suggesting benefit was pain in dysmenorrhea. This was one of the best-studied conditions and we found evidence of positive effects on pain in dysmenorrhea with inhaled EOs with and without massage, with moderate confidence.

We found several areas where EOs are potentially promising for particular populations and/or conditions – including labor/childbirth, hypertension, hemodialysis, stress, perioperative care, and sleep quality – in which inhaled EOs were inconsistently associated with positive effects across studies or across outcomes within a given domain (*eg*, positive effects for 1 measured psychological outcome but not another, or positive effects in some studies but not a majority). We also found evidence of potential effectiveness in the use of topical tea tree oil for tinea pedis.

However, we found insufficient evidence to characterize treatment effects in most of the conditions studied. The most common reasons we rated evidence as insufficient was a simple paucity of trials, small sample sizes, and methodologic limitations of the studies. On the other hand, aside from low-confidence evidence examining aromatherapy for anxiety in palliative care patients, we found very little evidence with which to characterize aromatherapy as ineffective. In other words, in broad terms, the literature examining aromatherapy does not yet appear to provide enough information to determine whether it has any effects for most conditions.

One challenge in interpreting and applying the aromatherapy literature is the variation in interventions across studies. There are many sources of intervention variation: the compounds used for aromatherapy, their concentrations, the equipment through which they are delivered, the frequency and duration of their application, their combination with co-interventions like massage, and the inhalation instructions provided to patients. In this evidence map, we were unable to determine the comparative effectiveness of different aromatherapy interventions for different conditions. Applying this evidence to clinical settings in the United States is also complicated by the lack of regulatory oversight and standardization of these interventions.

Determining how much of an intervention's effectiveness is a direct effect of the specific intervention and how much is due to the placebo effect may be less important if the intervention is low cost and has few adverse effects. The costs and cost-effectiveness of EO interventions were beyond the scope of our review, though compared with conventional treatments these are generally considered low-cost interventions. Inhaled-only and topical EO interventions could be administered by a variety of providers in a range of settings, whereas massage would add cost and specialization on the part of the provider.^{41,42} We have very little data about adverse effects from the included reviews, as they were seldom reported. Sensitive populations, such as those with asthma or allergies, may be at potentially greater risk of adverse effects from inhaled or topical EO interventions.⁴³⁻⁴⁵

Limitations

There are several limitations related to evidence map methodology and related to the body of evidence itself. These evidence maps provide a broad overview of the existing evidence compiled by SRs. These maps provide only broad “brushstrokes” regarding the potential benefits of these interventions. Evidence maps such as these are not designed to provide definitive conclusions about benefit, and there are several reasons for cautious interpretation: 1) we relied only on SRs and did not search for more recently published trials or conditions for which no SR has been written (so we cannot be definitive in our characterization of the evidence for each condition, nor is this an exhaustive list of conditions/populations for which aromatherapy has been used), 2) we cannot comment on the magnitude of treatment effect, 3) we relied on others’ study quality assessments, and 4) our measure of the level of confidence cannot approach the rigor represented by standardized approaches⁴⁶ given the previously listed constraints. One should be particularly circumspect about the “potential for positive effect” findings since these were – by design – weighted toward identifying any potential area of benefit to aid with research prioritization.

The body of evidence was itself limited in many ways. Many studies in the reviews were rated as having a high risk of bias because they failed to report quantitative measures, used inadequate placebos, or because the interventions were not well standardized. One explanation for the poor study quality provided by some practitioners of aromatherapy is that it does not lend itself well to standardization in the trial setting, because usual practice involves a great degree of personalization of dosage, dilution, and scent.^{22,35} The authors of the included reviews often noted insufficient patient blinding or the use of a non-odor placebo. Attention controls were seldom used.

There were also limitations within the SRs included in this report. Several SRs did not report effect sizes or p-values, stating only the presence or absence of a treatment effect, and whether the finding of difference was statistically significant. We relied on the reporting of the systematic reviews; therefore, it is possible that primary trials included in these reviews reported more detailed analyses, but this would not have been reflected in our report.

Research Gaps/Future Research

The maps highlight many potential areas for future research. The interventions and health conditions for which there was evidence of a “potential positive effect” may be one place to start to prioritize research, since these findings underscore potentially fruitful areas of research. The comparative effectiveness of different, standardized aromatherapeutic approaches should be examined especially in conditions for which there is potential promise. Future studies should capture potential adverse effects data, and the safety of aromatherapy should be examined in patients with comorbidities especially those of the respiratory tract. The use of a non-EO fragrance comparator would improve blinding and allow comparison of effects and harms of aromatherapy containing EO versus synthetically generated fragrance oils.

CONCLUSIONS

There is moderate confidence that aromatherapy is effective for pain in dysmenorrhea. We found potential positive effects of aromatherapy for pain in labor/childbirth; blood pressure reduction in those with hypertension; stress, depression, and sleep in patients on hemodialysis; stress in

healthy adults; anxiety in perioperative patients undergoing various surgery types; and sleep quality in various populations, with low to moderate confidence in the evidence. For EOs applied topically, there is moderate confidence in the potentially positive effect of tea tree oil for tinea pedis. There is insufficient evidence with which to determine whether aromatherapy or topically applied EOs is effective for all other examined conditions.

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