

INTEGRATIVE MEDICINE SECTION

Review Article

The Impact of Massage Therapy on Function in Pain Populations—A Systematic Review and Meta-Analysis of Randomized Controlled Trials: Part II, Cancer Pain Populations

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Abstract

Purpose. Pain is multi-dimensional and may be better addressed through a holistic, biopsychosocial

approach. Massage therapy is commonly practiced among patients seeking pain management; however, its efficacy is unclear. This systematic review and meta-analysis is the first to rigorously assess the quality of massage therapy research and evidence for its efficacy in treating pain, function-related and health-related quality of life in cancer populations.

Methods. Key databases were searched from inception through February 2014. Eligible randomized controlled trials were assessed for methodological quality using the SIGN 50 Checklist. Meta-analysis was applied at the outcome level. A diverse steering committee interpreted the results to develop recommendations.

Results. Twelve high quality and four low quality studies were subsequently included in the review. Results demonstrate massage therapy is effective for treating pain compared to no treatment [standardized mean difference (SMD) = -.20] and active (SMD = -0.55) comparators. Compared to active comparators, massage therapy was also found to be beneficial for treating fatigue (SMD = -1.06) and anxiety (SMD = -1.24).

Conclusion. Based on the evidence, weak recommendations are suggested for massage therapy, compared to an active comparator, for the treatment of pain, fatigue, and anxiety. No recommendations were suggested for massage therapy compared to no treatment or sham control based on the available literature to date. This review addresses massage therapy safety, research challenges, how to address identified research gaps, and necessary next steps for implementing massage therapy as a viable pain management option for cancer pain populations.

Key Words. Systematic Review; Meta-Analysis; Massage Therapy; Pain; Function; Health-Related Quality of Life

Introduction

Public Health Significance of Cancer Pain

Pain is the most common and debilitating symptom among cancer patients. While the exact prevalence of pain varies depending on the type and stage of cancer, research shows that pain generally affects over 50% of those undergoing cancer therapy and up to 90% with advanced cancer experience pain [1]. According to a 2007 meta-analysis, which pooled data from 52 studies, the prevalence of pain was found to be approximately 59% among patients undergoing active cancer treatment and over 50% across all cancer types, with the highest pooled prevalence of 70% among head/neck cancer patients [2]. These figures convey that cancer pain is perhaps not adequately addressed by the current healthcare system and underscore the significant challenges faced by treating oncologists and other medical professionals in the field of cancer pain management.

Cancer pain can range from mild to severe and from acute to chronic. Pain management can be challenging; not only can cancer pain be spontaneous, as in the case with the emergence of breakthrough pain [3] (i.e., sudden, transient exacerbation of pain intensity in patients with stable and controlled chronic pain) despite continued administration of analgesics [4], but it can also affect patients physically, emotionally, socially, and spiritually. Patients often experience significant anxiety and depression [5,6], as well as insomnia, fatigue, weakness, and other complications that can exacerbate each other, impair normal daily activities, and negatively impact quality of life [7–9].

Current Treatment Approaches and Challenges

Pharmacologic interventions (i.e., non-opiods, opiods, adjuvant medications), as well as interventional techniques (e.g., nerve blocks, local anesthetics, surgical interventions) represent the mainstay of treatment for cancer pain. Despite their wide use and clinical benefits for controlling pain, however, these interventions are also associated with potential risks for both drug addiction and unwanted side effects (e.g., nausea, vomiting, dizziness, confusion) [10]. Therefore, practitioners are challenged with determining the correct dosage that will adequately relieve pain without causing such side effects [11]. Studies have also suggested that medical professionals, including oncologists and nurses, may have inadequate tools, knowledge, and skills to accurately be able to assess patient's pain severity and administer the correct dosage of medications [11]. For example, a discrepancy often exists between patient and physician in judging both the severity of the patient's pain and the affected areas of daily function, with the physician generally underrating the patient's pain intensity and undertreating cancer pain [12]. In an effort to minimize this discrepancy, many healthcare facilities have begun to place a greater emphasis on obtaining frequent assessments of the patient's pain intensity, in the form of patient self-report on pain and pain-related needs.

Massage Therapy for Cancer Pain

Due to unsatisfactory results from conventional cancer pain management [6], as well as the growing recognition of the importance of establishing treatment goals based on patients' own criteria for meaningful and holistic pain relief across physical, functional, and psychosocial domains [8], a large number of cancer patients are seeking out and utilizing complementary and integrative medicine (CIM) therapies [6,13-15]. In fact, many cancer patients have turned to massage therapy [16] to help with not only physical relaxation and relief from physical pain but also emotional distress, functional ability, and overall quality of life. In response to a growing demand for a more holistic pain management approach for cancer patients, therapeutic massage is being used more in medical treatment programs to reduce pain and related symptoms, as well as enhance personal sense of wellbeing in such patients [17].

Despite its popularity and theoretical base supporting its use, however, there is ongoing debate and conflicting evidence regarding the efficacy of massage therapy for cancer pain. Some reviews have found that massage therapy does not significantly improve cancer pain [18,19], while others suggest a positive impact of massage therapy on relieving cancer symptoms and side effects associated with intensive cancer treatment and medications[20,21]. To date, there has not been a comprehensive systematic review that attempts to better understand both the scope of massage therapy as well its full effects on various outcomes associated with cancer pain that addresses the patient's needs from a holistic view.

Purpose

This current review provides a comprehensive, up-todate systematic review and meta-analysis that examines a variety of outcomes to address the multi-dimensional experience of pain in cancer patients from a biopsychosocial perspective. In doing so, the review: (a) clearly defines both concepts of (i) massage therapy, to dissolve taxonomy confusion and ensure transparency with eligibility criteria and (ii) function, as approached from a patient-centric perspective; (b) examines the efficacy of massage therapy for treating cancer patients experiencing acute or chronic pain that is affecting function-related (e.g., pain, activity, sleep, mood, stress) and other (e.g., health-related quality of life, physiological) outcomes of daily life; (c) describes the characteristics and safety of massage therapy as reported in the current literature, and whether they adhere to the proposed Standards for Reporting Interventions in Clinical Trials of Massage (STRICT-M) Checklist; (d) synthesizes the evidence to draw initial conclusions based on the current state of the evidence for its application; and (e) identifies

gaps in research areas to guide a future research agenda.

Methodology

Overview of Methodological Approach

A systematic review and meta-analysis was conducted using Samueli Institute's systematic review process known as the Rapid Evidence Assessment of Literature (REAL©) [22], which has been used by a variety of organizations to date [23-27]. Specifically, (a) the Evidence for Massage Therapy (EMT) Working Group, composed of a diverse group of stakeholders including a full steering committee and subject matter experts, contributed to defining the review's protocol (i.e., research question. concepts/definitions, eligibility criteria) to maximize the review's meaning and impact to the target audience; (b) the systematic review team followed the developed protocol to independently evaluate the quantity and quality of the available English, peer-reviewed literature in order to (c) present the results to the EMT Working Group who then interpreted the evidence to suggest recommendations for the field. The protocol for this systematic review is registered with PROSPERO under registration number CRD42014008867.

Concepts and Definitions

The authors agreed to use a broad scope when conducting the review, and consequently examined the state of the science regarding the impact of massage therapy on function for all individuals experiencing pain. Rather than restricting the population up front, the authors decided to allow the literature base to identify subgroup populations and dictate decisions surrounding which subgroups should be included and examined in the review. This systematic review focuses on the subgroup of cancer pain populations. Other populations, including those experiencing pain and seeking consultation from their general practitioner as well as surgical patients [28,29], are assessed in other articles within this series.

Pain

The authors agreed to rely on the Pain Management Task Force's definition for pain.

An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Pain is always subjective. Pain can be acute or chronic [30].

Massage Therapy

After reviewing several definitions of massage therapy [28,31,32], the authors decided to use the following broad definition of massage therapy to adequately

capture the majority of interventions typically recognized as massage therapy.

The systematic manipulation of soft tissue with the hands that positively affects and promotes healing, reduces stress, enhances muscle relaxation, improves local circulation, and creates a sense of well-being.

Function

Pain is a multidimensional experience that affects various function-related outcomes. Recognizing the need to approach pain from a biopsychosocial and patient-centered point of view in order to address the entire patient, the authors assess function-related outcomes of pain, such as activity, sleep, mood and stress as well as health-related quality of life (HrQoL) and physiological (i.e., outcomes relating to one's physiology including the physical and chemical phenomena and processes involved) outcomes.

Study Eligibility Criteria

Articles were included if they met all of the following criteria: (a) cancer patients experiencing pain, as defined above; (b) massage therapy, as defined above, administered (i) alone as a therapy; (ii) as part of a multi-modal intervention where massage effects can be separately evaluated; or (iii) with the addition of techniques commonly used with massage, as pre-defined by the EMT Working Group (i.e., external application of water, heat, cold, lubricants, background music, aromas, essential oils, and tools that may mimic the actions that can be performed by the hands); (c) sham, no treatment, or active comparator (i.e., those in which participants are actively receiving any type of intervention); (d) assessment of at least one relevant function outcome, as defined above; and (e) randomized controlled trial (RCT) study design published in the English language. Additionally, interventions were included if they were not necessarily labeled as massage or massage therapy but included the use of manual forces and soft-tissue deformation as well as gliding, torsion, shearing, elongation, oscillating, percussive, and joint movement methods (i.e., touch, compression, gliding, percussion, friction, vibration, kneading, movement, positioning, stretching, holding) [28]. Note that interventions solely performed by tools (e.g., chair massage) were excluded.

Search Strategy

Databases, including PubMed, CINAHL, Embase, and PsycInfo, were searched from database inception through February 2014 according to the broad research scope. Authors explored MeSH within MEDLINE and consulted with experts in the field to determine the best keywords to yield the most powerful search (see Figure 1 for PubMed search string). Variations of the search strategy for the remaining databases are available upon request from the primary author.

(pain) AND ("massage" OR massotherap* OR "musculoskeletal manipulation" OR "myofascial release" OR neuromuscular therap* OR "strain counterstrain" OR "trager" OR "proprioceptive neuromuscular facilitation" OR "bodywork" OR "rolfing" OR "structural integration" OR trigger point therap* OR "manual lymph drainage" OR manual therap* OR "lomi" OR hydrotherap* OR "passive motion" OR heat therap* OR "gliding" OR knead* OR "friction" OR "holding" OR "percussion" OR "vibration" OR "direct pressure" OR "skin rolling" OR "manual stretch" OR "manual stretches" OR "manual stretching" OR "contract-relax" OR "passive stretch" OR "passive stretching" OR "rocking" OR "traction")

Figure 1 PubMed Search String.

Study Selection

Three reviewers (LX, AP, CP) independently screened titles and abstracts of the citations yielded from the literature search according to the pre-defined eligibility criteria. A Cohen's kappa for inter-rated agreement of >0.90 was maintained throughout the entire screening phase. Disagreements about inclusion were resolved through discussion and consensus, by one of the review managers (CB, CC) or, ultimately, by involving the EMT Working Group.

Methodological Quality Assessment and Data Extraction

Methodological quality (i.e., risk of bias/internal validity) was independently assessed by three reviewers (LX, AP, CP) using the Scottish Intercollegiate Guidelines Network (SIGN) 50 Checklist [33] for RCTs, a validated and reliable assessment tool widely used in the literature. The External Validity Assessment Tool (EVAT©) [34] was used to measure the generalizability of the intervention's applicability to other individuals (i.e., external validity) and other settings (i.e., model validity) outside the confines of a study. The following descriptive data was also extracted from included studies: type and stage of cancer, sample entered/completed, intervention and control/comparison description and dosage, relevant function measures and corresponding results and statistics, effect sizes, and author's main conclusions. The authors also noted whether power calculations to achieve sufficient effect sizes and adverse events were reported. Mobius Analytics Systematic Review System (Mobius Analytics Inc, Ottawa, Ontario) was used for all data entry and execution of the systematic review.

Proposed STRICT-M Checklist and Analysis

The Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) [35] is a formal

extension of Consolidated Standards of Reporting Trials (CONSORT) [36] that expands the general content of item five (surrounding the intervention description specific to acupuncture) to improve the completeness of reporting interventions in controlled acupuncture trials. Because complete and accurate trial reports can facilitate translation and replicability, the authors extracted data similar to the STRICTA criteria and noted whether studies included this data in reporting. Subsequently, the authors refer to this STRICTA-based checklist as the proposed Standards for Reporting Interventions in Clinical Trials of Massage (STRICT-M) [28].

Data Synthesis and Analysis

Meta-Analysis

When reported, the sample size, mean or pre-post difference, and standard deviation for each treatment group was extracted. Effect sizes were calculated for each comparison (i.e., massage vs. active comparator, massage vs. sham, massage vs. no treatment) for the functional outcomes related to pain: pain intensity/severity, activity, stress, mood (anxiety), sleep (fatigue), and HrQoL, where available. If a study had more than one active comparator (i.e., physical therapy or acupuncture), the biostatistician randomly chose one active comparator for analysis by flipping a coin. A minimum of three studies was required to perform a meta-analysis for each subset of data analyzed. An unbiased estimate was calculated using Cohen's d effect size for subgroup analyses that pooled across several scales [37,38]. A pooled random-effects estimate of the overall effect size was estimated for all studies judged as clinically similar enough to warrant a meta-analysis. The individual trial outcomes were weighted by both within- and betweenstudy variation in this synthesis. For a reduction in pain intensity/severity, fatigue, and anxiety, a negative effect size favors massage therapy treatment group over the comparison arm (i.e., active comparator, sham or no treatment group). For improved activity (i.e., increase in range of motion) and HrQoL, a positive effect size favors the massage therapy treatment group over the comparison arm (i.e., active comparator, sham or no treatment group). Publication bias was also assessed using the Egger regression asymmetry test [38,39]. Heterogeneity was assessed using I² and tested via Q statistics. For pain intensity/severity, a clinical translation into the visual analog scale (VAS), 0-100, was conducted for clinical interpretation using a standard deviation of 25 points; a 20-mm difference on the VAS was considered clinically relevant [40]. All meta-analyses were conducted with Comprehensive Meta-analysis version 2.2 (Meta-analysis.com, Englewood, NJ).

Evidence Synthesis

The EMT working group and systematic review team convened to: (a) review the evidence revealed through the systematic review and meta-analysis, and (b) further synthesize the evidence in order to determine the overall (i) confidence in the estimate of the effect; (ii) magnitude of the effect; and (iii) evaluate safety as being reported in the results; in order to provide an overall recommendation concerning the benefit/risk for massage therapy. The conclusions reached and recommendations made are in no way to be construed as clinical guidelines, but are rather recommendations about the benefit/risk of massage therapy for cancer pain management, based solely on the evidence from the systematic review results.

Results

Characteristics of Included Studies

The database searches yielded 3,678 articles that examined three subgroups of populations including individuals with pain conditions for which they would generally seek treatment from their general practitioner, individuals with pain related to a surgical procedure and those with cancer pain. Results regarding the first two subgroups are reported elsewhere [28,29].

A total of 16 studies, ranging from 1990 through 2013 publication years, investigated the effect of massage therapy on cancer pain populations (see Figure 2 for Flow Chart of included studies). Massage techniques named as massage[10,41–45], massage therapy [46–52], Thai massage [53], therapeutic massage [54], and lymphatic drainage [55] were compared to several types of control/comparator arms including no treatment [10,47,48,51], standard care [46,53,54], attention [43,45,49], touch [50,54], usual care [10,52], caring presence [54], quiet time [42], reading [41], and an undescribed control [44]. Treatment dosages varied from one single 10-minute session to 15 daily 45-minute

sessions over a 3-week course. In the 16 studies, 31.5% were male and 68.5% were female with the mean age of 57.2 across the studies. See Supplementary Data Table S1 for full descriptions of all included studies.

Methodological Quality of Included Studies

According to the SIGN 50 criteria, the majority of studies seemed to have minimal to no risk of bias detected, with one high (++) and 11 acceptable (+) quality studies; four studies were low (0) quality. Most of the SIGN criteria were addressed either adequately or well (see Table 1). In fact, the majority of studies addressed an appropriate and clearly focused question, dropouts, baseline similarities, group differences, outcome reliability and validity, and intention-to-treat analyses. Studies were equally divided regarding reporting randomization procedures, with half addressing these processes either well or adequately and the remaining studies doing so poorly. Allocation concealment was poorly addressed by most studies and all five multi-site studies [41,42,44,50,52] addressed site differences poorly.

EVAT evaluates the generalizability of study results to other individuals and settings outside the confines of the study. Over half of studies described the recruitment (87.4%) and participation (53.8%) aspects of external validity adequately, meaning that the populations being studied and the source from which they came are understood well enough that results can be generalized to other patients in real-life settings. Similarly, model validity was adequately reported in 53% of the studies, indicating that the staff, places and facilities where patients were treated were representative of the treatment that the majority of patients would typically receive. See Table 2 for details.

STRICT-M Analysis

The EMT Working Group and review team convened to draft the proposed STRICT-M requirements, adapted from the STRICTA Checklist [35], and analyzed the systematic review's literature pool according to these proposed requirements [28]. All studies (100.0%) described the massage technique utilized and most (62.5%) included the rationale for selecting the provided massage treatment. While massage location (93.8%) and amount of pressure (68.8%) were described by most studies, other details were not. Only 18.8% and 31.3% of studies described the amount of time spent massaging each location, and the extent to which treatments varied, respectively. No studies used specific massage terms when describing the massage protocols or included information about the type of response sought. Despite this lack of detail, dosing regimens including frequency (75.0%), duration (93.8%), and number (93.5%) of treatment sessions over a specified time frame (87.5%) were described by almost all studies. 42.9% of the studies that used additional massage-related interventions

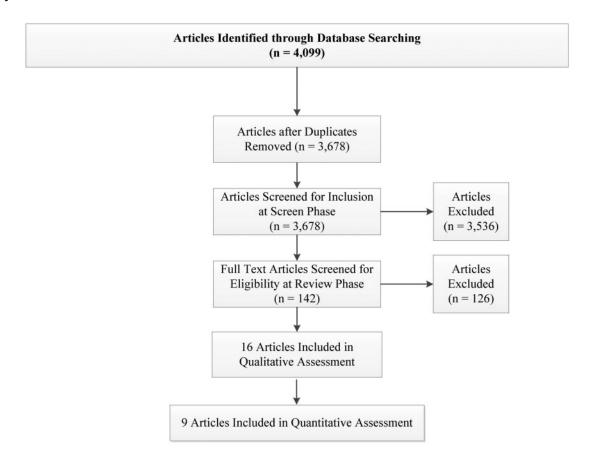


Figure 2 Flow Chart.

eligible for inclusion in this review (i.e., essential oils, aromatherapy) described these interventions well. All studies described the setting in which massage was performed. Although massage was primarily administered in a hospital (n=12) [42–51,53–55], it was also provided at the client/therapist's home (n=3) [10,41,52] and a hospice (n=1) [50] setting.

Four studies included one provider, while 12 included more than one provider; of the studies that included multiple providers, only four reported the exact number of providers and only one described the interaction between providers. Almost all studies described the type of massage practitioner (87.5%); however, provider qualifications were only described by 31.3% of studies. Most providers were massage therapists (n = 8) or some type of unspecified therapist (n=3). Other types of providers included a nurse (n=2), healing-arts specialist (n=1), caregiver (n=1), and a researcher trained in massage (n = 1). Based on the few studies that reported practitioner qualifications, years of experience ranged from six months to 10 years. Hours of supervised clinical experience and didactic training were not discussed by many studies; however, a few required practitioners to undergo some sort of training program specific to the study's protocol. See Table 3 for full detail of the STRICT-M analysis.

The control or comparator intervention was described by the majority of studies (87.5%); however, the rationale for using the selected interventions was only included by a few studies (12.5%). Dosage information including frequency (56.3%) and number (56.3%) of sessions over a specified time frame (81.3%) was addressed by most studies while duration of each treatment (43.8%) was covered by less than half of the studies.

Adverse Events

Five of the included studies [10,41,45,49,54] reported that no adverse events occurred during the trial, while one[50] reported two serious adverse events (i.e., respiratory infection, gastrointestinal bleed) that appeared to be unrelated to the massage therapy treatment. The remaining studies did not report or mention adverse events.

Results According to Functional Outcome

Pain

One high (++) [49], 11(+) acceptable [10,41,43–45,47,48,51,53–55], and four low (0) [42,46,50,52] quality studies investigated the effect of massage therapy on pain outcomes in metastatic cancer, colorectal cancer, advanced cancer, breast cancer, pediatric cancer, and

Table 1 SIGN 50 checklist quality assessment [33]

		Percentage (N)	
	Poor	Adequate	Well
Appropriate and clearly focused question	6.2% (1)	43.8% (7)	50.0% (8)
Randomization	50.0% (8)	31.2% (5)	18.8% (3)
Allocation concealment	75.0% (12)	18.8% (3)	6.2% (1)
Percentage of dropouts	31.2% (5)	25.0% (4)	43.8% (7)
Baseline similarities	_	12.5% (2)	87.5% (14)
Group differences	12.5% (2)	75.0% (12)	12.5% (2)
Outcome reliability/validity	12.5% (2)	12.5% (2)	75.0% (12)
Intention-to-treat analyses	43.8% (7)	31.2% (5)	25.0% (4)
Multi-site similarities	100.0% (5)	-	-

SIGN = Scottish Intercollegiate Guidelines Network.

SIGN criteria was modified to exclude blinding and was weighed accordingly because of this.

Table 2 EVAT quality assessment [34]

		Percentage	(N)	
	Poor	Adequate	Well	NA
Recruitment	6.3% (1)	87.4% (14)	6.3% (1)	0
Participation	30.8% (4)	53.8% (7)	15.4% (2)	3
Model validity	40.0% (6)	53.3% (8)	6.7% (1)	1

EVAT = External Validity Assessment Tool.

non-specified [41,43–46,48,52,54] cancer pain populations. Massage techniques primarily consisted of massage therapy, therapeutic massage, light Thai massage, and lymphatic drainage; 11 [41,43–45,49–55] of the 14 massage therapy studies were reportedly effective for treating cancer pain, while the remaining studies displayed non-significant results.

Activity

No studies investigated the effect of massage therapy on activity outcomes across cancer pain populations.

Sleep

Six acceptable (+) [41,44,51,53,54,56], one high (++) [49], and two low (0) [42,46] quality studies assessed the effect of massage therapy on sleep outcomes in cancer, metastatic cancer, colorectal cancer, breast cancer, and pediatric cancer pain populations. The primary technique, massage therapy, proved to be effective for cancer [41,46], metastatic cancer [49], colorectal cancer[53], and breast cancer[51] pain.

Stress, Mood, and Heath-Related Quality of Life

Of the 14 cancer pain population studies investigating the effect of massage on stress, mood, and/or HrQoL, there were one high (++) [49], nine acceptable

(+) [10,41,44,47,48,51,53-55], and four low (0) [42,46,50,52] quality studies. Massage techniques consisted of massage therapy, massage, Thai massage, and lymphatic drainage. Nine studies [41,42,44,46,48-51,53] displayed significant results for mood outcomes, six [10,41,51-53,55] for HrQoL outcomes, and three [41,46,52] for stress outcomes. Two studies [47,54] displayed non-significant results.

Physiological

Three acceptable (+) [53–55] and four low (0) [42,46,50,52] quality studies examined the effect of massage therapy, light Thai massage, therapeutic massage, or manual lymphatic drainage on cancer, colorectal cancer, or unilateral breast cancer-related lymphedema pain populations. The majority of these studies showed that massage therapy was effective for physiological outcomes [42,46,52–55].

Overall Evidence Synthesis

Of the 16 studies included in systematic review, nine studies provided sufficient data to be included and pooled in the meta-analysis assessing the effect of (a) massage therapy compared to no treatment for reducing pain intensity/severity and (b) massage therapy compared to other active comparators for reducing (i) pain intensity/severity, (ii) fatigue, and (iii) anxiety

Table 3 STRICT-M analysis

	Percentage (N
1. Massage Rationale	
a. Reasoning for treating provided	62.5% (10)
b. Extent to which treatment varied	31.3% (5)
2. Details of Massage Technique	()
a. Name and description of	100.0% (16)
massage technique	, ,
b. Details of intervention using terms	_
c. Location of massage	93.8% (15)
d. Amount of time spent massage	18.8% (3)
each location	
e. Description of pressure	68.8% (11)
f. Response sought	_ ` ` `
3. Treatment Regimen Related to Dosing	g
a. Number of treatment sessions	93.8% (15)
over what time	
b. Time frame (total duration)	87.5% (14)
c. Frequency	75.0% (12)
d. Duration of each treatment	93.8% (15)
4. Other Components of Treatment	
a. Details of massage-related interventions	42.9%
	(3 out of 7)
b. Massage equipment	_
c. Setting	93.8% (15)
5. Practitioner Background	
a. Type of practitioner	87.5% (14)
b. Qualifications	31.3% (5)
6. Control or Comparator Interventions	
a. Rationale for control	12.5% (2)
 b. Name and description of control 	87.5% (14)
c. Number of control sessions	56.3% (9)
d. Time frame (total duration)	81.3% (13)
e. Frequency	56.3% (9)
f. Duration of each treatment	43.8% (7)

outcomes at post-treatment. There was insufficient data to allow for meta-analysis comparing massage therapy to a sham treatment. Treatment comparators used for meta-analysis are denoted beside the author names in the forest plots (see Figures 3A-D for plotted meta-analysis results). Publication bias was detected in only the anxiety and fatigue analyses (see Figures 3C-D for Egger's test p-values). Although interpretation is challenging given the small number of studies pooled (n=3), publication bias still cannot be completely ruled out. All studies, regardless of whether their data was pooled for meta-analysis, were considered for the overall evidence synthesis if three or more studies were in a specific subgroup assessed.

Pain Intensity/Severity

Massage vs. No Treatment

Three studies, involving 167 cancer participants, compared the effect of massage therapy to no treatment for

pain intensity/severity. All three studies were pooled for the meta-analysis resulting in a standardized mean difference (SMD) of -0.20 (95% CI, -0.99 to 0.59; $I^2 = 82.60\%$) at post-treatment (see Figure 3A). Translated into the VAS, the reduction in pain intensity is -5.075 (95% CI, -24.80 to 14.63). Studies were quite heterogeneous. Despite all being of acceptable methodological quality, the study results were inconsistent; one producing a very large effect compared to no treatment (SMD = -0.813), another[44] producing a much smaller effect (SMD=-0.182), and a third [56] producing no effect (SMD=0.388) at all. Only one reported adverse events, noting none occurred. As such, massage therapy appears safe; however, more data is needed to fully understand safety. Given the small size and apparent heterogeneity and inconsistency across the pooled studies, no recommendation was made for massage compared to no treatment for reducing pain intensity/severity for cancer patients (see Table 4).

Massage vs. Active Comparator(s)

There were 10 studies involving 708 cancer patients comparing the effect of massage therapy on pain outcomes to active comparators (i.e., attention, usual care, standard treatment, a reading group comparator, and caring presence). Six of these studies (370 total patients) had sufficient data available to pool for a metaanalysis resulting in a SMD of -0.55 (95% CI, -1.23 to 0.14; $l^2 = 89.26\%$) for a reduction of pain intensity/severity. See Figure 3B. Translated into a VAS, the reduction in pain intensity is -13.63 (95% CI, -30.78 to 3.5). The majority of these studies consistently demonstrated massage therapy, performed by either a massage therapist or trained nurse, was more effective than the active comparator. Although one outlier [41] showed a reading group produced a larger effect on cancer pain than massage therapy, this effect may be due to the different nature of the massage intervention, which was designed as an instructional video for caregivers to administer massage techniques. Despite this outlier, the overall pooled studies favored massage therapy. All but two of the 10 studies were of either high or acceptable methodological quality.

Only five studies discussed adverse events, reporting that no such events occurred. Even though the evidence appears to favor massage therapy for cancer pain, the EMT Working Group suggested a weak recommendation in favor of massage compared to active comparator for reducing cancer pain intensity/severity. Further research is very likely to alter the estimate of the effect. Though the majority of studies demonstrated consistent results, heterogeneity within the pooled studies is concerning. Further information is needed to care for this special population; appropriate pressure, dosing, as well as what types of practitioners with what credentials are best for treating pain in cancer populations must be well understood before a strong recommendation can be made (see Table 4).

Sleep

Massage vs. Active Comparator(s): Fatigue

Six studies, involving 539 cancer patients, assessed sleep as measured by fatigue in cancer patients experiencing pain. Three of these studies (235 total patients) examining fatigue in cancer pain patients were pooled for this meta-analysis yielding a SMD of -1.06 (95% CI, -2.18 to 0.05; $I^2 = 92.81\%$). See Figure 3C. A large amount of heterogeneity is noted. Massage therapy showed a small positive effect for massage compared to reading [41] or caring presence [54], as well as a large positive effect when compared to standard treatment [46], which should be interpreted with caution. Further, massage appears safe with infrequent adverse events according to the four studies that reported on safety. Subsequently, a weak recommendation was provided for massage therapy to reduce fatigue for cancer patients experiencing pain (see Table 4). Adhering to reporting requirements such as the proposed STRICT-M and developing clear clinical practice guidelines for treating this special population is essential before making any further recommendations for cancer pain patients.

Stress, Mood, and Health-Related Quality of Life

Massage vs. Active Comparator(s): Anxiety

Eight studies, involving 620 cancer patients, examined stress, mood (anxiety), and HrQoL outcomes. The same three studies (234 total patients) included in the fatigue meta-analysis were pooled for this meta-analysis resulting in a SMD of -1.24 (95% CI, -2.44 to -0.03; l^2 = 93.56%). See Figure 3D. There is a large amount of heterogeneity within these three pooled studies, with two studies [41,46,54] producing relatively small effects and third producing a substantial positive effect; the latter should be interpreted cautiously given its low methodological quality and small sample size. Based on the four studies that reported on adverse events, massage appears safe with infrequent adverse events. Consequently, a weak recommendation in favor of massage therapy was provided for cancer patients dealing with anxiety; however, until clear guidelines are developed for practitioners working with cancer patients, caution is warranted (see Table 4).

Discussion

Based on this systematic review and meta-analysis, massage therapy was found to be relatively safe, with infrequent adverse events. Overall, massage therapy seems to be more effective than other active treatments evaluated for reducing pain intensity/severity, fatigue, and anxiety in cancer patients. There was insufficient evidence available to draw any conclusions surrounding massage therapy compared to either sham treatment or no treatment controls. The evidence synthesis could not be conducted on HrQoL, emotional stress, and activity outcomes due to an insufficient amount of studies

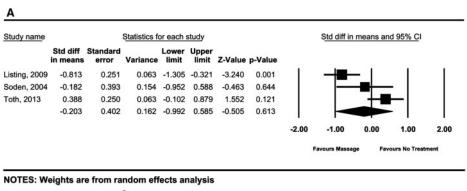
examining these outcomes. Future research should focus on evaluating these outcomes to better understand the total impact massage has on the whole person.

Methodology

Overall, the majority of studies were high or acceptable quality. Most aspects of internal validity were adequately addressed; however, many studies failed to either successfully carry out or describe allocation concealment procedures. Sufficient descriptions of similarities between multiple sites, when applicable, were also lacking. Similarly, half of the studies [41,42,45-49,51] did not mention blinding. Blinding of patients may not be appropriate or possible in massage trials; however, blinding of data collectors and outcome assessors (e.g., single blinding) is often achievable. Although this review excluded blinding from its risk of bias assessment, due to these challenges, the authors tracked whether studies mentioned blinding procedures, as such processes are a critical component of clinical trials that should, at the very least, be discussed: regardless of whether blinding is possible. authors should always state who was blinded, or, if blinding was not carried out, discuss attempts made toward blinding or justify their reasoning for excluding such procedures. Moreover, although external validity was detailed by most studies, model validity was not addressed by many, making it difficult to understand how the results of these studies may be replicated and massage therapy implemented into practice. Subsequently, the authors encourage future research adhere to CONSORT guidelines to avoid such methodological flaws. Following such guidelines helps ensure that critical study elements are not only carried out, but also reported on, allowing for translation and eventual implementation to occur.

Research Challenges

In order to successfully implement massage therapy into real-world settings, several factors (i.e., specifics of massage protocols including amount of time spent massaging specific locations as well as details of massagerelated interventions; adequate dosing and time of administration; practitioner type, qualifications, as well as licensing requirements for this special population) must be well-understood to clearly interpret the effect of massage on cancer patients. Although this information is essential for replication, many studies included in this systematic review failed to report on these items. For example, most studies described the type of practitioner; however, only a third of studies described the practitioner's qualifications. Although practitioner characteristics (e.g., qualifications, affiliation, experience, clinical expertise) can influence massage treatment effects [57] and are likely associated with an improvement in outcomes [58], this concept is difficult to explore as this information is typically underreported [59,60]. Practitioner qualifications and credentialing are especially important with cancer populations as oncology massage typically requires providers to have special training. In fact, several massage modifications related to positioning, pressure, pace,



Heterogeneity: Q-value = 11.50, I2 = 82.60%; Publication bias: Egger's test P-value = 0.99

В

Study name			Statistics for	or each s	tudy				Std diff in	means and	95% CI	
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value					
Ahles, 1999, Standard Treatmer	nt -2.466	0.462	0.213	-3.371	-1.560	-5.337	0.000	k—	- 1	T	- 1	T
Collinge, 2013, Reading	0.624	0.216	0.047	0.201	1.047	2.892	0.004	- 1			█	
Post-White 2003, Healing Touch	-0.277	0.186	0.035	-0.642	0.087	-1.490	0.136	- 1	_ →	■十	_	
Jane, 2011, Social Attention	-0.920	0.248	0.061	-1.405	-0.434	-3.710	0.000	- 1	_	= 2	- 1	
Weinrich, 1990, Attention	-0.283	0.380	0.144	-1.027	0.462	-0.745	0.457	- 1	\vdash	-		
Wilkie, 2000, Usual Care	-0.277	0.373	0.139	-1.009	0.454	-0.743	0.457	- 1	-	-		
	-0.545	0.350	0.122	-1.231	0.140	-1.560	0.119	- 1				- 1
								-2.00	-1.00	0.00	1.00	2.00
									Favours Massage	Fav	yours Active Co	ntrol

NOTES: Weights are from random effects analysis

Heterogeneity: Q-value = 46.58, I2 = 89.27%; Publication bias: Egger's test P-value = 0.27

С

Study name			Statistics 1	for each	study				Std diff in	means	and 95% CI	
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value					
Collinge, 2013, Reading	-0.295	0.207	0.043	-0.700	0.109	-1.430	0.153	- 1		-	- 1	- 1
Post-White, 2003, Caring Presenc	e -0.225	0.196	0.039	-0.610	0.160	-1.146	0.252		_ I - ī	■+	- 1	
Ahles, 1999, Standard Treatment	-3.066	0.514	0.264	-4.073	-2.059	-5.970	0.000	k			- 1	- 1
	-1.063	0.568	0.323	-2.177	0.050	-1.872	0.061	—	$\overline{}$	-	l l	
								-2.00	-1.00	0.00	1.00	2.00
									Favours Massage		Favours Active Cor	strol

NOTES: Weights are from random effects analysis

Heterogeneity: Q-value = 27.81, I² = 92.81%; Publication bias: Egger's test P-value = 0.01

D

Study name			Statistics 1	for each	study				Std diff in	means	and 95% CI	
	Std diff in means	Standard error	Variance		Upper limit	Z-Value	p-Value					
Collinge, 2013, Reading	-0.353	0.207	0.043	-0.759	0.053	-1.704	0.088	T	-	₩	- 1	- 1
Post-White, 2003, Caring Presenc	e -0.268	0.197	0.039	-0.653	0.118	-1.361	0.174		-	■+	- 1	- 1
Ahles, 1999, Standard Treatment	-3.589	0.572	0.327	-4.709	-2.468	-6.278	0.000	k	9-20		- 1	- 1
	-1.235	0.614	0.377	-2.438	-0.032	-2.012	0.044	-		_		- 1
								-2.00	-1.00	0.00	1.00	2.00
									Favours Massage	F	avours Active Co	ntrol

NOTES: Weights are from random effects analysis

 $Heterogeneity: Q-value = 31.10, \ I^2 = 93.57\%; \ Publication \ bias: \ Egger's \ test \ P-value = 0.00$

Figure 3 (A) Results of massage vs. no treatment meta-analysis for cancer populations experiencing pain: pain intensity/severity at post-treatment (sample size analyzed, N=176). (B) Results of massage vs. active comparator(s) meta-analysis for cancer populations experiencing pain: pain intensity/severity at post-treatment (sample size analyzed, N=370). (C) Results of massage vs. active comparator(s) meta-analysis for cancer populations experiencing pain: sleep (fatigue) at post-treatment (sample size analyzed, N=235). (D) Results of massage vs. active comparator(s) meta-analysis for cancer populations experiencing pain: mood (anxiety) at post-treatment (sample size analyzed, N=234).

Evidence synthesis Table 4

Outcom <i>e/</i> Comparison	Number of Participants Completed (N)	*Confidence in the Estimate of the Effect (N)	[†] Effect Size	[‡] Reported Studies Safety GRADE (N)	[§] Strength of the Recommendation
PAIN¶	167 (3)	C	0 00 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(1)	No recommendation
vs. No realine to vs. Active Comparator(s)	708 (10)) U	-0.55 (95% CI, -1.23, 0.14), 6 studies	+2 (5) +2 (5)	Weak, in favor
vs. Active Comparator(s) 539 (6) C STRESS MOOD HEALTH-BELATED CITAL ITY OF	539 (6) REI ATED OIIAI ITV	C - IFF	Fatigue: -1.06 (95% CI, -2.18, 0.05), 3 studies	+2 (4)	Weak, in favor
vs. Active Comparator(s)	620 (8)	i i	Anxiety: -1.24 (95% CI, -2.44, -0.03), 3 studies	+2 (4)	Weak, in favor

Definitions for scoring are based on Samueli Institute's Overall Synthesis Evaluation Criteria (adapted from other standard synthesis methods).

(A) Further research is very unlikely to change our confidence in the estimate of effect, (B) further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate, (C) further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate, and (D) any estimate of effect is very uncertain.

Safety ranges from (+2) appears safe with infrequent adverse events and interactions to (- 2) appears to have serious safety concerns that include frequent and serious adverse Calculated as the standardized mean difference using Cohen's d effect size estimation where 0.2 is considered a small, 0.5 a medium, and 0.8 a large overall effect. events and/or interactions.

⁸Ranges from Strong Recommendation in Favor indicating that the EMT Working Group is very certain that benefits do outweigh risks and burdens to Strong Recommendation Against indicating that the EMT Working Group is very certain that benefits do not outweigh the risks and burdens. ^{II}Negative effect indicates improvement in massage intervention compared to control intervention.

or location of massage may need to be considered. It could be that practitioners may need to work around medical devices and be aware of concerns such as medical devices, side effects from drug or surgical treatments, and compromised bone integrity, lymph nodes, and blood cell counts. Similarly, individuals with cancer are often affected by additional cancer-related conditions that require substantial adjustments be made to ensure the patient's comfort and/or safety [61]. Massage therapists must know what particulars to elicit from the patient and respond accordingly. To date, this is not well understood.

Specific intervention details and safety are necessary for replication and validation of the trial's results, building a future research agenda and making decisions regarding implementation. Researchers and clinicians are unable to make recommendations to patients based on inconsistent or missing data. As such, the authors encourage researchers to utilize standard reporting guidelines (i.e., proposed STRICT-M Checklist), as well as CONSORT Guidelines when developing protocols and reporting clinical trials to ensure critical study elements are carried out and reported. In fact, this review demonstrated the wide variety in the types, styles, dosages, and naming conventions of massage that made it difficult to define "massage." Adhering to the proposed STRICT-M would help standardize the language used to describe massage, thereby enabling readers to better understand how to conceptualize massage as a therapy.

Future research should also focus on identifying appropriate controls in order to best determine the efficacy of massage. The majority of studies compared massage to another active therapy and reported massage was superior to most comparators. Further comparative effectiveness studies should be conducted to better understand these comparisons. Additionally, no studies included in this review performed cost analyses; the authors recommend that future studies conduct cost analyses to determine which intervention is most practical and appropriate for implementation.

No studies compared massage to sham therapy, and only a handful of studies compared it to no treatment. Several challenges surround selecting control groups suitable for massage therapy. For example, no treatment control groups do not control for nonspecific effects of attention and touch, resulting in massage interventions tending to be more successful than such controls. Wait list controls, moreover, do not control for placebo effects, and treatment as usual controls often assign individuals to care that they may have already previously tried and found unsuccessful. As such, massage should be assessed against controls that are equally credible, acceptable, and seemingly identical in order to ensure positive effects are truly attributable to massage. Sham controls (e.g., sham massage, light touch) are promising; however, there is debate whether touch control is a true placebo, as touch elicits nonspecific psychological effects. Future research should focus on identifying appropriate control groups to better understand the efficacy of massage, and whether it is appropriate to use for this patient population. Further, patient expectation was only measured by one study [56] in this review; the authors also encourage future trials to include questions about patient and practitioner expectation, as expectation can contribute to a placebo effect.

Not only is it important to identify appropriate comparators in order to ensure impactful results, but utilizing standardized, valid, and reliable patient-reported outcomes is also essential to successful healthcare. Using such outcomes helps decision-makers make evidencebased decisions for cost-effective treatments that are meaningful to the patient and focused on whole person healing. The National Institute of Health's Patient Reported Outcomes Measurement Information System (PROMIS) was designed to develop reliable and valid patient-reported items to evaluate patient-reported symptoms and health outcomes meaningful to patient function [62]. The Pain Assessment Screening Tool and Outcomes Registry (PASTOR) [63] is an example of a clinical pain assessment tool that utilizes PROMIS domains in order to standardize approaches to pain management. Such assessment tools are not only patientcentered, but are also less time consuming than using multiple individual assessment tools. This current review examined PROMIS and PASTOR domains to pre-define the function-related outcomes of interest. The authors encourage researchers to utilize measures that include PROMIS domains in all future massage therapy clinical trial work to not only ensure patient-centered care is at the forefront of research, but to also create both effective and easy translation and combinability of future results for the massage field.

In addition, while the authors used a clinically important cut-off point of 20-mm for the VAS for the reduction in pain, this should be interpreted with caution. What constitutes a clinically important change will vary for each individual; the whole-person perspective should be incorporated into that change-factor assessing globally not only pain reduction, but also psychological, physical, social, spiritual functioning as well. Since massage is considered complementary, we encourage the field to evaluate pain using measures beyond pain intensity when evaluating the success on any therapeutic approach to pain.

Applicability

Lastly, it is important to note that a recent meta-analysis was published reporting the effect of massage therapy on cancer pain [21] while this current review was being executed. There are important similarities to note. Both this current review and Lee et al. included similar studies, with the exception of a few that were not within the scope of this current review (i.e., controlled clinical trials, shiatsu or reflexology massage studies). The authors agree with Lee et al. on the importance of identifying appropriate control groups to guide future research in

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this field, as well as reporting practitioner characteristics in all future studies to be able to interpret the results for real-world applicability. The authors believe this current review adds to this work by not only including a more recent search, but also examining a variety of outcomes and controls, rather than the specific outcomes (i.e., cancer pain) and controls (i.e., no treatment or conventional care) that Lee et al. investigated. For example, the current review includes a narrower definition of massage therapy; unlike the Lee et al. analysis, this review did not include reflexology or shiatsu, as these therapies did not meet the review's definition of massage since these approaches have their own certification and council of schools and have fought to be recognized as separate from "massage." Further, Lee et al. was more interested with the population, performing subgroup analyses on types of cancer and causes of cancer pain. Conversely, this review focused on function-related outcomes and HrQoL, taking the stance that pain is multi-dimensional and must be approached holistically by examining such outcomes in order to fully understand the impact of massage for those experiencing pain. Lee et al. also performed subgroup analyses on types of massage: the authors avoided such analyses given the heterogeneity of massage types and inconsistencies in the field regarding the definition of massage. As such, the authors believe that massage, as a whole, first needs to be understood before examining specific types of massage and conducting comparative effectiveness research.

Despite these differences in protocols, both meta-analyses demonstrated favorable effects for massage on cancer pain, and the two approaches complement each other. The Lee et al. meta-analysis, however, reported much larger effects overall. Because results of meta-analyses can differ greatly depending on the source of data used for the meta-analysis, these differences could be due to the aforementioned differences in protocols (e.g., outcomes and comparators assessed) as well as some additional differences pertaining to the analytical techniques and the ways in which these procedures were carried out. Because of this, results should always be interpreted with caution, and methodology should always be explicitly stated in all reports.

Suggested Next Steps for Future Research

- Encourage researchers to follow the CONSORT Checklist when developing protocols and reporting trial findings to facilitate a complete and transparent report of the trial, aiding in their critical appraisal and interpretation.
- 2. Consider the proposed STRICT-M Checklist and adapt it for use in future trials; focus on practitioner qualifications and credentialing, and the special considerations required for this population.
- 3. Consider using PROMIS patient-reported outcome measures in future massage therapy clinical trials.

- 4. Sort through the issue of heterogeneity in the current literature base, considering items 1–3, and make recommendations regarding standard criteria for future protocol development.
- Conduct comparative effectiveness research, incorporating cost benefit analyses, on the use of massage therapy in cancer populations.

Conclusion

This is the first systematic review to assess functionrelated outcomes and HrQoL in cancer pain populations. Massage therapy appears to be promising for reducing pain intensity/severity, fatigue, and anxiety in cancer populations compared to the active comparators evaluated in this systematic review. Patients should consider massage therapy as a therapeutic option to help manage their cancer pain. Specific factors surrounding the massage protocol, as well as selection of appropriate controls and standard outcomes, need to be well-understood before definitive clinical conclusions and recommendations regarding the usage and implementation of massage can be made for cancer pain at a policy level. This review's promising results warrant investment of time and resources into future research aimed at addressing these aforementioned gaps in order to ultimately consider massage therapy a standard treatment for cancer populations experiencing pain.

Supplementary Data

Supplementary Data may be found online at http://pain medicine.oxfordjournals.org

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References

- 1 Lesage P, Portenoy RK. Trends in cancer pain management. Cancer Control 1999;6(2):136–45.
- 2 van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, et al. Prevalence of pain in patients with cancer: A systematic review of the past 40 years. Ann Oncol 2007;18(9):1437–49.

- 3 Margarit C, Julia J, Lopez R, et al. Breakthrough cancer pain—Still a challenge. J Pain Res 2012;5:559–66.
- 4 Smith H. A comprehensive review of rapid-onset opioids for breakthrough pain. CNS Drugs 2012;26 (6):509–35.
- 5 O'Mahony S, Goulet J, Kornblith A, et al. Desire for hastened death, cancer pain and depression: Report of a longitudinal observational study. J Pain Symptom Manage 2005;29(5):446–57.
- 6 Archie P, Bruera E, Cohen L. Music-based interventions in palliative cancer care: A review of quantitative studies and neurobiological literature. Support Care Cancer 2013;21(9):2609–24.
- 7 Coleman EA, Goodwin JA, Coon SK, et al. Fatigue, sleep, pain, mood, and performance status in patients with multiple myeloma. Cancer Nurs 2011;34 (3):219–27.
- 8 Dalal S, Hui D, Nguyen L, et al. Achievement of personalized pain goal in cancer patients referred to a supportive care clinic at a comprehensive cancer center. Cancer 2012;118(15):3869–77.
- 9 Reyes-Gibby CC, Wang J, Spitz M, et al. Genetic variations in interleukin-8 and interleukin-10 are associated with pain, depressed mood, and fatigue in lung cancer patients. J Pain Symptom Manage 2013;46 (2):161–72.
- 10 Levy MH. Pharmacologic treatment of cancer pain. New Engl J Med 1996;335(15):1124–1132.
- 11 Jho HJ, Kim Y, Kong KA, et al. Knowledge, practices, and perceived barriers regarding cancer pain management among physicians and nurses in Korea: A nationwide multicenter survey. PLoS One 2014;9(8):e105900. doi:10.1186/1475-2891-13-106.
- 12 Cleeland CS, Gonin R, Hatfield AK, et al. Pain and its treatment in outpatients with metastatic cancer. N Engl J Med 1994;330(9):592–6.
- 13 Syrjala K, Abrams J, Polissar N, et al. Patient training in cancer pain management using integrated print and video materials: A multisite randomized controlled trial. Pain 2008;135(1–2):175–86.
- 14 Furlan A, Yazdi F, Tsertsvadze A, et al. A systematic review and meta-analysis of efficacy, cost-effectiveness, and safety of selected complementary and alternative medicine for neck and low-back pain. Evid Based Complement Alternat Med 2012:953139. doi:10.1155/2012/953139.

- 15 Broom A, Kirby E, Sibbritt D, Adams J, Refshauge K. Use of complementary and alternative medicine by mid-age women with back pain: A national cross-sectional survey. BMC Complement Alternat Med 2012;12(98). doi:10.1186/1472-6882-12-98.
- 16 Moyer C, Rounds J, Hannum J. A meta-analysis of massage therapy research. Psychol Bull 2004;130(1): 3–18.
- 17 Sagar S, Dryden T, Wong R. Massage therapy for cancer patients: A reciprocal relationship between body and mind. Curr Oncol 2007;14(2):45–56.
- 18 Lee MS, Lee EN, Ernst E. Massage therapy for breast cancer patients: A systematic review. Ann Oncol 2011;22(6):1459–61.
- 19 Pan YQ, Yang KH, Wang YL, Zhang LP, Liang HQ. Massage interventions and treatment-related side effects of breast cancer: A systematic review and meta-analysis. Int J Clin Oncol 2014;19(5):829–41.
- 20 Ernst E. Massage therapy for cancer palliation and supportive care: A systematic review of randomised clinical trials. Support Care Cancer 2009;17(4):333–7.
- 21 Lee SH, Kim JY, Yeo S, Kim SH, Lim S. Meta-analysis of massage therapy on cancer pain. Integr Cancer Ther 2015;14(4):297–304.
- 22 Crawford C, Boyd C, Jain S, Khorsan R, Jonas W. Rapid evidence assessment of the literature: Streamlining the systematic review process and creating utility for evidence-based health care. BMC Res Notes 2015;8:631. doi:10.1186/s13104-015-1604-z.
- 23 Costello B, Lentino C, Boyd C, et al. The effectiveness of melatonin for promoting healthy sleep: A rapid evidence assessment of the literature. Nutr J 2014;13(106). doi:10.1186/1475-2891-13-106.
- 24 Buckenmaier C III, Crawford C, Lee C, Schoomaker E. Are active self-care complementary and integrative therapies effective for management of chronic pain? A rapid evidence assessment of the literature and recommendations for the field. Pain Med 2014; 15(Suppl 1):S1–S113.
- 25 Lee C, Crawford C, Wallerstedt D, et al. The effectiveness of acupuncture research across components of the trauma spectrum response (tsr): A systematic review of reviews. Syst Rev 2012;1 (46). doi:10.1186/2046-4053-1-46.
- 26 York A, Crawford C, Walter A, et al. Acupuncture research in military and veteran populations: A rapid

Massage Therapy for Cancer Pain Populations

- evidence assessment of the literature. Med Acupunct 2011;23(4):229–36.
- 27 Zeno S, Crawford C, Lee C, Purvis D, Deuster P. The effectiveness of warm-up exercises for physical fitness testing (in the military). Med Sci Sports Exerc 2013;45(7):1369–76.
- 28 Crawford C, Boyd C, Paat C, et al. The impact of massage therapy on function in pain populations—A systematic review and meta-analysis of randomized controlled trials: Part I, patients experiencing pain in the general population. Pain Med. doi:10.1093/pm/pnw099.
- 29 Boyd C, Crawford C, Paat C, et al. The impact of massage therapy on function in pain populations—A systematic review and meta-analysis of randomized controlled trials: Part III, surgical pain populations. Pain Med. doi:10.1093/pm/pnw101.
- 30 Office of the Army Surgeon General: Pain Management Task Force. Pain management task force final report: Providing a standardized DOD and VHA vision and approach to pain management to optimize the care for warriors and their families. Washington, DC: Office of the Army Surgeon General; 2010.
- 31 Coalition of National Massage Therapy Organizations. The entry level analysis project. 2015. Available at: www.elapmassage.org (accessed November 1, 2015).
- 32 Massage Therapy Body of Knowledge Task Force. Body of knowledge. 2015. Available at: www. mtbok.org (accessed November 1, 2015).
- 33 Scottish Intercollegiate Guidelines Network (SIGN). A guideline developer's handbook. 2001. Available at: http://www.sign.ac.uk/methodology/checklists.html (accessed November 1, 2015).
- 34 Khorsan R, Crawford C. How to assess the external validity and model validity of therapeutic trials: A conceptual approach for systematic review methodology. Evid Based Complement Alternat Med 2014:694804. doi:10.1155/2014/694804.
- 35 MacPherson H, Altman D, Hammerschlag R, et al. Revised standards for reporting interventions in clinical trials of acupuncture (stricta): Extending the consort statement. Acupunct Med 2010;28(2): 83–93.
- 36 The CONSORT Group. The consolidated standards of reporting trials (consort) statement. 2010. Available at: http://www.consort-statement.org/ (accessed November 1, 2015).

- 37 Cohen, J. Statistical Power Analysis for the Behavioral Sciences. 2nd edition. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
- 38 Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315(7109):629–34.
- 39 Higgins J, Thompson S, Deeks J, Altman D. Measuring inconsistency in meta-analyses. BMJ 2003;327(7414):557–60.
- 40 Farrar JT, Portenoy RK, Berlin JA, Kinman JL, Strom BL. Defining the clinically important difference in pain outcome measures. Pain 2000;88(3):287–94.
- 41 Collinge W, Kahn J, Walton T, et al. Touch, caring, and cancer: Randomized controlled trial of a multimedia caregiver education program. Support Care Cancer 2013;21(5):1405–14.
- 42 Post-White J, Fitzgerald M, Savik K, et al. Massage therapy for children with cancer. J Pediatr Oncol Nurs 2009;26(1): 16–28.
- 43 Rosen J, Lawrence R, Bouchard M, et al. Massage for perioperative pain and anxiety in placement of vascular access devices. Adv Mind Body Med 2013; 27(1):12–23.
- 44 Soden K, Vincent K, Craske S, Lucas C, Ashley S. A randomized controlled trial of aromatherapy massage in a hospice setting. Palliat Med 2004;18(2): 87–92.
- 45 Weinrich SP, Weinrich MC. The effect of massage on pain in cancer patients. Appl Nurs Res 1990;3(4): 140–5.
- 46 Ahles TA, Tope DM, Pinkson B, et al. Massage therapy for patients undergoing autologous bone marrow transplantation. J Pain Symptom Manage 1999; 18(3):157–63.
- 47 Billhult A, Bergbom I, Stener-Victorin E. Massage relieves nausea in women with breast cancer who are undergoing chemotherapy. J Altern Complement Med 2007;13(1):53–7.
- 48 Campeau MP, Gaboriault R, Drapeau M, et al. Impact of massage therapy on anxiety levels in patients undergoing radiation therapy: Randomized controlled trial. J Soc Integr Oncol 2007;5(4):133–8.
- 49 Jane S-W, Chen S-L, Wilkie DJ, et al. Effects of massage on pain, mood status, relaxation, and sleep in taiwanese patients with metastatic bone pain: A randomized clinical trial. Pain 2011;152(10):2432–42.

- 50 Kutner JS, Smith MC, Corbin L, et al. Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer: A randomized trial. Ann Intern Med 2008;149(6):369–79.
- 51 Listing M, Reisshauer A, Krohn M, et al. Massage therapy reduces physical discomfort and improves mood disturbances in women with breast cancer. Psychooncology 2009;18(12):1290–9.
- 52 Wilkie DJ, Kampbell J, Cutshall S, et al. Effects of massage on pain intensity, analgesics and quality of life in patients with cancer pain: A pilot study of a randomized clinical trial conducted within hospice care delivery. Hosp J 2000;15(3):31–53.
- 53 Khiewkhern S, Promthet S, Sukprasert A, Eunhpinitpong W, Bradshaw P. Effectiveness of aromatherapy with light thai massage for cellular immunity improvement in colorectal cancer patients receiving chemotherapy. Asian Pac J Cancer Prev 2013;14(6):3903–7.
- 54 Post-White J, Kinney ME, Savik K, et al. Therapeutic massage and healing touch improve symptoms in cancer. Integr Cancer Ther 2003;2 (4):332–44.
- 55 Williams AF, Vadgama A, Franks PJ, Mortimer PS. A randomized controlled crossover study of manual lymphatic drainage therapy in women with breast cancer-related lymphoedema. Eur J Cancer Care 2002;11(4):254–61.
- 56 Toth M, Marcantonio ER, Davis RB, et al. Massage therapy for patients with metastatic cancer: A pilot

- randomized controlled trial. J Altern Complement Med 2013;19(7):650-6.
- 57 Russell NC, Sumler SS, Beinhorn CM, Frenkel MA. Role of massage therapy in cancer care. J Altern Complement Med 2008;14(2):209–14.
- 58 Furlan A, Brosseau L, Imamura M, Irvin E. Massage for low back pain. Cochrane Database Syst Rev 2002;(2):CD001929.
- 59 Haraldsson B, Gross A, Myers C, et al. Massage for mechanical neck disorders. Cochrane Database Syst Rev 2006;(3):1–75.
- 60 Ezzo J. What can be learned from cochrane systematic reviews of massage that can guide future research. J Altern Complement Med 2007;13(2): 291–5.
- 61 Society for Oncology Massage (s4om). 2015. Available at: http://www.s4om.org/faq (accessed November 1, 2015).
- 62 National Institutes of Health. Promis: Patient reported outcomes measurement information system. 2015. Available at: http://commonfund.nih.gov/promis/overview (accessed November 1, 2015).
- 63 Defense & Veterans Center for Integrative Pain Management (DVCIPM). Pain assessment screening tool and outcomes registry (pastor). 2015. Available at: http://www.dvcipm.org/clinical-resources/pain-as sessment-screening-tool-and-outcomes-registry-pas tor (accessed November 1, 2015).