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Evidence Brief: The Comparative Effectiveness of Selected Complementary and Integrative Health (CIH) Interventions for Preventing or Reducing Opioid Use in Adults with Chronic Neck, Low Back, and Large Joint Pain

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PREFACE

The VA Evidence-based Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of particular importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. QUERI provides funding for four ESP Centers, and each Center has an active University affiliation. Center Directors are recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Centers. The ESP is governed by a Steering Committee comprised of participants from VHA Policy, Program, and Operations Offices, VISN leadership, field-based investigators, and others as designated appropriate by QUERI/HSR&D.

The ESP Centers generate evidence syntheses on important clinical practice topics. 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 ESP disseminates these reports throughout VA and in the published literature; some evidence syntheses have informed the clinical guidelines of large professional organizations.

The ESP Coordinating Center (ESP CC), located in Portland, Oregon, was created in 2009 to expand the capacity of QUERI/HSR&D and is charged with oversight of national ESP program operations, program development and evaluation, and dissemination efforts. The ESP CC establishes standard operating procedures for the production of evidence synthesis reports; facilitates a national topic nomination, prioritization, and selection process; manages the research portfolio of each Center; facilitates editorial review processes; ensures methodological consistency and quality of products; produces “rapid response evidence briefs” at the request of VHA senior leadership; collaborates with HSR&D Center for Information Dissemination and Education Resources (CIDER) to develop a national dissemination strategy for all ESP products; and interfaces with stakeholders to effectively engage the program.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP CC Program Manager, at Nicole.Floyd@va.gov.

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This report is based on research conducted by the Evidence-based Synthesis Program (ESP) Coordinating Center located at the **Portland VA Health Care System, Portland, OR,** funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

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EXECUTIVE SUMMARY

Over the past 2 decades, there has been a dramatic increase in opioid-related overdose deaths, dependence, and misuse. As a result, there is intense interest in non-opioid alternatives for treating chronic pain. Select Complementary and Integrative Health (CIH) interventions may be a reasonable non-opioid treatment option in general, if they can improve pain at a magnitude comparable to opioids, but without serious side effects. Whether CIH interventions can reduce chronic opioid use is of great interest in the fight against the opioid epidemic.

The evidence base regarding the effectiveness of select CIH interventions for reducing opioid use is extremely limited. No study has evaluated the effectiveness of select CIH interventions for reducing new opioid use, stopping opioids entirely, or for reducing opioid use below any particular morphine equivalent dose (MED) threshold. Compared to sham, in patients already using a dosage below 80 mg MED, there is low-strength evidence that certain electro-acupuncture modalities can reduce opioid dose after 6 to 10 weeks of treatment. This was found both in a group of Australian patients with various forms of chronic pain undergoing a planned opioid tapering and in a group of Veterans with advanced knee osteoarthritis taking opioids for an unknown duration. But these effects were not sustained 5-9 months following acupuncture discontinuation (Table ES1). Single studies of massage, meditation, and yoga provided insufficient evidence to draw conclusions about their effects on opioid dose because (1) they lacked details about opioid type, dose, and frequency and (2) relied on self-assessments from unblinded patients, with no effort to match the intervention to a sham treatment group, which could have led to more favorable assessments in the experimental groups. We found no studies that evaluated the impact of tai chi or classic acupuncture on opioid use.

Additional research is needed to better understand the effectiveness of select CIH interventions for reducing opioid use in Veterans. To best remedy key limitations of current evidence, future research should seek to: (1) evaluate the most clinically relevant outcomes of reducing new use, stopping opioids entirely, and/or reducing opioid use below relevant MED threshold(s) using suggested measurement methods, (2) simultaneously measure a complete set of key outcomes, including impact on pain, pain-related function, quality of life, and harms, including potential consequences of reducing opioid use, (3) clarify whether the effectiveness of CIH varies depending on the timing of their integration, and (4) identify particular subpopulations that are more or less likely to benefit from CIH to reduce opioid use and whether variation in benefit varies by CIH type.

Background

To inform VA's research initiative to evaluate non-opioid alternative approaches to pain management, its Health Services Research and Development Service (HSR&D) is planning a state-of-the-art (SOTA) conference for November 2016 to help define future directions of research for all non-opioid alternative approaches to pain management. To inform their interim April 2016 Expert SOTA Planning Meeting, HSR&D commissioned the Evidence-based Synthesis Program Coordinating Center (ESP CC) to conduct an evidence brief on the effectiveness of select Complementary and Integrative Health (CIH) interventions (*ie*, acupuncture, massage, meditation, tai chi, and yoga) for reducing opioid use in adults with chronic neck, low back, and large joint pain.

Methods

To identify studies, we reviewed bibliographies from recent good-quality systematic reviews and supplemented this with a Medline search for more recent studies. We used prespecified criteria for study selection, data abstraction, and rating internal validity and strength of the evidence. See our PROSPERO protocol for our full methods.

Table ES1. Characteristics and Findings of Acupuncture Studies

Author Year Risk of Bias N Pain type	Interventions	Opioid type and dose	Impact on opioid use	Pain, quality of life, functional status, adverse events
Sator-Katzenschlager 2004 [1] Unclear N = 61 LBP	Auricular acupuncture with electrical stimulation (EA) or without stimulation (CO)	Tramadol ≤ 400 mg daily	EA reduced # opioid tablets consumed throughout intervention: EA = 6 vs CO = 150 (P < .001)	EA reduced pain (10-point VAS scale) at 18 wks: EA = 1 vs CO = 4 (P < 0.05) EA reduced well-being impairment (10-point VAS scale) at 18 wks: EA = 1 vs CO = 5 (P < 0.05) Adverse events: none observed
Weiner 2013 [2] Unclear N = 190 Veterans with Knee OA	Periosteal stimulation therapy, with boosters (PST+PST) or without boosters (PST+control) or control PST without boosters (control)	Opioid type NR: average 0.47 doses/wk	Opioid consumption at 10 wks PST+PST similar to Control PST: 0.018 (95% CI -0.19 to 0.23) PST+control reduced consumption vs Control PST : -0.27 (95% CI -0.48 to -0.054)	9 m outcomes: PST+PST improved WOMAC pain (MD 1.5, 95% CI 0.069 to 3.0), but not SF-36 physical component (MD -1.2; 95% CI -2.8 to 0.041) vs Control PST PST+control did not improve WOMAC pain (MD 1.1, 95% CI -.32 to 2.6) or SF-36 physical component (MD -1.3; 95% CI -3.0 to 0.28) vs Control
Zheng 2008 [3] Unclear N = 35 NMCP	Electroacupuncture (REA) or sham electroacupuncture (SEA)	Codeine, Methadone, Oxycodone, Morphine, & Tramadol Dose (mg/d morphine equivalent): REA = 65.9/d SEA = 42.2/d	REA reduced OLM consumption (change from baseline, mg/d morphine equivalent) at 8 wks: REA = -25.7 vs SEA = -10.9 20 wks: REA = -16.7 vs SEA = -8.1	REA reduced pain (scale NR): Change from baseline at 8 wks: -0.8 REA vs -0.7 SEA (P = .001) Adverse events: 33 events REA and 19 events SEA

EA: Auricular acupuncture with electrical stimulation; CO: Auricular acupuncture without electrical stimulation; PST: Periosteal stimulation therapy; LBP: Low back pain; VAS: Visual Analog Scale; OA: Osteoarthritis; WOMAC: Western Ontario & McMaster Universities Osteoarthritis Index Evidence Brief; NMCP: Non-malignant chronic pain; REA: Electroacupuncture; SEA: Sham electroacupuncture; OLM: Opioid-like medications; NR: Not reported

INTRODUCTION

PURPOSE

In October, 2015, the White House announced that the VA would lead an initiative to evaluate non-opioid alternative approaches to pain management. [https://www.whitehouse.gov/the-press-office/2015/10/21/fact-sheet-obama-administration-announces-public-and-private-sector] To inform this initiative, the VA Health Services Research and Development Service (HSR&D) is planning a state-of-the-art (SOTA) conference for November 2016 to help define the future directions of research for all non-opioid alternative approaches to pain management. In April 2016, HSR&D will convene an Expert SOTA Planning Meeting, and commissioned the Evidence-based Synthesis Program Coordinating Center (ESP CC) to conduct an evidence brief on select Complementary and Integrative Health (CIH) interventions to inform that meeting.

Key goals of the April planning meeting are to identify: (1) preliminary consensus policy conclusions based on what is known about CIH approaches to reduce opioid use, (2) preliminary gaps in evidence, (3) a research agenda for National Center for Complementary and Integrative Health (NCCIIH)/Department of Veterans Affairs (VA)/Department of Defense (DOD) collaboration for CIH approaches to pain management and comorbidities, and (4) key questions for more in-depth examination at the November 2016 SOTA. For the November 2016 SOTA, additional work will be done to evaluate all non-pharmacological approaches, including cognitive behavioral therapy (CBT) and additional key outcomes, including pain, function, PTSD, sleep, and quality of life.

BACKGROUND

The Opioid Overdose Epidemic

Opioid analgesics are a class of prescription medications (morphine, hydrocodone, oxycodone, *etc*) that the FDA has classified as controlled substances (Schedule 2 drug) due to their high potential for abuse and dependence. Between 1999 and 2011, the United States saw a 319% increase in deaths due to prescription opioid analgesic-related overdoses. Because this increase far exceeded that for deaths due to heroin (+149%) and cocaine (+22%) and it outnumbered motor vehicle crash and gunshot-related deaths,[4] in 2012 the CDC characterized the problem as an epidemic.[5] Compared to the general US population, VHA patients may have an elevated risk of death due to prescription opioid overdose (crude rate per 100,000 person-years = 1.96 vs 10.49; standardized mortality ratio 1.96, 95% CI 1.83 to 2.08).[6]

The increase in opioid prescribing that began in the late 1990s is frequently cited as a key determinant of increased opioid-related overdose mortality.[7] The causes of increased prescribing have been widely debated and are likely numerous. Recent data from 3 large health care systems, including the VHA, have shown that higher doses are a risk factor for prescription opioid overdose deaths[8-10] and suicide.[11] Among Veterans taking opioids for pain, compared to those prescribed a Morphine Equivalent Dose (MED) of < 20 mg, risk of death increased for MED 20 to < 50 mg (HR 1.88; 95% CI 1.33 to 2.67), 50 to < 100 mg (HR 4.63, 95% CI 3.18 to 6.74), and ≥ 100 mg (HR 7.18; 95% CI 4.85 to 10.65).[10] Studies examining the association between opioid dose and death have categorized dose in a variety of ways for a variety of reasons, but evidence has not yet identified a clear dose "threshold" for overdose risk.[12] Rather, evidence seems to

suggest that risk increases as dose increases, starting with very low doses. The new CDC guidelines recommend additional caution at 50 mg and avoidance of prescribing > 90 mg, but acknowledge that there is no threshold for risk.[13]

Many factors contribute to opioid-related mortality. A systematic review identified 3 categories of potential determinants of increased opioid-related mortality in the United States and Canada from 1990 to 2013[14]: (1) *Prescriber behaviors*: increased prescriptions and sales of opioids, prescribing higher doses of opioids, prescribing oxycodone, prescribing methadone, and prescribing at high volumes, (2) *User behavior and characteristics*: history of substance abuse, diversion, doctor or pharmacy shopping, drug substitution, polydrug toxicity, sociodemographic characteristics (men, non-Hispanic Whites and American Indian/Alaska Natives, middle-aged individuals, those living in rural areas, and those of lower socioeconomic status), and (3) *Environmental and systemic determinants*: area urbanization or socioeconomic status, geography, endorsement by guideline, policies and consensus statements of expanded opioid prescription, implementation of educational interventions and prescription drug monitoring programs, and expanded media coverage.

Because the reasons for increased opioid-related overdose mortality are numerous, diverse, and complex, interventions to reduce opioid-related overdose mortality must vary in their targets. To emphasize its public health importance, in its Fiscal Year 2016 budget, the White House Administration increased funding by $133 million for efforts to combat the prescription opioid epidemic. This funding will support multifaceted efforts to improve education and training, tracking and monitoring, prevention and overdose response, treatment, and enforcement and supply.

Chronic Pain and the Complexity of Chronic Opioid Therapy

Chronic pain may occur in up to 50% of Veterans treated in primary care.[15] Chronic pain is characterized by a persistence of greater than 3 months[16] and its treatment may vary based on patient demographics and comorbidities (*eg*, alcohol or substance use and other mental health and medical disorders).[17] Among individuals with chronic pain, about 25% will develop related life problems, including increasing physical, emotional, and social dysfunction that requires more intensive, multimodal treatment.[18]

Developing evidence-based guidance on how and when to use opioids for chronic non-cancer pain management is difficult because there is little evidence that opioids are effective in maintaining pain relief over long periods of time and inconclusive evidence as to whether opioids can improve long-term functioning and quality of life.[17,19] Clinical policies and practice try to balance the risks of overdose, drug interactions, and complications such as falls and accidental death against the risk of undertreatment of pain.[20] Between 2009 and 2012, many professional society and health care agencies, including the VA/DoD, updated their guidelines to better address opioid risk mitigation, focusing on dosing targets and strategies for identifying signs of misuse.[21] According to Nuckols et al, 9 fair- to good-quality guidelines consistently agree on the following treatment strategies: (1) use of upper dosing thresholds (generally 90-100 mg MED, but some up to 200 mg MED), (2) cautions with certain medications, (3) attention to drug-drug and drug-disease interactions, and (4) use of risk assessment tools, treatment agreements, and urine drug testing for mitigating high-risk use. However, implementation of the

recommended approaches is problematic because the evidence on the effectiveness of such strategies remains weak[21] and questions continue about whether dosing threshold initiatives may be generating a new unanticipated consequence – the emergence of withdrawal symptoms that may lead to aberrant opioid-seeking behaviors that may result in use of illicit opioids.[22,23]

To identify which patients may benefit most from expanded use of non-opioid alternatives, there is a need to first understand who is most at risk for complications related to opioid use. More medical, psychiatric, and substance use disorders and specifically neuropathy, low back pain, nicotine dependence disorders, and guideline-discordant care have been associated with high-dose opioid use both within and outside of the VA.[24,25] In Veterans receiving opioids, receipt of benzodiazepines has been associated with an increased risk of overdose death[26] and mental health disorders, pharmacotherapy, impaired drug metabolism or excretion, pulmonary disorders, specific opioid characteristics, and recent hospital visits have been associated with serious opioid-induced respiratory depression.[27]

Potential Mechanism for CIH in Mitigating High-risk Opioid Use

CIH encompasses a broad range of therapies, including physical modalities (*eg*, acupuncture, massage, chiropractic manipulation), relaxation and mind/body therapies (*eg*, meditation, mindfulness, guided imagery), movement-based therapies (*eg*, yoga, tai chi, other exercise), creative arts therapies, nutritional counseling, self-care, and other naturopathic treatments and herbal medicines.[28] These treatments are used in a variety of pain conditions, including musculoskeletal, arthritis, headache, and fibromyalgia pain, as well as depression, posttraumatic stress disorder (PTSD), and substance use disorders.[29]

Limited evidence suggests that select CIH interventions may be reasonable non-opioid treatment options in general because: (1) CIH is possibly under-utilized in patients prescribed opioids and (2) compared to usual care, magnitude of pain reduction for CIH is potentially comparable to opioids, but without serious side effects. The potential mechanism for CIH interventions in mitigating high-risk opioid use is that if CIH interventions were to effectively treat pain, then physicians could prescribe fewer or lower dose opioids and/or patients could take fewer or lower dose opioids. Although there is already high use of and willingness to try certain CIH modalities among Veterans with chronic non-cancer pain (CNCP) in general,[30] studies show under-use of CIH in patients prescribed opioids.[31,32] Although studies directly comparing CIH and opioids are lacking,[17,33] the most recent and relevant systematic reviews[33-44] show that when CIH interventions are each respectively compared to a common control group of usual care, they have similar magnitudes of pain improvement (SMD range = 0.46 to -3.65). However, it is unclear how applicable CIH's efficacy is to patients taking opioids – particularly at high doses – because CIH studies have often excluded entirely or involved very few and poorly characterized patients prescribed opioids, and there is some evidence that *non-use* of opioids may be a strong predictor of CIH efficacy.[45] For the April SOTA meeting, a small group of CIH and pain researchers will provide a more rigorous synthesis of evidence on the effects of CIH on pain.

We found, however, that opioid-specific guidelines (see Supplemental Materials)[13,46-62] seldom refer directly to CIH treatments. Some guidelines instruct providers to ask themselves, prior to prescribing opioids, "are alternative treatment options available?", but no specific CIH treatments are listed as a possible "alternative" treatment to consider. General chronic pain

guidelines more commonly reference specific CIH interventions – most frequently acupuncture,[54-59] followed by massage,[54,55,58,61] and yoga.[54,55,58] The VHA's current Pain Management Directive (2009-053) also generally mentions CIH as a potential non-pharmacological treatment option, but like other guidelines, does not specify *when* to initiate CIH in relation to opioids. All seem to imply CIH use as generally adjunctive to opioids. National CIH organizations, such as the National Center for Complementary and Integrative Health in the United States and the Complementary Medical Association in United Kingdom, have not yet issued CIH-specific guidelines.

Possible roles for CIH in mitigating high-risk opioid use are: (1) to reduce opioid use in general, by initiating CIH *prior* to initiating opioids, (2) to reduce dose escalation, by integrating adjunctive CIH during the initiation and titration phases and/or as a supplemental therapy for pain exacerbations during stable opioid therapy, and (3) to help manage withdrawal symptoms and potential pain exacerbation during planned opioid dose reduction or complete withdrawal.

Key Considerations in Measuring the Effectiveness of CIH to Reduce Opioid Use

The goal of reducing opioid use is to reduce risk of overdose deaths, dependence, misuse, and other serious complications. In some cases, this means stopping opioids entirely. Because of the link between increased opioid dose and prescription opioid overdose deaths,[8-10] another potentially meaningful indicator of CIH success in reducing opioid use may be to show reductions below relevant and justified MED thresholds. However, given the central goal of risk reduction and the lack of an established magnitude of dose reduction that is agreed upon as clinically important, any mean dose decrease is a reasonable proxy to consider.

Some risks of reducing opioid dose and use may be under-treatment of pain resulting in reduced quality of life and function, the emergence of withdrawal symptoms – potentially related to an opioid use disorder - that may lead to aberrant opioid-seeking behaviors that may result in use of illicit opioids,[23] and perception of withholding care. These potential consequences must be weighed against reductions in opioid use.

There is a need to clarify the applicability of CIH's effects to Veterans who are most representative of patients prescribed high-dose opioids: predominantly male, white, middle-aged, overweight, and with multiple moderate-severe pain problems and high levels of medical and psychiatric comorbidity. Also of interest is determining whether: (1) type or location of pain, (2) patient demographics (*eg*, age, race, ethnicity, gender), and (3) patient comorbidities (including past or current alcohol or substance use disorders, mental health disorders, medical comorbidities, and high risk for addiction) may modify the effectiveness of CIH for reducing opioid use and whether there is variation by CIH type or timing of use (*eg*, *prior* to initiating opioids; early intervention to prevent "chronification"; or as an adjunct to opioid therapy during initiation, titration, or for exacerbations, or after opioid failure).

SCOPE

The objective of this evidence brief is to summarize the evidence on the effectiveness of select Complementary and Integrative Health (CIH) interventions (acupuncture, massage, meditation, tai chi, and yoga) for reducing opioid use in adults with chronic neck, low back, and large joint pain. The ESP Coordinating Center investigators and representatives of the SOTA committee

worked together to identify the population, interventions, comparators, outcomes, timing, setting, and study design characteristics of interest. The SOTA committee approved the following key questions and eligibility criteria to guide this review:

KEY QUESTIONS

Key Question 1: In adults with chronic neck, low back, and large joint pain who have never used opioids, what is the comparative effectiveness of selected CIH interventions for reducing new opioid use?

Key Question 2: In adults with chronic neck, low back, and large joint pain who have never used opioids, what are the comparative harms of selected CIH interventions for reducing new opioid use?

Key Question 3: In adults with chronic neck, low back, and large joint pain who have never used opioids, how do the comparative effects of selected CIH interventions for reducing new opioid use vary depending on: (1) the specific type or location of pain; (2) patient demographics (*eg*, age, race, ethnicity, gender); (3) patient comorbidities (including past or current alcohol or substance use disorders, mental health disorders, medical comorbidities, and high risk for addiction)?

Key Question 4: In adults using opioids for chronic neck, low back, and large joint pain, what is the comparative effectiveness of selected CIH interventions for reducing opioid use?

Key Question 5: In adults using opioids for chronic neck, low back, and large joint pain, what are the comparative harms of selected CIH interventions for reducing opioid use?

Key Question 6: In adults using opioids for chronic neck, low back, and large joint pain, how do the comparative effects of selected CIH interventions for reducing new opioid use vary depending on: (1) the specific type or location of pain; (2) patient demographics (*eg*, age, race, ethnicity, gender); (3) patient comorbidities (including past or current alcohol or substance use disorders, mental health disorders, medical comorbidities, and high risk for addiction)?

ELIGIBILITY CRITERIA

The ESP included studies that met the following criteria:

- ***P****opulation:* Adults with chronic non-cancer neck or low back and large joint pain (*eg*, shoulders, elbows, hips, knees, and ankles)[1]
- ***I****ntervention*: Massage, acupuncture, meditation, yoga, and tai chi
- ***C****omparator*: No restrictions
- ***O****utcomes:* Primary = reducing new or ongoing use or dosage of opioids, including physician prescribing or patient consumption; Secondary = pain, functional capacity, quality of life, adverse events

[1] ACR/EULAR classification from Aletaha et al 2010 in *Arthritis & Rheumatism*.

- ***T****iming:* No restrictions
- ***S****etting*: No restrictions
- ***S****tudy design:* No restrictions

METHODS

An evidence brief differs from a full systematic review in that the scope is narrowly defined and some traditional review methods may be streamlined in order to synthesize evidence within a shortened timeframe. An evidence brief does not outline the full context in which the information is to be used and does not present a comprehensive assessment of knowledge on the topic. Brief or rapid review methodology is still developing and there is not yet consensus on what represents best practice.

To identify published articles relevant to the key questions, we primarily relied on reference lists from the large volume of recent and relevant ESP evidence maps and systematic reviews. We started with the 4 evidence maps developed by the ESP on acupuncture, meditation, tai chi, and yoga.[41-44] For massage and to identify newer systematic reviews for the other 4 interventions, our research librarian then searched Ovid MEDLINEÒ, Cochrane Database of Systematic Reviews, PubMed, PsycINFO, and CINAHL from 2014 forward. To identify newer primary studies published subsequent to the prior systematic review searches, our research librarian searched MEDLINE® using terms for the CIH interventions and chronic pain. We determined search start dates for new primary studies based on the end dates of previous systematic reviews: 2009 for acupuncture, 2014 for massage, and 2010 for meditation, tai chi, and yoga. We limited the search to published and indexed articles involving human subjects available in the English language. Additional citations were identified through consultation with content experts. See Supplemental Materials for complete search strategies for both our systematic review and primary study searches.

To identify additional unpublished or ongoing studies or existing programs that have evaluated or will evaluate the effects of specific CIH interventions to reduce opioid use, our research librarian searched the following non-bibliographic database sources: known authors, organization websites, government websites, conference proceedings, academic medical center websites, and Google. We identified known authors by noting authors who repeatedly appeared as authors on relevant publications, as well as through discussion with topic experts. Relevant organizations were identified through mention in recent media publications on the topic, since that captured current programs and research that might not be included in academic literature. We included government agencies that have conducted research on, or provided funding for research on, the opioid crisis. Relevant professional societies that publish conference proceedings were also included, namely the American Pain Society. Also, we searched for programs that connected complementary and alternative treatments to traditional Western medicine programs. Finally, between February 8, 2016 and February 19, 2016, we used Google to identify relevant websites, organizations, programs, and experts in the field. Some keywords used include “opioids epidemic,” “opioids crisis,” “narcotics,” “complementary and alternative medicine,” “integrative medicine,” “yoga,” “acupuncture,” “massage,” “programs,” “centers,” and “interventions.”

Study selection was based on the eligibility criteria described above. Titles and abstracts were reviewed by one investigator. Full-text articles were reviewed by one investigator and checked by another. All disagreements were resolved by consensus.

We used Cochrane's Risk of Bias Tool to rate the internal validity of controlled trials.[63] We abstracted prespecified data from all included studies and results for each included outcome. All data abstraction and internal validity ratings were first completed by one reviewer and then checked by another. All disagreements were resolved by consensus.

We graded the strength of the evidence based on the AHRQ Methods Guide for Comparative Effectiveness Reviews.[64] This approach incorporates 4 key domains: risk of bias (includes study design and aggregate quality), consistency, directness, and precision of the evidence. It also considers other optional domains that may be relevant for some scenarios, such as a dose-response association, plausible confounding that would decrease the observed effect, strength of association (magnitude of effect), and publication bias. Strength of evidence is graded for each key outcome measure and ratings range from high to insufficient, reflecting our confidence that the evidence reflects the true effect.

A draft version of this report was reviewed by 6 technical experts as well as clinical leadership. Their comments and our responses are presented in the Supplemental Materials.

The complete description of our full methods can be found on the PROSPERO international prospective register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO/; registration number CRD42016033177).

RESULTS

LITERATURE FLOW

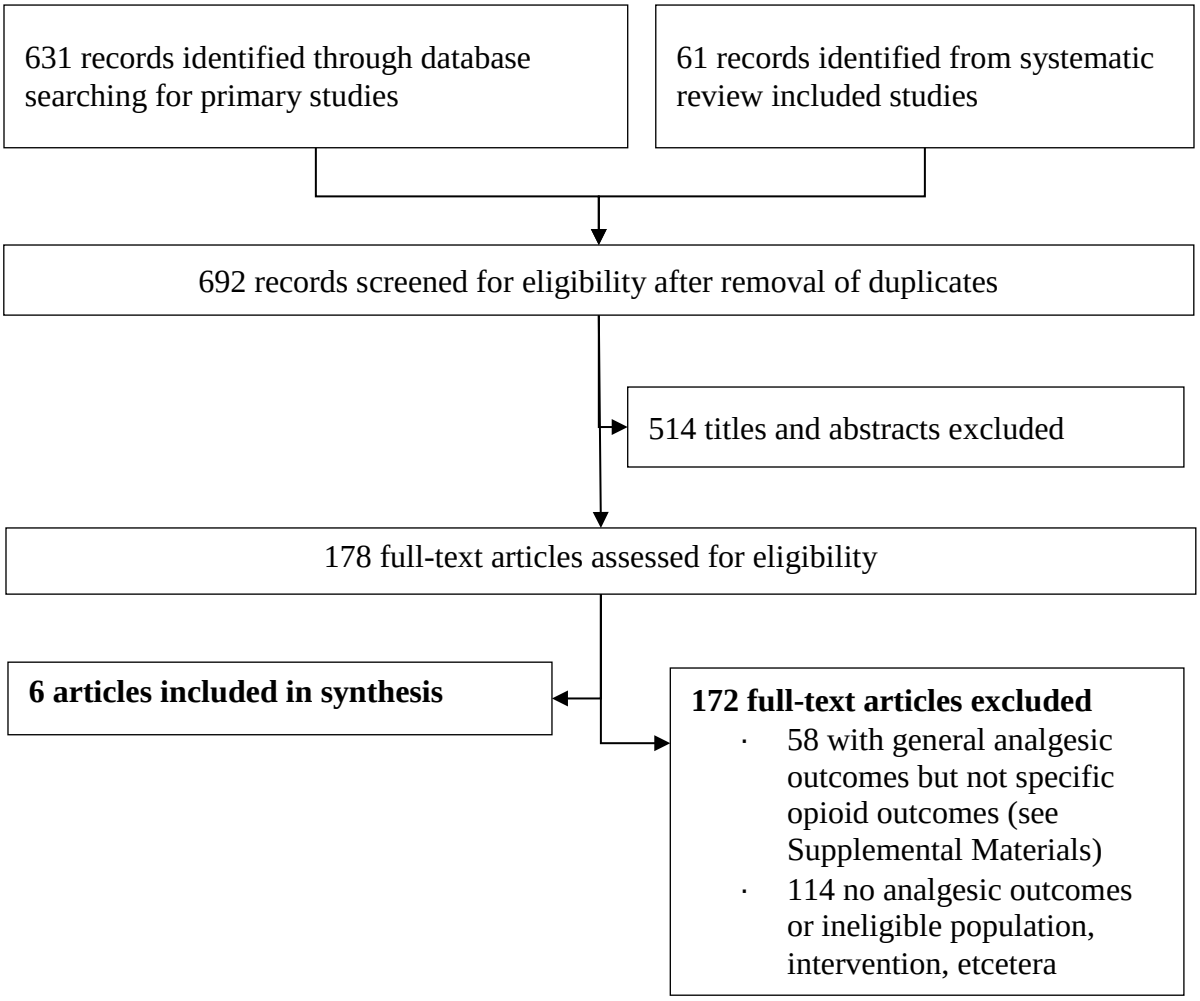
Table 1 displays the number of systematic reviews we reviewed in each intervention area. Overall, most SRs identified did not specifically report analgesic use as an outcome.

Table 1. Identified and Reviewed Systematic Reviews

Source	Total # SRs identified	#SRs reviewed full-text	# SRs evaluating analgesic use	# Primary studies identified
Acupuncture				
ESP map	26	26	4	48
Update search	333	24	0	
Massage				
Search	178	25	0	6
Meditation				
ESP map	9	9	0	1
Update search	65	7	0	
Tai chi				
ESP map	14	14	0	3
Update search	35	11	0	
Yoga				
ESP map	3	3	0	3
Update search	52	6	0	

Figure 1 shows the results of our searches for primary studies. We included a total of 6 studies: 3 on acupuncture, 1 on massage, 1 on meditation, and 1 on yoga. No studies were identified for tai chi.

Figure 1. Literature Flow Chart



Numerous CIH studies measured analgesic use as a secondary outcome, but the majority did not isolate opioid use and prevalence of opioid use at baseline was generally minimal (< 10%). The exceptions were 6 studies that we included in this review that did isolate opioid use.[1-3,65-67]

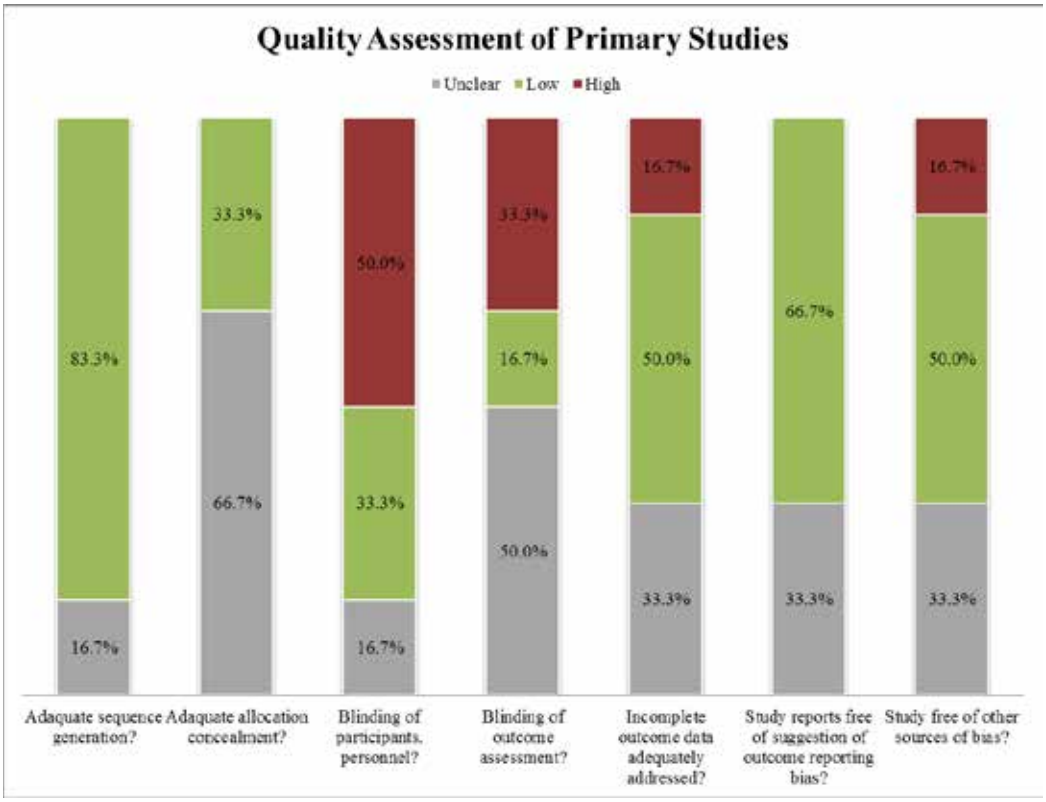
Supplemental searching of non-bibliographic database sources (see Supplemental Materials for details, including website links) did not identify any additional unpublished or ongoing studies or existing programs that have evaluated or will evaluate the effects of specific CIH interventions to reduce opioid use. For example, in 2014, NIH's National Center for Complementary and Alternative Medicine, the National Institute on Drug Abuse, and the Veteran Affairs Health Services Research and Development announced that they are providing an estimated $21.7 million over 5 years to 13 projects that explore nondrug approaches to managing pain.[68] Although 4 programs include mindfulness as an intervention, none of those mention evaluation of impact on opioid use. We also identified a protocol for an ongoing large-scale NIH-funded study that will compare the effects of usual care to a primary care-embedded interdisciplinary pain program designed to help patients who are on long-term opioids adopt self-management skills and limit their opioid use (NCT02113592). The protocol specifies morphine equivalents as a planned tertiary outcome measure. Although the intervention includes a yoga-based adapted

movement component, the analysis will not be able to isolate its effects from among those of the other multiple components (*ie*, behavioral health, nurse case management, physical therapy, and pharmacy). Also, although we are aware of many existing programs that offer CIH for pain management, it was unclear how CIH was used in relationship to prescribed opioids within these programs.[69-71] We are also aware of programs that routinely use multidisciplinary approaches to help reduce reliance on pharmacological treatments for pain.[73,74] But we were unable to identify clear descriptions of their approaches to using specific CIH interventions or data on their effectiveness.

We found the published literature to provide little useful information for determining the effectiveness of CIH interventions for reducing opioid use. This is because: (1) very few studies evaluated opioid use in isolation from overall analgesic use, and (2) in those that did, details on key opioid use characteristics (*eg*, timing of initiation, daily opioid dose, and duration of use) were missing altogether[65-67] or nonspecific,[2] or the studies suffered from other methodological limitations.[1,3] Details on key opioid use characteristics were likely limited because, with one exception,[3] studies were not designed to measure opioid use as a key outcome. All studies that evaluated opioid use were randomized controlled trials.

Figure 2 displays the quality indicators of the included studies. Half of the studies were rated high risk of bias[65-67] and half were rated as unclear risk of bias.[1-3] The most common methodological limitations were: (1) lack of blinding of participants, personnel, and outcome assessors, combined with lack of a sham or placebo group, which could have led to more favorable assessments in the intervention groups, and (2) increased risk of attrition bias due to high (47% to 52%) or differential (> 20%) exclusion of outcome data. See the Supplemental Materials for detailed data abstraction, quality assessment, and strength of evidence tables.

Figure 2: Quality Assessment of Included Studies



KEY QUESTIONS 1-3: CIH FOR REDUCING NEW OPIOID USE

We found no studies assessing CIH interventions for reducing new opioid use.

KEY QUESTIONS 4-6: CIH FOR MANAGING EXISTING OPIOID USE

Acupuncture

Acupuncture is the only included CIH intervention with any studies that reported at least some information on opioid characteristics.[1-3] Although actual mean baseline MED were only reported in one study (42.2-65.9 mg/d),[3] based on very low numbers of daily mean doses (0.07-0.12) in the other 2 studies, we can assume that opioid dose was very low in these studies.[1,2] Compared to sham, there is low-strength evidence that certain acupuncture modalities have shown some modest promise for reducing opioid dose during the 8-10 week treatment periods, both in Veterans with advanced knee osteoarthritis using a mean of 0.47 weekly doses of unspecified opioids,[2] and in patients with various forms of chronic pain from an Australian chronic pain center undergoing planned opioid tapering (Table 2).[3] However, these effects were not sustained 5-9 months following acupuncture discontinuation.

In 190 Veterans with advanced knee osteoarthritis, compared to sham, stimulation of the periosteum (PST) facilitated by acupuncture needles once a week for 10 weeks led to a small reduction in the number of weekly opioid doses (mean difference, -0.27; 95% CI -0.48 to -0.054) immediately after treatment period.[2] But these results weren't sustained at 9 months (mean difference, -0.20; 95% CI -0.23 to 0.19). Adding boosters every 2 weeks and then monthly

following the initial 10-week treatment period did not further reduce weekly opioid doses compared to sham. Strengths of this study include: (1) this is the only study in a VA population, and (2) intended patient blinding was formally assessed and documented as successful. For other outcomes measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), PST without boosters did not improve pain, function, or quality of life at 10 weeks or 9 months. PST with boosters led to a statistically significant lower mean WOMAC pain score at 9 months (6.2 vs 7.7; mean difference, 1.5; 95% CI 0.069 to 3.0); however, the clinical importance of a 1.5-point difference is unclear. A 20-30% improvement has been suggested as a threshold for minimum clinically important difference in pain[19] and both the PST booster group (8.9 at baseline to 6.2 at 9 months; 30% reduction) and the control group (10.6 at baseline to 7.7 at 9 months; 27% reduction) are in that range. PST with boosters did not improve quality of life or function. An advantage of this study is that it is highly applicable to patients prescribed opioids in the VA as it involved a VA population that was mostly male (85%), had a mean age of 67 years, had been suffering moderate pain for a mean of 6 years, and had a mean Comorbidity Cumulative Illness Rating of 4.4 (number of items with a score of moderate or higher).

In 35 patients with various forms of chronic pain from an Australian chronic pain center undergoing planned opioid tapering, compared to sham, electroacupuncture for 20 minutes twice a week for 6 weeks did not lead to a statistically significant reduction in opioid MED either at the end of treatment or at 20 weeks.[3] Strengths of this study include: (1) this is the only study designed to measure opioid use as a primary outcome, (2) this is the only study we found that reported opioid type (*ie*, codeine, methadone, oxycodone, morphine, and tramadol) and MED, but MED was greater in the real acupuncture group than in the sham group (461.6 mg MED/wk or 65.9mg/d versus 295.5mg MED/w or 42.2mg/d), (3) patients recorded medication use daily, rather than retrospectively for the previous week, and (4) intended patient blinding was formally assessed and documented as successful. In the intention-to-treat population, the reduction in opioid MED was 39% in the real acupuncture group and 26% in the sham group, which likely did not reach statistical significance because of the small sample size. However, the difference may have been biased in favor of the real acupuncture group because of the greater starting MED (65.9 mg MED/d vs 42.2 mg MED/d). Real electroacupuncture did not significantly improve pain, depression, or quality of life, and functional capacity was not evaluated. The applicability of this study to patients prescribed opioids in the VA is unclear. Patients were 50% male and in their early 50s, with a mean pain duration of 15 years. Mean pain intensity was 5 based on a patient diary visual analogue scale (VAS), but the VAS scale upper limit was not reported. Comorbidities were not reported.

In the third trial with at least some detail on opioid dosing, in 61 low back pain patients seen at an Austrian university-based pain center, auricular acupuncture with electrical stimulation reduced total mean number of tramadol 50 mg rescue medication tablets consumed over an 18-week period compared to acupuncture without electrical stimulation (6 versus 150; $P < .001$).[1] Acupuncture was performed once weekly for 6 weeks. A strength of this study is that patients recorded medication use 3 times daily, rather than just once daily or retrospectively for the previous week. However, the lack of a sham or placebo group is an important limitation of this study, which limits our ability to attribute the opioid reductions to the acupuncture itself, rather than other nonspecific features of study participation. Other benefits of electroacupuncture included reduced pain at 18 weeks (VAS estimated from Figure 2A: 1 versus 4; $P < .05$), more patients returning to full-time work (77% vs 25%; $P = .0032$), and reduced impairment in well-

being (VAS estimated from figure 2B: 1 vs 5; P < .05). The applicability of these findings to patients prescribed opioids in the VA is also unclear as patients were 30% male and comorbidities were not reported.

Massage

There is insufficient evidence to draw conclusions about the effects of massage on opioid use. In 401 Group Health Cooperative members with chronic low back pain, compared to usual care, structural or relaxation massage did not reduce the proportion of patients who reported any narcotic analgesic use in the preceding week immediately following 10 weeks of treatment, or after 26 or 52 weeks of follow-up (Table 2).[65] The meaningfulness of this finding is unclear, however, as details are lacking about opioid type, dose, and frequency. The other key limitation of this study is that it has a high risk of performance and detection biases that could have led to more favorable assessments in the massage groups. This is because opioid use was retrospectively assessed for the previous week based only on unmasked patient self-report and there was not a sham treatment group.

Meditation

There is insufficient evidence to draw conclusions about the effects of meditation on opioid consumption. Compared to waitlisted usual care, in 25 patients with failed back surgery syndrome (FBSS) an 8-week mindfulness stress reduction (MBSR) program, including weekly classroom learning and audiotape-guided meditation for 45 minutes per day for 6 days a week, led to reduced overall analgesics medication use (Table 2).[66] However, this finding has little usefulness for determining impact specifically on opioid use, due to limitations in the measurement method. The 4-point medication use scale included ratings specific to both non-opioid and opioid use (0 = no analgesic use, 1 = less than daily non-opioid analgesic use, 2 = daily non-opioid analgesic use, *3 = less than daily opioid use, and 4 = daily opioid use*). However, we can't determine whether the point reductions (0.4-1.5) observed related to opioid use because baseline levels were not reported. For example, the 1.5-point reduction in the MBSR group could have reflected a change from daily non-opioid use to no analgesic use. A better way to capture opioid use would have been to evaluate proportion of patients who scored a 3 or 4, as both ratings specifically reflecting opioid use. Even then, without details of opioid type and dose, we can't assess whether the reductions are truly meaningful. Interpretation of these findings is also limited by their general high risk of performance and detection biases caused by reliance on self-rated outcomes from unblinded patients and the lack of a sham treatment.

Yoga

There is insufficient evidence to draw conclusions about the effects of yoga on opioid consumption. In 95 predominantly low-income female minorities with moderate-severe chronic low back pain from an academic safety-net hospital and 5 affiliated federally qualified community health centers in Boston, changes from baseline in proportion of patients using opioids after 12 weeks of once-weekly or twice-weekly yoga were small and not different between groups (Table 2).[67] Interpretation of these findings is limited by: (1) the lack of information about opioid type and dose, (2) their general high risk of performance and detection biases caused by reliance on self-rated outcomes from unblinded patients, (3) the lack of a sham treatment group, (4) low and differential adherence to the yoga treatment (once-weekly = 65% vs twice-weekly = 44%, P = .040), (5) potential contamination of effects by use of other CIH (*eg*,

47% used massage), and (6) unknown influence of paying subjects $25 every 3 weeks for their participation.

Table 2: Summary of Findings

Author Year Risk of Bias N Pain type	Interventions	Applicability (% male, age, comorbidities, pain severity and duration)	Opioid type and dose	Impact on opioid use	Pain, quality of life, functional status, adverse events
Acupuncture					
Sator-Katzenschlager 2004 [1] Unclear N = 61 LBP	Auricular acupuncture with electrical stimulation (EA) or without stimulation (CO)	Unclear: 30% male, age=53.6; moderate pain for 4.6y; comorbidities NR	Tramadol: ≤ 400 mg daily	ê Opioid consumption (# tablets) throughout intervention: EA = 6 vs CO = 150 (P < .001)	ê Pain (VAS scale out of 10) at18 wks: EA = 1 vs CO = 4 (P < .05) ê Well-being impairment (scale out of 10) at 18 wks: EA = 1 vs CO = 5 (P < .05) Adverse events: none observed
Weiner 2013 [2] Unclear N = 190 Knee OA	Periosteal stimulation therapy, with boosters (PST+PST) or without boosters (PST+control) or control PST without boosters (control)	High: VA population, 85% male in mid to late 60s with comorbidities	Opioid type NR: average 0.47 doses/wk	Opioid consumption (baseline adjusted differences in # weekly doses compared to control) at 10 wks: = PST+PST: 0.018 (95% CI -0.19 to 0.23) ê PST+control: -0.27 (95% CI -0.48 to -0.054)	Baseline adjusted differences compared with control at 9 m PST+PST improved WOMAC pain (MD 1.5, 95% CI 0.069 to 3.0), but not SF-36 physical component (MD -1.2; 95% CI -2.8 to 0.041) vs Control PST PST+control did not improve WOMAC pain (MD 1.1, 95% CI -.32 to 2.6) or SF-36 physical component (MD -1.3; 95% CI -3.0 to 0.28) vs Control PST Adverse events: 4 adverse events attributable to PST and control PST
Zheng 2008 [3] Unclear N = 35 NMP	Electroacupuncture (REA) or sham electroacupuncture (SEA)	Unclear: 50% male in early 50s, 15 years duration; pain intensity unclear – measured on VAS scale, average = 5, but not clear on VAS upper limit; Comorbidities NR	Codeine, Methadone, Oxycodone, Morphine, & Tramadol Dose (mg/d morphine equivalent): REA = 65.9/d	ê OLM consumption (change from baseline, mg/d morphine equivalent) at 8 wks: REA = -25.7 vs -10.9 SEA and 20 wks: REA = -16.7 vs SEA = -8.1	ê Pain (scale NR): Change from baseline at 8 wks: -0.8 REA vs -0.7 SEA (P = .001) Adverse events: 33 events REA and 19 events SEA

Author Year Risk of Bias N Pain type	Interventions	Applicability (% male, age, comorbidities, pain severity and duration)	Opioid type and dose	Impact on opioid use	Pain, quality of life, functional status, adverse events
			SEA = 42.2/d		
Massage					
Cherkin 2011 [65] High N = 401 LBP	Structural massage (SM), relaxation massage (RM), or usual care (UC)	Unclear: 35.67% male, age=47; moderate pain (5.67/10 on symptom bothersome scale), 75.6% LBP longer than 1 year; co-morbidities NR	NR	= narcotic analgesic consumption (% narcotic analgesics in past week, change from baseline) at 10 wks: SM = -12.4 vs RM = -12.0 vs UC = -7.2 at 52 wks: SM = -12.2 vs RM = -12.1 vs UC = -8.1	= Pain (change from baseline symptom bothersomeness score out of 10): at 10 wks: -1.8 SM vs -2.1 RM vs -0.6 UC at 52 wks: -1 SM vs -1.7 RM vs -1.6 UC é Quality of life (% patient global rating of improvement): at 10 wks: SM = 36.1 (28.8 to 45.) vs RM = 39.4 (31.8 to 48.7) vs UC = 3.8 (1.6 to 9.0) UC (P = <.001) at 52 wks: SM = 26.1 (19.8 to 34.6) vs RM = 36.2 (29.1 to 45.0) vs UC = 20.5 (14.5 to 29.0) UC (P = .013) Adverse events: 7% SM and 4% RM patients
Mindfulness					
Esmer 2010 [66] High N = 25 FBSS	Mindfulness-based stress reduction (MBSR) or usual care	Unclear: 56% male, age=55.08; moderate-severe pain (23.64/30 on VAS pain scale), duration less than 2 years; co-morbidities NR	NR	ê Analgesic medication use at 12-wks (4-point scale: 0 = no analgesic to 4 = daily narcotics): MBSR = -1.5 vs Control = 0.4 (P < .001)	ê Pain (change in VAS 30-point scale) at 12 wks: MBSR = -6.9 vs control = -0.2 (P < .021) é Quality of life: Change in CPAQ (108-point scale) at 12 wks: MBSR = 7.0 vs control = -6.7 (P < .014) é Functional status (change in RMDQ 24-point scale) at 12 wks: MSBR=-3.6 vs control = 0.1 (P < .005)
Yoga					
Saper 2013 [67] High N = 95 LBP	Yoga, once weekly classes or twice weekly classes	Unclear: 28% male, age=47.5; moderate pain (6.9/11 in previous week), duration=43% longer	NR	= Opiate (% change from baseline) at 12 wks: Yoga 1x/wk = 0 vs Yoga 2x/wk = 2; NS	=Pain (change from baseline out of 11) at 12 wks: 1x/wk classes -2.1 (95% CI -2.9 to -1.3) vs 2x/wk classes -2.4 (95% CI -3.1 to -1.8); Between group difference: 0.3 (95% CI -0.2 to 0.8)

Author Year Risk of Bias N Pain type	Interventions	Applicability (% male, age, comorbidities, pain severity and duration)	Opioid type and dose	Impact on opioid use	Pain, quality of life, functional status, adverse events
		than 1 year; co-morbidities NR			= Quality of life (SF-36 mental mean change from baseline) at 12 wks: 1x/wk classes 4.0 (1.3 to 6.7) vs 2x/wk classes 2.5 (-0.7 to 5.7); Between group difference: 1.5 (-2.6 to 5.6) =Adverse events: 27% 1x/wk classes, 34% 2x/wk classes (P = 0.47)

EA: Auricular acupuncture with stimulation; CO: Auricular acupuncture without stimulation; LBP: Low back pain; OA: Osteoarthritis; PST: Periosteal stimulation therapy; NR: Not reported; NMP: Non-malignant pain; REA: Electroacupuncture; SEA: Sham electroacupuncture; OLM: Opioid-like medication; VAS: Visual Analog Scale; WOMAC: Western Ontario & McMaster Universities Osteoarthritis Index; CPAQ: Chronic Pain Acceptance Questionnaire; RMRQ: Roland Morris Disability Questionnaire; SF-36: Short Form-36 Health Survey; SM: Structural massage; RM: Relaxation massage; UC: Usual care; MSBR: Mindfulness-based stress reduction; FBSS: Failed back surgery syndrome

KEY MESSAGES

1. The evidence base regarding the effectiveness of select CIH interventions for reducing opioid use in patients with chronic pain is extremely limited. No study has evaluated the effectiveness of select CIH interventions for reducing new opioid use, stopping opioids entirely, or for reducing opioid use below any particular morphine equivalent dose (MED) threshold.

2. Compared to sham, in patients already using dosage below 80 mg MED, there is low-strength evidence that certain electro-acupuncture modalities can reduce opioid dose immediately after 6- to 10-week treatment periods, both in a group of Australian patients with various forms of chronic pain undergoing a planned opioid tapering and in a group of Veterans with advanced knee osteoarthritis who were taking opioids for an unknown duration. But these effects were not sustained 5-9 months following acupuncture discontinuation.

3. Single studies of massage, meditation, and yoga provided insufficient evidence to draw conclusions about their effects on opioid dose because: (1) they lacked details about opioid type, dose, and frequency, and (2) relied on self-assessments from unblinded patients, with no effort to match the intervention to a sham treatment group, which could have led to more favorable assessments in the experimental groups.

4. We found no studies of the effects of classic acupuncture or tai chi on opioid use.

5. We found no studies that evaluated whether the effectiveness of CIH varies depending on: (1) type or location of pain, (2) patient demographics (*eg*, age, race, ethnicity, gender), or (3) patient comorbidities (including past or current nicotine, alcohol, or substance use disorders, mental health disorders, medical comorbidities, and high risk for addiction).

6. We did not identify any existing or developing programs primarily designed to offer CIH interventions *before* opioids or to reduce opioid use. Several programs exist to promote use of interdisciplinary approaches, including CIH interventions, but are not designed to isolate the effects of the CIH interventions and measure changes in opioid use as secondary outcome.

IMPLICATIONS FOR FUTURE RESEARCH

Additional research is needed to better understand the effectiveness of select CIH interventions for reducing opioid use in Veterans. Patient self-report methods for measuring opioid use varied substantially across studies, generally without providing a rationale for how they were selected: recall periods ranging from multiple times daily up to monthly, proportion of patients with any use, daily, or less than daily use, and number of weekly doses. To determine how to select and strengthen patient self-report methods for measuring opioid use, we suggest considering use of well-validated processes, optimized question response formats and recall periods, taking steps to address social desirability concerns, avoiding interview-based assessments, and accounting for self-report challenges such as cognitive functioning, burden, and setting.[75] Potentially, incorporation of the patient perspective and preference in selecting measurement methods may

further improve patient satisfaction and the reliability of their self-report. To improve clinical relevance, future studies should report opioid type, dose, and frequency. In addition to opioid use outcomes, to best assess the overall net benefit of CIH interventions, future studies should simultaneously evaluate a more complete set of key outcomes, including their impact on pain, pain-related function, quality of life, and harms.

A dataset such as Morasco et al used to study clinical characteristics of Veterans prescribed high doses of opioid medications (Veterans Integrated Service Network-20 Data Warehouse)[24] potentially could be further evaluated to assess the effects of CIH use on opioid dose. Although the Morasco study focused on patient demographics and clinical characteristics, variables could be added to represent CIH use to evaluate their potential association with progression of opioids from traditional to high doses. However, as a concern with reducing opioid dose and use is the possible increase in risk of under-treatment of pain and other undesirable outcomes such as reduced quality of life, function, and switch to other opioids (such as heroin), we recommend additional studies that simultaneously measure these potential consequences.

To improve our knowledge about the state of CIH practice in relation to opioids, research is needed to identify whether the effectiveness of CIH varies depending on the timing of their integration. To facilitate this, future studies should seek to more clearly characterize when their populations initiated CIH in relation to opioids using the framework for opioid treatment management from the VA/DoD guideline: (1) early intervention *prior* to initiating opioids, to prevent "chronification," (2) as an adjunct during initiation, titration, for exacerbations, or after opioid failure, or (3) to facilitate opioid withdrawal.

Future research should also seek to clarify whether there are particular subpopulations that are more or less likely to benefit from CIH to reduce opioid use and whether variation in benefit varies by CIH type. Key characteristics of interest include: (1) type or location of pain, (2) patient demographics (*eg*, age, race, ethnicity, gender), and (3) patient comorbidities (including past or current nicotine, alcohol, or substance use disorders, mental health disorders, medical comorbidities, and high risk for addiction). We also suggest investigation of how patient motivation, mobility, and geography may impact benefit from CIH to reduce opioid use. This is because these factors may impact Veterans' abilities to successfully access skilled practitioners of CIH treatments.

Research into potential barriers to CIH implementation may also be useful. Several CIH therapies require a higher level of provider time and patient effort than treatment with opioids. Access to skilled practitioners of CIH treatments may vary depending on patient motivation, mobility, geography, and cost. CIH treatments vary in their required levels of active patient and provider engagement and this variation may ultimately impact feasibility, adherence, and effectiveness. The "passive" nature of acupuncture and massage may seem more approachable to patients. But they both require direction by and presence of a provider and potentially more frequent clinic visits and higher cost. These features may be more difficult to navigate for Veterans in rural areas with transportation limitations. However, both treatments could potentially be provided in patients' homes. Yoga and tai chi have the potential advantage of being the least provider-intensive, as both can be delivered in Veterans' home via various modalities (*eg*, internet streaming, videotape, *etc*). But yoga and tai chi also require the greatest

amount of patient motivation and physical activity and may be at least initially the most difficult for patients with lower mobility and greater pain.

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QUERI

Evidence Brief: The Comparative Effectiveness of Selected Complementary and Integrative Health (CIH) Interventions for Preventing or Reducing Opioid Use in Adults with Chronic Neck, Low Back, and Large Joint Pain

Supplemental Materials

April 2016

Prepared for:
Department of Veterans Affairs
Veterans Health Administration
Quality Enhancement Research Initiative
Health Services Research & Development Service
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VA HEALTH CARE Defining EXCELLENCE in the 21st Century

TABLE OF CONTENTS

EXISTING GUIDELINES

Guideline	Reference to non-pharmacological or alternative care?	Type of reference to CAM (nonspecific, general, or specific)	Recommended timing of use
Opioid-specific guidelines			
APS-AAPM [1]	Yes	Nonspecific - "continuing discussion with the patient regarding alternatives to COT (strong recommendation, low-quality evidence)"	Throughout--"continuing discussion"
Canadian National Use Guideline Group [2]	Yes	Nonspecific - for adolescent patients, opioid therapy may be considered when "non-opioid alternatives have failed"	Alternative options must be tried prior to opioid treatment
CDC[3]	Yes	Nonspecific – “Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.”	Initiation – preferred therapy
ICSI [4]	Yes	Nonspecific - "Physical, psychological, interventional or other appropriate non-opioid therapies"	During initiation
UMHS [5]	Yes	Nonspecific - "referral for individual behavioral and psychological intervention may be all that is required"	Initiation ("Begin with [non-pharmacologic therapies] (*eg*, exercise, heat, sleep hygiene))
VA/DoD [6]	Yes	Nonspecific - mentions "adjuvant therapies" and "non-pharmacologic modalities", but doesn't mention CAM in general or any specific types of CAM	During initiation, titration, and for exacerbations.
UDOH [7]	Yes	Nonspecific - "Alternatives to opioid treatment should be tried…before initiating opioid treatment" Physical therapy provided as example of non-pharma alternatives	Recommended trying prior to use

Guideline	Reference to non-pharmacological or alternative care?	Type of reference to CAM (nonspecific, general, or specific)	Recommended timing of use
ASIPP [8]	Yes	Nonspecific - "To establish medical necessity for OT, it is essential to have information of multiple modalities of treatments available including conservative, various other alternatives, and consultations (including physical and behavioral modalities, interventional pain management techniques, and others) if necessary"	When establishing medical necessity (Initiation?)
AGS [9]	No	N/A	N/A
WA State AMDG[10]	Yes	Specific – Mindfulness, meditation, yoga, acupuncture “In addition to medication, therapies should include physical activation and behavioral health interventions”	Unclear – No reference to timing with opioids
General chronic pain guidelines			
APS/ACP [11]	Yes	Specific - "For patients who do no improve with self-care options, clinicians should consider addition of non-pharmacologic therapy with proven benefits--acupuncture, massage therapy, spinal manipulation, yoga, cognitive-behavioral therapy, or progressive relaxation"	Unclear - No reference to timing with opioids
AAPM [12]	Yes	Specific - Yoga, Mindfulness, Meditation, Relaxation, Acupuncture, Massage	During - "Therapy for chronic pain ranges from single modality approaches for the straightforward patient to comprehensive interdisciplinary care for the more challenging patient. Therapeutic components such as pharmacologic, interventional, psychological and physical have been found to be most effective when performed in an integrated manner. Continuation or modification of pain management depends on the physician’s evaluation of progress toward treatment objectives. If the patient's progress is unsatisfactory, the physician should assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities."

Guideline	Reference to non-pharmacological or alternative care?	Type of reference to CAM (nonspecific, general, or specific)	Recommended timing of use
ICSI [13]	Yes	Specific - Acupuncture Nonspecific - Complementary therapies, complementary medicine management, non-pharmacologic management, Exercise therapy	During - "Medications are not the sole focus of treatment in managing pain. They should be used when needed to meet overall goals of therapy **in conjunction** with other treatment modalities: psychosocial and spiritual management, rehab and functional management, non-pharmacologic and complementary medicine, and intervention management."
Colorado DWC [14]	Yes	Specific - Acupuncture, Nonspecific - "Interdisciplinary rehabilitation programs" (programs that evaluate and treat multiple conditions including neurological and psychological issues example)	Unclear - Non-operative therapeutic procedures listed first in the guidelines, however no indication as to the order recommended
VA/DoD [15]	Yes	Specific - Massage, Acupuncture, Yoga	Unclear - No reference to timing with opioids; Algorithm lists discussing pharmacologic and non-pharmacologic treatment options in the same step
AGS [16]	Yes	Specific - Mindfulness, Acupuncture	During - "used as adjunctive therapies"
ASIPP [17]	No	NA	NA
NICE [18]	Yes	Specific - Manual therapy including spinal therapy and massage; Also recommend "movement instruction" and "stretching"	Unclear - "Provide people with advice and information to promote self-management of LBP; Take into account the person's expectations and preferences when considering recommended treatments"

APS: American Pain Society; AAPM: American Academy of Pain Medicine; ICSI: Institute for Clinical Systems Improvement; UMHS: University of Michigan Health System; VA: Veteran Affairs; DoD: Deparment of Defense; UDOH: Utah Department of Health; AGS: American Geriatrics Society; ASIPP: American Society of Interventional Pain Physicians; ACP: American College Physicians; DWC: Division of Workers Compensation; NICE: National Institute for Health and Care Excellence; CDC: Centers for Disease Control and Prevention; AMDG: Agency Meidcal Directors' Group

SEARCH STRATEGIES

SYSTEMATIC REVIEWS

Acupuncture

Ovid MEDLINE

Search Strategy:

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1 exp Acupuncture/ or acupuncture.mp. (15370)

2 Cochrane database of systematic reviews.jn. or search.tw. or meta-analysis.pt. or Medline.tw. or systematic review.tw. (267064)

3 (pain or knee pain or ankle pain or hip pain or chronic pain or elbow pain or shoulder pain or neck pain or back pain or low back pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (403904)

4 1 and 2 and 3 (467)

5 limit 4 to yr="2013 -Current" (41)

Cochrane Database of Systematic Reviews

Search Strategy:

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1 acupuncture.mp. [mp=title, abstract, full text, keywords, caption text] (448)

2 (pain or knee pain or ankle pain or hip pain or chronic pain or elbow pain or shoulder pain or neck pain or back pain or low back pain).mp. [mp=title, short title, abstract, full text, keywords, caption text] (3966)

3 1 and 2 (316)

4 limit 3 to last 3 years (124)

PubMed

(("acupuncture"[MeSH Terms] OR "acupuncture"[All Fields] OR "acupuncture therapy"[MeSH Terms] OR ("acupuncture"[All Fields] AND "therapy"[All Fields]) OR "acupuncture therapy"[All Fields]) AND ("pain"[MeSH Terms] OR "pain"[All Fields])) AND systematic[sb] AND ("2013/01/01"[PDAT] : "2015/12/21"[PDAT]))

-168 articles on 12/21/2015

Massage

Ovid MEDLINE

Database: Ovid MEDLINE(R) without Revisions <1996 to January Week 1 2016>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <January 18, 2016>

Search Strategy:

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1 Massage/ (2977)

2 massage therapy.mp. (793)

3 massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (6868)

4 1 or 3 (6868)

5 2 or 3 (6868)

6 reflexology.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (319)

7 3 or 6 (6960)

8 effleurage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (33)

9 3 or 8 (6872)

10 3 or 6 or 8 (6964)

11 petrissage.mp. (14)

12 10 or 11 (6964)

13 tapotement.mp. (4)

14 anma.mp. (11)

15 3 or 14 (6875)

16 6 or 8 or 15 (6971)

17 aquatic bodywork.mp. (1)

18 3 or 17 (6869)

19 ashiatsu.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

20 ayurvedic massage.mp. (4)

21 3 or 20 (6868)

22 balinese massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

23 bowen technique.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (8)

24 3 or 23 (6873)

25 Breema.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

26 biodynamic massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2)

27 3 or 26 (6868)

28 champissage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

29 craniosacral therapy.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (40)

30 3 or 29 (6893)

31 esalen massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

32 foot massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (44)

33 3 or 32 (6868)

34 Hilot massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

35 Kum Nye.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

36 lomilomi.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (5)

37 3 or 36 (6869)

38 lymphatic drainage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1751)

39 manual lymphatic drainage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (133)

40 3 or 39 (6972)

41 medical massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (11)

42 3 or 41 (6868)

43 metamorphic technique.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

44 myofascial release.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (121)

45 3 or 44 (6957)

46 postural integration.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1)

47 3 or 46 (6869)

48 namaste massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

49 prostate massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (43)

50 3 or 49 (6868)

51 shiatsu.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (64)

52 3 or 51 (6905)

53 sports massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (23)

54 3 or 53 (6868)

55 stone massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1)

56 structural integration.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (119)

57 3 or 56 (6982)

58 swedish massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (52)

59 3 or 58 (6868)

60 tantric massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)

61 thai massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (27)

62 3 or 61 (6868)

63 Chinese massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (19)

64 traditional chinese massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (5)

65 63 or 64 (19)

66 3 or 63 (6868)

67 Trager approach.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1)

68 trigger point massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (5)

69 3 or 68 (6868)

70 tui na.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (13)

71 3 or 70 (6871)

72 Watsu.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (5)

73 3 or 72 (6872)

74 (effluerage or anma or aquatic bodywork or bowen technique or craniosacral therapy or lomilomi or manual lymphatic drainage or myofascial release or postural integration or reflexology or shiatsu or structural integration or tui na or watsu).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (827)

75 massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (6868)

76 74 or 75 (7349)

77 (pain or knee pain or ankle pain or hip pain or chronic pain or elbow pain or shoulder pain or neck pain or back pain or low back pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (398856)

78 76 and 77 (1751)

79 Cochrane database of systematic reviews.jn. or search.tw. or meta-analysis.pt. or Medline.tw. or systematic review.tw. (262068)

80 78 and 79 (212)

81 (pregnancy or cancer or child or newborn or infant).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2363442)

82 80 not 81 (154)

Cochrane Database of Systematic Reviews

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to January 13, 2016>

Search Strategy:

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1 (effluerage or anma or aquatic bodywork or bowen technique or craniosacral therapy or lomilomi or manual lymphatic drainage or myofascial release or postural integration or reflexology or shiatsu or structural integration or tui na or watsu).mp. [mp=title, abstract, full text, keywords, caption text] (82)

2 massage.mp. [mp=title, abstract, full text, keywords, caption text] (316)

3 1 or 2 (341)

4 (pain or chronic pain or knee pain or ankle pain or hip pain or elbow pain or shoulder pain or back pain or low back pain or neck pain).mp. [mp=title, abstract, full text, keywords, caption text] (3940)

5 3 and 4 (268)

6 (cancer or pregnancy).mp. [mp=title, abstract, full text, keywords, caption text] (3454)

7 5 not 6 (135)

8 (child or infant or newborn).mp. [mp=title, abstract, full text, keywords, caption text] (3069)

9 7 not 8 (107)

CINAHL

#	Query	Limiters/Expanders	Results
S5	S3 AND S4	Limiters - Publication Type: Meta Analysis, Systematic Review Search modes - Boolean/Phrase	154

S4	pain OR neck pain OR back pain OR low back pain OR elbow pain OR shoulder pain OR hip pain OR knee pain OR ankle pain	Search modes - Boolean/Phrase	182,782
S3	S1 OR S2	Search modes - Boolean/Phrase	14,844
S2	massage	Search modes - Boolean/Phrase	13,538
S1	effluerage or anma or aquatic bodywork or bowen technique or craniosacral therapy or lomilomi or manual lymphatic drainage or myofascial release or postural integration or reflexology or shiatsu or structural integration or tui na or watsu	Search modes - Boolean/Phrase	1,837

Meditation

Conducted the week of 1/4/2016-1/8/2016

Ovid MEDLINE

Search Strategy:

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1 exp Meditation/ (1775)

2 meditation.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (3117)

3 exp Mindfulness/ (689)

4 mindfulness.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2861)

5 (pain or chronic pain or knee pain or ankle pain or hip pain or elbow pain or shoulder pain or back pain or low back pain or neck pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (403904)

6 2 or 4 (4943)

7 5 and 6 (521)

8 Cochrane database of systematic reviews.jn. or search.tw. or meta-analysis.pt. or Medline.tw. or systematic review.tw. (267064)

9 7 and 8 (50)

10 limit 9 to yr="2014 -Current" (20)

11 cancer.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (950774)

12 10 not 11 (14)

Cochrane Database of Systematic Reviews

Search Strategy:

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1 meditation.mp. [mp=title, abstract, full text, keywords, caption text] (124)

2 mindfulness.mp. [mp=title, abstract, full text, keywords, caption text] (90)

3 (pain or chronic pain or knee pain or ankle pain or hip pain or elbow pain or shoulder pain or back pain or low back pain or neck pain).mp. [mp=title, abstract, full text, keywords, caption text] (3966)

4 1 and 2 and 3 (27)

5 limit 4 to last 2 years (15)

6 cancer.mp. [mp=title, abstract, full text, keywords, caption text] (2112)

7 5 not 6 (7)

CINAHL

Search ID#	Search Terms	Search Options	Results
S8	S5 AND S6	Limiters - Publication Type: Meta Analysis, Review, Systematic Review; Published Date: 20140101-20161231	11
S7	S5 AND S6		497
S6	S3 OR S4		182, 371
S5	S1 OR S2		5,288
S4	ankle pain OR knee pain OR hip pain OR elbow pain OR shoulder pain OR neck pain OR back pain OR low back pain		34,771
S3	pain OR chronic pain		182,371
S2	meditation		3,638
S1	mindfulness		2,484

PsycINFO

Search Strategy:

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1 exp Meditation/ (3530)

2 meditation.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (6180)

3 exp Mindfulness/ (5275)

4 mindfulness.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (7347)

5 1 or 2 (6180)

6 3 or 4 (7347)

7 (pain or knee pain or ankle pain or hip pain or chronic pain or elbow pain or shoulder pain or neck pain or back pain or low back pain).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (79675)

8 meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/ (3789)

9 ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab. (19049)

10 ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab. (7218)

11 ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab. (3019)

12 (data synthes* or data extraction* or data abstraction*).ti,ab. (1458)

13 (handsearch* or hand search*).ti,ab. (842)

14 (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab. (3244)

15 (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab. (659)

16 (meta regression* or metaregression*).ti,ab. (770)

17 (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw. (35317)

18 (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw. (14326)

19 (meta-analysis or systematic review).md. (25796)

20 (comparative adj3 (efficacy or effectiveness)).ti,ab. (1514)

21 (outcomes research or relative effectiveness).ti,ab. (2934)

22 ((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab. (145)

23 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 (64496)

24 2 or 4 (11661)

25 7 and 23 and 24 (36)

26 limit 25 to yr="2014 -Current" (11)

PubMed

Search ((meditation OR mindfulness)) AND (pain OR "chronic pain" OR "knee pain" OR "ankle pain" OR "hip pain" OR "elbow pain" OR "shoulder pain" OR "back pain" OR "low back pain" OR "neck pain") Filters: Systematic Reviews; Publication date from 2014/01/01 to 2016/01/06

Results: 22

Tai Chi

Ovid MEDLINE

Database: Ovid MEDLINE(R) without Revisions <1996 to December Week 5 2015>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <January 11, 2016>

Search Strategy:

---

1 Tai Ji/ (708)

2 tai chi.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1010)

3 1 or 2 (1090)

4 Pain/ (70617)

5 exp Pain/ (204677)

6 (pain or knee pain or ankle pain or hip pain or chronic pain or elbow pain or shoulder pain or neck pain or back pain or low back pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (398419)

7 5 or 6 (428674)

8 3 and 7 (146)

9 Cochrane database of systematic reviews.jn. or search.tw. or meta-analysis.pt. or Medline.tw. or systematic review.tw. (261616)

10 8 and 9 (35)

11 limit 10 to yr="2014 -Current" (10)

12 (tai chi or taichi or tai ji or taiji or taijiquan or shadow boxing).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1142)

13 1 or 2 or 12 (1142)

14 7 and 9 and 13 (35)

Cochrane Database of Systematic Reviews

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to January 08, 2016>

Search Strategy:

---

1 (tai chi or taichi or tai ji or taiji or taijiquan or shadow boxing).mp. [mp=title, abstract, full text, keywords, caption text] (84)

2 (pain or knee pain or ankle pain or hip pain or chronic pain or elbow pain or shoulder pain or neck pain or back pain or low back pain).mp. [mp=title, abstract, full text, keywords, caption text] (3938)

3 1 and 2 (59)

4 limit 3 to last 2 years (35)

CINAHL

#	Query	Limiters/Expanders	Last Run Via	Results
S3	S1 AND S2	Limiters - Publication Type: Meta Analysis, Systematic Review; Published Date: 20140201-20160131 Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	4
S2	tai chi or tai-chi or tai ji or tai-ji or taiji or t'ai chi or t' ai chi or taijiquan or shadow boxing	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,540
S1	pain OR neck pain OR back pain OR low back pain OR elbow pain OR shoulder pain OR hip pain OR knee pain OR ankle pain	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	182,540

PubMed

Search	Query	Results
#3	#1 AND #2	11
#2	Search (pain OR "neck pain" OR "back pain" OR "low back pain" OR "shoulder pain" OR "elbow pain" OR "hip pain" OR "knee pain" OR "ankle pain") Filters: Systematic Reviews; Publication date from 2014/02/01 to 2016/01/11	4076
#1	Search ("tai chi" OR "tai-chi" OR "tai ji" OR "tai-ji" OR "taiji" OR "t'ai chi" OR "t' ai chi" OR "taijiquan" OR "shadow boxing") Filters: Systematic Reviews; Publication date from 2014/02/01 to 2016/01/11	64

Yoga

Run: Week of 1/11/16-1/15/16
Ovid MEDLINE

Search Strategy:

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1 exp Yoga/ (1342)

2 yoga.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2521)

3 hatha.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (118)

4 vinyasa.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (8)

5 3 or 4 (123)

6 2 or 5 (2521)

7 astanga.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (6)

8 (pain or knee pain or ankle pain or hip pain or chronic pain or elbow pain or shoulder pain or neck pain or back pain or low back pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (398472)

9 1 or 2 (2521)

10 2 and 8 (391)

11 Cochrane database of systematic reviews.jn. or search.tw. or meta-analysis.pt. or Medline.tw. or systematic review.tw. (261673)

12 10 and 11 (51)

13 limit 12 to yr="2014 -Current" (15)

14 limit 13 to english language (13)

Cochrane Database of Systematic Reviews

Search Strategy:

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1 yoga.mp. [mp=title, abstract, full text, keywords, caption text] (162)

2 (astanga or ovinyasa or hatha).mp. [mp=title, abstract, full text, keywords, caption text] (16)

3 1 or 2 (162)

4 (pain or knee pain or ankle pain or hip pain or chronic pain or elbow pain or shoulder pain or neck pain or back pain or low back pain).mp. [mp=title, abstract, full text, keywords, caption text] (3938)

5 1 and 4 (113)

6 limit 5 to last 2 years (33)

CINAHL

#	Query	Limiters/Expanders	Last Run Via	Results
S7	S5 NOT S6	**Limiters** - Publication Type: Meta Analysis, Systematic Review; Published Date: 20140701-20160131 **Search modes** - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	2
S6	Cancer OR pregnancy OR child	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	785,393
S5	S2 AND S4	**Limiters** - Publication Type: Meta Analysis, Systematic Review; Published Date: 20140701-20160131 **Search modes** - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	6
S4	pain OR neck pain OR back pain OR low back pain OR elbow pain OR shoulder pain OR hip pain OR knee pain OR ankle pain	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	182,540

S3	S1 OR S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	5,407
S2	yoga	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	5,407
S1	(MH "Yoga+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	5,011

PubMed

History Download history C

Search	Add to builder	Query	Items found
#11	Add	Search **(((((yoga AND systematic[sb] AND ("2014/07/01"[PDat] : "2016/01/13"[PDat]))) AND ((pain OR "neck pain" OR "low back pain" OR "back pain" OR "hip pain" OR "elbow pain" OR "shoulder pain" OR "knee pain" OR "ankle pain" OR "joint pain"))) AND systematic[sb] AND ("2014/07/01"[PDat] : "2016/01/13"[PDat]))) NOT (((pregnancy OR cancer OR child)) AND systematic[sb] AND ("2014/07/01"[PDat] : "2016/01/13"[PDat]))** Filters: **Systematic Reviews; Publication date from 2014/07/01 to 2016/01/13**	4
#10	Add	Search **(pregnancy OR cancer OR child)** Filters: **Systematic Reviews; Publication date from 2014/07/01 to 2016/01/13**	13232
#9	Add	Search **((yoga AND systematic[sb] AND ("2014/07/01"[PDat] : "2016/01/13"[PDat]))) AND ((pain OR "neck pain" OR "low back pain" OR "back pain" OR "hip pain" OR "elbow pain" OR "shoulder pain" OR "knee pain" OR "ankle pain" OR "joint pain"))** Filters: **Systematic Reviews; Publication date from 2014/07/01 to 2016/01/13**	9
#8	Add	Search **yoga** Filters: **Systematic Reviews; Publication date from 2014/07/01 to 2016/01/13**	96

PRIMARY STUDIES

Acupuncture

Database: Ovid MEDLINE(R) without Revisions <1996 to January Week 4 2016>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <February 03, 2016>

Search Strategy:

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1 exp Acupuncture Therapy/ or exp Acupuncture/ or acupuncture.mp. (16323)

2 (chronic pain or non-cancer pain or neck pain or shoulder pain or back plain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (60940)

3 1 and 2 (1194)

4 limit 3 to yr="2015 -Current" (111)

5 limit 4 to english language (98)

6 (cancer or pregnancy or labor or infant$ or newborn$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1812077)

7 5 not 6 (93)

8 limit 3 to (english language and yr="2009 -Current") (552)

9 8 not 6 (521)

10 (comment or letter or case report or editorial).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1251839)

11 9 not 10 (429)

12 (news or historical article or patient education).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (352160)

13 11 not 12 (418)

14 (surgery or postoperative or post-traumatic stress disorder or mental health or mental illness).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (955471)

15 13 not 14 (388)

16 (chronic pain or non-cancer pain or neck pain or shoulder pain or back pain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (72816)

17 1 and 16 (1312)

18 limit 17 to (english language and yr="2009 -Current") (597)

19 6 or 10 or 12 or 14 (3933781)

20 18 not 19 (414)

Massage

Database: Ovid MEDLINE(R) without Revisions <1996 to January Week 4 2016>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <February 03, 2016>

Search Strategy:

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1 (chronic pain or non-cancer pain or neck pain or shoulder pain or back plain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (60940)

2 (cancer or pregnancy or labor or infant$ or newborn$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1812077)

3 (effluerage or anma or aquatic bodywork or bowen technique or craniosacral therapy or lomilomi or manual lymphatic drainage or myofascial release or postural integration or reflexology or shiatsu or structural integration or tui na or watsu).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (832)

4 massage.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (6902)

5 3 or 4 (7387)

6 1 and 5 (522)

7 6 not 2 (489)

8 limit 7 to (english language and yr="2014 -Current") (100)

9 (case report$ or comment or letter).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1766260)

10 8 not 9 (89)

11 (chronic pain or non-cancer pain or neck pain or shoulder pain or back pain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (72816)

12 5 and 11 (594)

13 12 not 2 (546)

14 limit 13 to (english language and yr="2014 -Current") (109)

15 14 not 9 (98)

Meditation

Database: Ovid MEDLINE(R) without Revisions <1996 to January Week 4 2016>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <February 03, 2016>

Search Strategy:

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1 (chronic pain or non-cancer pain or neck pain or shoulder pain or back plain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (60940)

2 (cancer or pregnancy or labor or infant$ or newborn$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1812077)

3 exp Meditation/ (1758)

4 meditation.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (3069)

5 meditat$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (3609)

6 3 or 4 or 5 (3609)

7 1 and 6 (126)

8 7 not 2 (116)

9 limit 8 to (english language and yr="2013 -Current") (47)

10 (case report$ or comment or letter).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1766260)

11 9 not 10 (44)

12 (chronic pain or non-cancer pain or neck pain or shoulder pain or back pain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (72816)

13 6 and 12 (135)

14 2 or 10 (3355938)

15 13 not 14 (117)

16 limit 15 to (english language and yr="2013 -Current") (47)

Tai Chi

Database: Ovid MEDLINE(R) without Revisions <1996 to January Week 4 2016>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <February 03, 2016>

Search Strategy:

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1 (chronic pain or non-cancer pain or neck pain or shoulder pain or back plain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (60940)

2 (tai chi or taichi or tai ji or taiji or taijiquan or shadow boxing).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1143)

3 1 and 2 (38)

4 (cancer or pregnancy or labor or infant$ or newborn$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1812077)

5 limit 3 to yr="2010 -Current" (28)

6 limit 5 to english language (26)

7 6 not 4 (22)

8 (chronic pain or non-cancer pain or neck pain or shoulder pain or back pain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (72816)

9 2 and 8 (43)

10 limit 9 to (english language and yr="2010 -Current") (31)

11 10 not 4 (27)

Yoga

Database: Ovid MEDLINE(R) without Revisions <1996 to January Week 4 2016>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <February 03, 2016>

Search Strategy:

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1 (chronic pain or non-cancer pain or neck pain or shoulder pain or back plain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (60940)

2 (cancer or pregnancy or labor or infant$ or newborn$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1812077)

3 exp Yoga/ (1346)

4 yoga.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2546)

5 hatha.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (121)

6 vinyasa.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (8)

7 5 or 6 (126)

8 4 or 7 (2546)

9 astanga.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (6)

10 3 or 4 (2546)

11 8 or 9 (2550)

12 1 and 11 (152)

13 limit 12 to (english language and yr="2010 -Current") (112)

14 13 not 2 (106)

15 (case report$ or comment or letter).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1766260)

16 14 not 15 (102)

17 (chronic pain or non-cancer pain or neck pain or shoulder pain or back pain or low back pain or elbow pain or hip pain or knee pain or ankle pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (72816)

18 11 and 17 (184)

19 limit 18 to (english language and yr="2010 -Current") (137)

20 2 or 15 (3355938)

21 19 not 20 (121)

GREY LITERATURE

Grey Literature Search – Opioids Rapid Review

"Opioid Epidemic"

A. Guidelines

a. Guidelines.gov
b. New CDC guideline currently being drafted- listed below under "CDC"
c. Nuckols 2014 review of guidelines- already identified

B. Organizations' websites

a. RWJF
b. Samueli Institute- "a nonprofit organization in Alexandria, Virginia, with a mission that includes applying academic rigor to research on healing, well-being and resilience; and translating evidence into action for the US military and large-scale health systems.
    i. President of the Samueli Institute is Wayne B. Jonas, MD, a retired US Army lieutenant colonel
    ii. Referenced in a few different articles; Dr. Jonas seems to partner with Eric Schoomaker
c. UCSF Osher Center for Integrative Medicine
    i. This program is part of the UCSF Medical Center, but I'm not sure how integrated it is into other practices, like primary care. Given that it's physically part of the space, I would think there would be higher rates of referral, but I don't see anything that indicates that on their website.
    ii. According to their "Integrative Medicine Consultation" webpage, their providers are trained and board-certified in both traditional and alternative medicine, but do not serve as PCPs. They will work with PCPs, but in place of.
    iii. They make no mention of opioids.
    iv. This seems like something that the patient must seek out and initiate, but I'm wondering if other centers at UCSF mention the Osher Center as an option instead of medication.
        1. UCSF's Pain Medicine department links to the Osher Center as a "related clinics and centers".
            a. They list the Osher Center in resources both for patients and for providers, implying that both groups can request/should be aware of the Osher Center's services.
d. PAINS Project: "Never Only Opioids: The imperative for early integration of non-pharmacological approaches and practitioners in the treatment of patients with pain" Fall 2014, policy brief
    i. Article about the policy brief.
    ii. This organization focuses on alleviating chronic pain in many different modalities and recognizes the burden of medication-only solutions to pain. Their focus is on public health initiatives to reduce the individual and societal burden of pain, and if that happens to involve CAM, they are supportive. But they are not solely focused on CAM interventions, and it

looks like the bulk of their work in the area is focused in the policy brief listed above.

C. Government websites

a. The White House: $1.1 billion towards opioids and heroin epidemic as of February 2, 2016
   i. https://www.whitehouse.gov/the-press-office/2016/02/02/president-obama-proposes-11-billion-new-funding-address-prescription
   ii. Specifically discusses medication-assisted treatments, does not mention any other treatment or prevention strategy specifically anywhere (therapy, CAM, etc)

b. CDC
   i. Draft CDC Guideline for Prescribing Opioids for Chronic Pain
      1. The comment period ended 1/13/2016 for public comments
      2. Not totally clear on the timeline- it still needs to go through a Federal Partner Review and Peer Review process

c. NIH
   i. NIH's National Center for Complementary and Alternative Medicine (NCCAM), the National Institute on Drug Abuse (NIDA) and the VA HSRD have provided $21.7 million over 5 years (article dated late 2014) to "explore nondrug approaches to managing pain and related health conditions such as post-traumatic stress disorder (PTSD), drug abuse, and sleep issues".
      1. 13 projects throughout the country
         a. Several include CAM interventions that we are interested in- mostly meditation
      2. NIH and VA address pain and related conditions in U.S. military personnel, veterans and their families: Research will focus on nondrug approaches
      3. This link goes to the list of programs

d. IOM
   i. Report: Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research (June 2011)
      1. This report does discuss opioids and CAM modalities, however the interface for finding these references within the full text report is very difficult to use. It's hard to tell (**yet**) how much the report discusses these two concepts *together*.

e. VA HSRD
f. DoD
g. Clinicaltrials.gov

D. Known authors

a. Amy S.B. Bohnert PhD
   i. Look at studies in progress
   ii. 84 documents in Scopus
      1. Many of her most highly cited articles are about suicide in veterans, with some link to substance abuse or pain
   iii. 991 "cited by" references
   iv. Look at her contributing authors

1. Scopus says:
    a. Mark Andrew Ilgen (42)
    b. Frederic C. Blow (22)
    c. Dana Ganoczy (12)
    d. Marcia M. Valenstein (11)
    e. Kara Zivin Zivin (10)

b. Karen Sherman
c. Lynn DeBar

E. Search for what individual states are doing

a. The CDC gave $20 million to 16 states to study prevention strategies aimed at fostering safe prescribing practices
    i. Minnesota: Joint Statement on Pain Management
    ii. Oregon: From Pills to Pins: How Oregon is Changing How It Deals with Back Pain
        1. Refers to the Quest Center in Portland
    iii. Which states, what are they doing, has anything been assessed yet?

F. Conferences and meeting proceedings

a. American Pain Society Complementary and Alternative Medicine Special Interest Group
    i. This year's conference is in May
    ii. Database of previous abstracts- these are pretty searchable. I looked at the 2015 group and searched for each of the interventions. A number of abstracts came up, but none were spot-on. Looking at past years might be useful.
b. COIN conference
c. IHI conference abstracts (Institute for Healthcare Improvement)

G. Findings from Google that could be related/useful

a. http://www.huffingtonpost.com/john-weeks/open-letter-to-barack-oba_2_b_9152892.html
    i. John Weeks- An Open Letter to Barack Obama on Your $1.1 billion Opioid Initiative: The Imperative for Integrative Medicine
        1. Published 2/5/2016
    ii. This article has a wealth of references to useful websites/programs/information
b. A Call to Action on Integrative Health and Medicine Policy: Advancing the Legacy of US Senator Tom Harkin
    i. Symposium at Georgetown University 9/29/2014
    ii. Eric Schoomaker gives the keynote speech again (article above says it's an 'expanded' version of the speech we already saw)
        1. References opioids in his talk, but no research
    iii. "Non-discrimination in healthcare"- a phrase that seems to refer to equating insurance coverage of Western medicine and CAM; possibly refers specifically to language in the ACA
    iv. Josephine Briggs talk "Building the Capacity for Real World Effectiveness Research for Integrative Health" (she's the director of the National Center for Complementary and Integrative Health) references opioids

c. Betty Ford high-level addiction programs

H. Programs that support/provide CAM interventions instead of/in concert with pharmaceutical pain relief

a. Las Vegas Recovery Center
   i. Not associated with any medical center
   ii. Focused on getting people off opiates by using holistic approaches to pain relief, including "physical, emotional, psychological and spiritual" approaches
   iii. It's an inpatient program
      1. Starts with a "medically managed withdrawal and detoxification" process
      2. Interventions we are interested in:
         a. Massage
         b. Meditation
         c. Acupuncture
         d. Yoga
   iv. There is some sort of assessment going on, but the graphs that are provided as the Pain Outcome Profile Reports don't really give any context as to what is being analyzed. In my opinion, they are presented in a vacuum and look like pain levels are decreasing, but it's hard to tell why, exactly.
   v. In an explanation of who gets admitted to the program, there is no reference to physician referrals.

b. RiverMend Health Centers- Georgia - Non-Opioid Pain Management Program
   i. RiverMend Health Center is a behavioral health and addiction treatment program; does not explicitly talk about referrals from medical doctors or how patients can get into this program
   ii. Focuses on people who are addicted to pain medication or people who are seeking alternative treatments for their chronic pain
   iii. Includes:
      1. Acupuncture
      2. Meditation
      3. Yoga
      4. Massage

LIST OF EXCLUDED STUDIES

Primary studies reporting medication use but no opioid-specific outcomes

#	Citation
1.	Brinkhaus B, Witt CM, Jena S, et al. Acupuncture in patients with chronic low back pain: a randomized controlled trial. *Archives of Internal Medicine.* 2006;166(4):450-457.
2.	Carlsson CP, Sjölund BH. Acupuncture for chronic low back pain: a randomized placebo-controlled study with long-term follow-up. *The Clinical journal of pain.* 2001;17(4):296-305.
3.	Cherkin DC, Eisenberg D, Sherman KJ, et al. Randomized trial comparing traditional Chinese medical acupuncture, therapeutic massage, and self-care education for chronic low back pain. *Archives of Internal Medicine.* 2001;161(8):1081-1088.
4.	Cherkin DC, Sherman KJ, Avins AL, et al. A randomized trial comparing acupuncture, simulated acupuncture, and usual care for chronic low back pain. *Archives of Internal Medicine.* 2009;169(9):858-866.
5.	Childs JD, Fritz JM, Flynn TW, et al. A clinical prediction rule to identify patients with low back pain most likely to benefit from spinal manipulation: a validation study. *Annals of internal medicine.* 2004;141(12):920-928.
6.	Christensen B, Iuhl I, Vilbek H, Bülow HH, Dreijer N, Rasmussen H. Acupuncture treatment of severe knee osteoarthrosis. A long-term study. *Acta Anaesthesiologica Scandinavica.* 1992;36(6):519-525.
7.	Coan RM, Wong G, Coan PL. The acupuncture treatment of neck pain: a randomized controlled study. *The American journal of Chinese medicine.* 1981;9(04):326-332.
8.	Coan RM, Wong G, Ku SL, et al. The acupunture treatment of low back pain: a randomized controlled study. *The American journal of Chinese medicine.* 1980;8(01n02):181-189.
9.	de Abreu Venancio R, Guedes Pereira Alencar Jr F, Zamperini C. Botulinum toxin, lidocaine, and dry-needling injections in patients with myofascial pain and headaches. *CRANIO®.* 2009;27(1):46-53.
10.	de Abreu Venâncio R, Guedes Pereira Alencar Jr F, Zamperini C. Different substances and dry-needling injections in patients with myofascial pain and headaches. *CRANIO®.* 2008;26(2):96-103.
11.	Dyson-Hudson TA, Shiflett SC, Kirshblum SC, Bowen JE, Druin EL. Acupuncture and Trager psychophysical integration in the treatment of wheelchair user's shoulder pain in individuals with spinal cord injury. *Archives of physical medicine and rehabilitation.* 2001;82(8):1038-1046.
12.	Ferreira ML, Ferreira PH, Latimer J, et al. Comparison of general exercise, motor control exercise and spinal manipulative therapy for chronic low back pain: a randomized trial. *Pain.* 2007;131(1):31-37.
13.	Foster NE, Thomas E, Barlas P, et al. Acupuncture as an adjunct to exercise based physiotherapy for osteoarthritis of the knee: randomised controlled trial. *Bmj.* 2007;335(7617):436.
14.	Grant DJ, Bishop-Miller J, Winchester DM, Anderson M, Faulkner S. A randomized comparative trial of acupuncture versus transcutaneous electrical nerve stimulation for chronic back pain in the elderly. *Pain.* 1999;82(1):9-13.
15.	Haake M, Müller H-H, Schade-Brittinger C, et al. German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. *Archives of Internal Medicine.* 2007;167(17):1892-1898.
16.	Harrison RE, Page JS. Multipractitioner upledger craniosacral therapy: descriptive outcome study 2007–2008. *The Journal of Alternative and Complementary Medicine.* 2011;17(1):13-17.
17.	Hemmilä HM. Bone setting for prolonged neck pain: a randomized clinical trial. *Journal of manipulative and physiological therapeutics.* 2005;28(7):508-515.
18.	Hoiriis KT, Pfleger B, McDuffie FC, et al. A randomized clinical trial comparing chiropractic adjustments to muscle relaxants for subacute low back pain. *Journal of manipulative and physiological therapeutics.* 2004;27(6):388-398.
19.	Hurley DA, McDonough SM, Dempster M, Moore AP, Baxter GD. A randomized clinical trial of

	manipulative therapy and interferential therapy for acute low back pain. *Spine.* 2004;29(20):2207-2216.
20.	Hurwitz EL, Morgenstern H, Kominski GF, Yu F, Chiang L-M. A randomized trial of chiropractic and medical care for patients with low back pain: eighteen-month follow-up outcomes from the UCLA low back pain study. *Spine.* 2006;31(6):611-621.
21.	Ilbuldu E, Cakmak A, Disci R, Aydin R. Comparison of laser, dry needling, and placebo laser treatments in myofascial pain syndrome. *Photomedicine and Laser Therapy.* 2004;22(4):306-311.
22.	Jull G, Stanton W. Predictors of responsiveness to physiotherapy management of cervicogenic headache. *Cephalalgia.* 2005;25(2):101-108.
23.	Jull G, Trott P, Potter H, et al. A randomized controlled trial of exercise and manipulative therapy for cervicogenic headache. *Spine.* 2002;27(17):1835-1843.
24.	Jüni P, Battaglia M, Nüesch E, et al. A randomised controlled trial of spinal manipulative therapy in acute low back pain. *Annals of the rheumatic diseases.* 2009;68(9):1420-1427.
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EVIDENCE TABLES

DATA ABSTRACTION OF INCLUDED PRIMARY STUDIES

Data Abstraction of RCTs

Author Year N Setting	Pain type, duration	Patient Characteristics	Intervention(s)	Treatment regiment, duration, setting, follow-up	Opioid use outcomes	Other outcomes: pain, functional capacity, quality of life, adverse events
Cherkin 2011[19] N=401 Integrated healthcare system	Nonspecific chronic low back pain ≥ 3 m	35.67% male Age = 47y 86.34% white	Relaxation massage (RM) Structural massage (SM) Usual care (UC)	Once per week in office treatment for 10 wks for 50-60 min + recommended at-home exercises Follow-up at 10, 26, and 52 wks	% narcotic analgesic use in past week (95% CI): 10-wks: 4.6 (3.0 to 7.3) SM vs 5.0 (3.0 to 8.5) RM vs 5.8 (3.4 to 9.9) UC; P = .69 26-wks: 5.0 (3.4 to 7.5) SM vs 4.6 (2.7 to 8.1) RM vs 5.2 (3.1 to 8.7) UC; P = .93 52-wks: 4.8 (3.1 to 7.3) SM vs 4.9 (3.1 to 7.9) RM vs 4.9 (2.7 to 8.7) UC; P = .99	Pain: Change from baseline SB score (points out of 10): 10 wks: -1.8 SM vs -2.1 RM vs -0.6 UC; 26 wks: -1.4 SM vs -1.3 RM vs -1.2 UC; 52 wks: -1 SM vs -1.7 RM vs -1.6 UC Functional capacity: Change from baseline RDQ score (points out of 23): 10 wks: -3.6 SM vs -5.6 RM vs -1.5 UC; 26 wks: -3.4 SM vs -5.2 RM vs -2.3 UC; 52 wks: -2.9 SM vs -5.6 RM vs -3.1 UC Adverse events: 4% RM and 7% SM of patients reported adverse events

Author Year N Setting	Pain type, duration	Patient Characteristics	Intervention(s)	Treatment regiment, duration, setting, follow-up	Opioid use outcomes	Other outcomes: pain, functional capacity, quality of life, adverse events
Esmer 2010[20] N=25 Spine and rehabilitation center	Failed back surgery syndrome: persistent leg and/or back pain despite history of surgery ≤ 2 y	56% male Age = 55.08y 100% white	Mindfulness-based stress reduction (including meditation)	Once per week in classroom for 1.5-2.5h for 8 wks + one additional 6h session in sixth week; required homework assignments + encouraged daily meditation using guided audiotapes Follow-up at 12 and 40 wks	Change in analgesic medication use at 12-wks (4-point scale: 0 = no analgesic to 4 = daily narcotics): -1.5 intervention vs 0.4 control (P < .001)	Pain: Change in VAS at 12-wks (30-point scale): -6.9 intervention vs -0.2 control (P < .021) Functional capacity: Change in RMDQ at 12-wks (24-point scale): -3.6 intervention vs 0.1 control (P < .005) Quality of life: Change in CPAQ at 12-wks (108-point scale): 7.0 intervention vs 6.7 control (P < .014)
Saper 2013[21] N=95 Academic hospital and 5 affiliated community health centers	Nonspecific chronic low back pain ≥ 12 wks	28% male Age=47.5y 17% white	Yoga	Once or twice weekly, 75 min yoga class in classroom for 12 wks + daily home practice for 30 min with audio CD and handbook Follow-up at 12 wks	% opiate use change from baseline at 12 wks: 0 once/wk class vs 2 twice/wk class (estimated from Figure 4). No significant change in from baseline. No significant between group differences	Pain: Intensity (scale NR) Mean change from baseline at 12 wks: -2.1 (-2.9 to -1.3) once/wk class vs -2.4 (-3.1 to -1.8) twice/wk classes Functional capacity: Change in RMDQ (23 point scale) at 12 wks: -5.1 (-7.0 to -3.2) once/wk class vs -4.9 (-6.5 to -3.3) twice/wk class Quality of life: Change in SF-36 physical at 12 wks: 6.4 (3.9 to 9.2) once/wk class vs 6.3 (4.1 to 8.4) twice/wk class Adverse events: 27% once/wk class vs 34% twice/wk class participants (P = 0.47)

Author Year N Setting	Pain type, duration	Patient Characteristics	Intervention(s)	Treatment regiment, duration, setting, follow-up	Opioid use outcomes	Other outcomes: pain, functional capacity, quality of life, adverse events
Sator-Katzenschlager 2004[22] N= 61 University-based pain center	Chronic low back pain ≥ 6 m	30% male Age=53.6y Race NR	Auricular acupuncture with electrical stimulation with P-Stim™ device (EA) or without (CO)	Once per wk at home for 48h for 6 wks Follow-up at 3 m after series	Consumption of tramadol rescue medication during entire investigation (# tablets): EA = 6 vs CO = 150 (P < .001)	Pain: VAS at 18 wks (estimated from Figure 2A): 1 EA vs 4 CO (P < 0.05) Functional capacity: Return to full-time work: 77% EA vs 25% CO (P = 0.0032) Quality of life: Well-being impairment VAS at 18 wks (estimated from figure 2B): 1 EA vs 5 CO (P < 0.05) Adverse events: none
Weiner 2013[23] N=190 VA Pittsburgh Healthcare System	Knee OA with moderate intensity pain ≥ 3 m	84.7% male 66.6 y 70.5 % white	Periosteal stimulation therapy w/ boosters (PST & PST) vs PST w/ no boosters (PST & control) vs control PST w/ no boosters (control)	PST or control PST for 30 min 1once/wk for 10 wk followed by 6 m of boosters or no boosters Follow-up at 3, 6, & 9 m follow-up	Baseline adjusted differences compared w/ control: 10 wks: PST & PST = 0.018 (-0.19 to 0.23) PST & control = -.27 (-0.48 to -0.054)	Baseline adjusted differences compared with control: Pain: WOMAC score: 10 wks: PST & PST = 1.1 (CI -.34 to 2.5); PST & control = 1.3 (CI -.10 to 2.8) Functional capacity: WOMAC difficulty performing daily activities (Scale 0-68): 10 wks: PST & PST = 2.5 (-1.9 to 6.9); PST & control = 1.8 (-2.6 to 6.2) SF-36 mental health composite: 10 wks: PST & PST = -0.34 (-2.9 to 2.2); PST & control = -0.46 (-3.1 to 2.1) Adverse events: 4 adverse events attributable to PST and control PST

Author Year N Setting	Pain type, duration	Patient Characteristics	Intervention(s)	Treatment regiment, duration, setting, follow-up	Opioid use outcomes	Other outcomes: pain, functional capacity, quality of life, adverse events
Zheng 2008[24] N=35 Pain management center	Non-malignant pain > 3 m	51.5% male 49.7 y Race NR	Electroacupuncture (REA) or sham electroacupuncture (SEA)	30 min. treatment & 20 min stimulation time twice/wk for 6 wks Follow-up at16 & 20 wks	OLM consumption (mg/wk morphine equivalent) 8 wks: 281.4 REA vs 219.1 SEA (P < .001) 20 wks: 344.7 REA vs 239.0 SEA (P = .022)	Pain: average (scale NR) 8 wks: Change from baseline -0.8 REA vs -0.7 SEA (P = .001) Adverse events: 33 REA vs 19 SEA

SB: Symptom Bothersomeness Scale; RDQ: Roland Disability Questionnaire; VAS: Visual Analog Scale; RMRQ: Roland Morris Disability Questionnaire; CPAQ: Chronic Pain Acceptance Questionnaire; SF-36: Short Form-36 Health Survey; WOMAC: Western Ontario & McMaster Universities Osteoarthritis Index; OA: Osteoarthritis; NR: Not Reported

QUALITY ASSESSMENT OF INCLUDED PRIMARY STUDIES

Quality Assessment of RCTs

Author Year	Adequate sequence generation?	Adequate allocation concealment?	Blinding of participants, personnel and outcome assessors?	Formal assessment of adequacy of the blind?	Incomplete outcome data adequately addressed?	Study reports free of suggestion of outcome reporting bias?	Study free of other sources of bias?	Risk of bias?
Cherkin 2011[19]	Low; Randomized to treatment/control, then statistician-generated randomization blocked on massage therapist	Low; Centralized	High; Therapist personnel unblinded, massage participants blinded as to type of massage received, usual care participants unblinded	High; Opioid use assessed weekly by unblinded patients; no sham group	Low; 5-9% lost to follow-up. Multiple imputation to account for missing values.	Low; Primary and secondary outcomes were stated in protocol and completed as stated.	Unclear; Patients in relaxation massage group had higher RDQ at baseline, although the difference (>1) is not clinically relevant according to the definitions of the study (>2).	High

Author Year	Adequate sequence generation?	Adequate allocation concealment?	Blinding of participants, personnel and outcome assessors?	Formal assessment of adequacy of the blind?	Incomplete outcome data adequately addressed?	Study reports free of suggestion of outcome reporting bias?	Study free of other sources of bias?	Risk of bias?
Esmer 2010[20]	Unclear; No description of how random assignments were generated	Unclear; Not described	High; Participants unblinded	Unclear; Statistical analysis of patient-completed questionnaires was performed by statistician blinded to patient intervention status.	High; High attrition rate between randomization and analysis (11/21 from control; 4/19 from intervention) with no explanation given of how that was incorporated in analysis. Numbers reported in flow diagram do not add up, and the text of the study seems to ignore the intervention-side attrition rate when reporting on intervention compliance rates.	Unclear	Low; No significant differences at baseline between analyzable intervention and control groups.	High
Saper 2013[21]	Low; Computer created randomization schedule	Unclear; Not described	High; Participants and study staff who scheduled classes unblinded	High; All outcome data provided from participants through questionnaires; no sham	Low; 96% follow-up	Low	High; Low and differential adherence: once-weekly=65% vs twice-weekly=44%, P = 0.040; not adjusted for in analysis	High

Author Year	Adequate sequence generation?	Adequate allocation concealment?	Blinding of participants, personnel and outcome assessors?	Formal assessment of adequacy of the blind?	Incomplete outcome data adequately addressed?	Study reports free of suggestion of outcome reporting bias?	Study free of other sources of bias?	Risk of bias?
Sator-Katzenschlager 2004[22]	Low; Computer-generated random number tables	Unclear; Not described	Low; Patients and investigators. Everyone wore the device, stimulator activated independent technician. Both groups believed they were receiving stimulation: 100% vs 97%	Low	Unclear; Early discontinuation: EA=6% for noncompliance and CO=13% for lack of efficacy. Stated that all 61 were analyzed but no info about how missing data imputed	Low	Low; Higher baseline pain in control group (8.0 vs 7.5; P = 0.021). But magnitude of difference small and in opposite direction of overestimating EA	Unclear
Weiner 2013[23]	Low; Computer generated stratified randomization	Low; Allocation determined for each participant once deemed eligible w/ next assignment concealed within electronic database until next participant was deemed eligible	Unclear; Research assistant doing scheduling masked; do not explicitly use the language that participants are "blinded or masked", however they give in-depth explanation of 3 groups and how they tried to "control for treatment expectancy," No detail on adequacy of the blind	Unclear; Research coordinator who collected outcome data was kept masked to treatment groups; however medication use was patient-reported, with no verification – and we are unclear about patient blinding	Low; Even though attrition was low (~7% overall, 2% to 10%), used multiple imputation in sensitivity analyses	Low; Clinical registration protocol made available and both primary and secondary outcomes clearly described and reported	Unclear; Characteristics similar in all 3 groups except scores on the catastrophizing scale of the Cognitive Strategies Questionnaire and WOMAC pain at baseline, with those in the PST and control PST boosters group having more catastrophizing and the control PST group having more knee pain.	Unclear

Author Year	Adequate sequence generation?	Adequate allocation concealment?	Blinding of participants, personnel and outcome assessors?	Formal assessment of adequacy of the blind?	Incomplete outcome data adequately addressed?	Study reports free of suggestion of outcome reporting bias?	Study free of other sources of bias?	Risk of bias?
Zheng 2008[24]	Low; Computer-generated block randomization	Unclear; Methods of concealment not described	Low; Participants and personnel blinded. Blinding assessed and no significant differences between groups.	Unclear; Blinding of outcome assessors not described	Unclear; 22-47% lost to follow-up. Used LOCF in intention to treat analysis	Unclear	Unclear; greater starting MED in intervention group? 461.6 MED/week versus 295.5 MED/week	Unclear

RDQ: Roland Disability Questionnaire WOMAC: Western Ontario & McMaster Universities Osteoarthritis Index; LOCF: Last observation carried forward; MED: morphine equivalent dose

STRENGTH OF EVIDENCE FOR INCLUDED STUDIES

SOE Grade	Study Design: No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Issues	Findings
Acupuncture								
Auricular acupuncture with or without electrical stimulation for low back pain: Low	1RCT, N=61[22]	Unclear	Direct	Unknown	Imprecise	Undetected	None	ê Opioid consumption (# tablets) throughout intervention: EA = 6 vs. CO = 150 (P < .001)
Electroacupuncture vs sham for opioid tapering in patients with various types of pain: Low	1 RCT; N=35[24]	Unclear	Direct	Unknown	Imprecise	Undetected	None	No difference; reduction in opioid MED 39% vs 26%; NSD
Periosteal stimulation therapy, with boosters (PST+PST) or without boosters (PST+control) or control PST without boosters (control) in Veterans with knee OA: Low	1 RCT; N=190[23]	Unclear	Direct	Unknown	Imprecise	Undetected	None	Opioid consumption (baseline adjusted differences in # weekly doses compared to control) at 10 wks: Reduced for PST without boosters, but not with boosters = PST+PST: 0.018 (-0.19 to 0.23) ê PST+control: -0.27 (-0.48 to -0.054)
Massage								
Structural massage relaxation massage, or usual care in low back pain: Insufficient	1 RCT; N=401[19]	High	Direct	Unknown	Imprecise	Undetected	None	= narcotic analgesic consumption (% narcotic analgesics in past week, change from baseline) at10 wks: SM = -12.4 vs RM = -12.0 vs UC = --7.2 at 52-wks: SM = -12.2 vs RM = -12.1 vs UC = -8.1

SOE Grade	Study Design: No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Issues	Findings
Meditation								
Mindfulness-based stress reduction (MBSR) or usual care in patients with failed back surgery syndrome: Insufficient	1 RCT; N=25{Esmer, 2010 #19	High	Direct	Unknown	Imprecise	Undetected	None	ê Analgesic medication use at 12-wks (4-point scale: 0 no analgesic - 4 daily narcotics): MBSR = -1.5 vs. Control = 0.4 (P < .001)
Yoga								
Yoga once vs twice weekly in patients with low back pain: Insufficient	1 RCT; N=95[21]	High	Direct	Unknown	Imprecise	Undetected	None	= Opiate (% change from baseline) at 12 wks: Yoga 1x/wk = 0 vs. Yoga 2x/wk = 2; NS

MED: morphine equivalent dose; OA: Osteoarthritis

PEER REVIEW COMMENT TABLE

Comment #	Reviewer #	Comment	*Author Response*
Are the objectives, scope, and methods for this review clearly described?			
1	1	Yes	*None*
2	2	Yes	*None*
3	3	Yes	*None*
4	4	Yes	*None*
5	5	Yes	*None*
6	6	Yes	*None*
7	7	Yes	*None*
8	8	Yes	*None*
Is there any indication of bias in our synthesis of the evidence?			
9	1	No	*None*
10	2	No	*None*
11	3	No	*None*
12	4	No	*None*
13	5	No	*None*
14	6	No	*None*
15	7	No	*None*
16	8	No	*None*
Are there any published or unpublished studies that we may have overlooked?			
17	1	No	*None*
18	2	No	*None*
19	3	No	*None*
20	4	Yes - No studies directly relating to CIH/opioids but perhaps some studies missed that relate to background and discussion information - I have attached what may be of interest or what may add to the accuracy or completeness of the document	*We thank the reviewer for providing these very recent citations – we have added all suggested citations.*
21	5	No	*None*
22	6	No	*None*
23	7	Might look into work from the Cleveland Clinic on interdisciplinary rehab programs and reduced opioid dose, Same with Standford and work by Beth Darnall.	*Added that we are aware of these programs, but that we were unable to identify clear descriptions of their approaches to using specific CIH interventions or data on their effectiveness*
24	8	No	*None*

Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.			
25	1	On page 6 lines 35-36 reference is made to the National Center for Complementary and Integrative Health and to the National Center for Complementary and Alternative Medicine. The way it is written seems to imply that these are two different organizations rather than one organization that has undergone a recent name change.	*Removed* National Center for Complementary and Alternative Medicine.
26	2	ES line 7: Awkward lead in -- I would state that the increase in opiod prescribing over the past two decades has been accompanied by dramatic increase in problems related to opiod use, including overdose-related death, dependence, and misuse. As a result, there is intense interest in non-opiod alternatives for treating chrinic pain.	*Revised as suggested.*
27	2	ES line 26: Separate this into two sentences	*Done.*
28	2	Table ES1: 2nd row: Confusing row in table -- not clear what comparisons are for down arrows, what do = sign mean?	*Replaced symbols with words and made other improvements*
29	2	Page 13, line 29: Is one is looking at opiod use as an outcome, could one argue that sham controls are less necessary since we don't necessarily care if some of the effect is due to placebo if it reduces the use of opiods?	*We appreciate this reviewer's point. But, this section is referring only to the potential methodological limitations of these studies, which is only one of our considerations about the usefulness of the evidence. Regardless of how we view the importance of the sham controls, the bigger problem with this evidence is that it was generally comprised of single small studies with limited applicability.*
30	2	Page 16, line 22: what are shams for massage?	*Light touch*

31	3	The target population and interventions are clearly defined. The outcome—opioid use—is not a clinical outcome, it's more of a treatment process variable. Also, opioid use isn't clearly defined; it could mean physician prescribing, patient consumption, or both. The topic is somewhat odd in its focus on the ability of one category of clinical interventions (CIH therapies) to prevent use of another category of clinical interventions (opioid medications). The cause and effect relationship isn't clear here as it is for most ESP reviews. Should we assume the mechanism is that CIH interventions would effectively treat pain so physicians would prescribe fewer or lower dose opioids or so patients would take fewer of their prescribed opioids? Are we interested in patient-level effects, prescriber-level effects, policy-level effects, or all three? Clarity on these issues would improve the relevance and utility of the report.	*We appreciate the reviewer's point about the outcome of opioid use, but think that the rationale of evaluating non-opioid interventions for pain with the goal of reducing opioid use will be intuitive for most prescribers. The recent CDC guideline on opioid prescribing also highlights this goal. The report abstract starts with "Primary care clinicians find managing chronic pain challenging. Evidence of long-term efficacy of opioids for chronic pain is limited. Opioid use is associated with serious risks, including opioid use disorder and overdose."* *Added clarification to opioid use outcome inclusion criteria that we intended to include both physician prescribing and patient consumption. We also added clarification to the Introduction section about the potential mechanism of CIH for reducing opioid use.*
32	3	The text related to opioid dosing is inaccurate and contradictory in places. On the last paragraph of page 4, "higher doses" are described in parentheses as 100-120 ME mg, although the data presented in the next sentence demonstrates increased risk of death starting at 20 ME mg. On page 5, guidelines' "upper dosing thresholds" are described as "generally 90-120 mg MED, but some up to 200 MED." On page 7, a link is described between overdose and an "80-120 MED threshold." 80 mg is used subsequently in the text as a cutoff for high dose or threshold for risk. Studies examining dose-death associations have categorized dose in a variety of ways for a variety of reasons, but I am aware of no evidence that suggests an actual inflection point or "threshold" for overdose risk. Rather, evidence seems to suggest that risk increases as dose increases, starting with very low doses. The new CDC guidelines describe in detail the rationale for their recommendations of additional caution at 50 mg and avoidance of prescribing >90 mg, while acknowledging that there is no threshold for risk. For the purposes of this review, it may be best to avoid choosing a dose cutoff. If one is selected, it should be much more clearly justified.	*Agreed. Removed suggested dose threshold of 80-120 MED. Added new CDC guidelines as a reference and acknowledgement that risk generally increases with dose and there is no evidence of a "universal" threshold for risk*
33	3	Page 4, 4th paragraph, 1-2 sentences: The causes of increased opioid prescribing are a matter of hot debate, but I'm not aware of changes in laws and regulations that played a major role. The role of the Joint Commission's pain standards in this prescribing practice change is controversial. More commonly stated causes are misleading and aggressive promotion of new opioid products (e.g., Oxycontin) and advocacy for more aggressive treatment of pain. Speculating on this matter is likely to detract from the purpose of the report.	*Changed to: "The causes of increased prescribing have been widely debated and are likely numerous."*

34		Page 5, lines 30-31: I don't believe reliable estimates of chronic pain in male and female VHA patients have been published. The citation is not specific.	*Changed to: Chronic pain may occur in up to 50% of Veterans treated in primary care.[Kerns 2013]*
35	3	Page 5, final paragraph, first sentence: The lack of evidence for opioids should not make it more difficult to develop "evidence-based guidance for chronic non-cancer pain management." There are many studies that provide evidence on many different treatments for chronic pain. The difficulty is in developing guidance on when and how to use opioids.	*Changed to: Developing evidence-based guidance on how and when to use opioids for chronic non-cancer pain management is difficult…*
36	3	Page 6, paragraph 3: It seems obvious that opioid-specific guidelines would focus on opioids; by definition, other therapies are outside their scope. "Chronic pain" is not one condition, but an umbrella term that covers an experience common to a number of conditions, such as chronic back pain, osteoarthritis pain, fibromyalgia, peripheral neuropathic pain, and headache. Guidelines addressing specific chronic pain conditions are the appropriate place to look for recommendations on use of CIH in chronic pain. (This comment also applies to key message #2)	*We appreciate the reviewer's point, but as clinicians are also obligated to discuss alternatives when consenting for opioid treatment, opioid-specific guidelines generally address considering alternatives. Our point is that CIH is not cited specifically as an alternative as other non-opioid treatments such as CBT are.*
37	3	Page 6, last paragraph, first sentence: These statements seem to lack any basis in the literature: "(1) CIH is under-utilized in opioid users and (2) compared to usual care, magnitude of pain reduction for CIH is comparable to opioids" What evidence suggests that CIH is under-utilized in opioid users? What is the magnitude of pain reduction for opioids vs. usual care and for CIH vs. usual care	*Changed to: "Select CIH interventions may be reasonable non-opioid treatment options in general because (1) CIH is possibly under-utilized in opioid users and (2) compared to usual care, magnitude of pain reduction for CIH is potentially comparable to opioids, but without serious side effects." The rest of this paragraph provides the supporting details and citations for these statements.*
38	3	Highlighting a hypothetical connection of opioid dose reduction with heroin use seems overly speculative.	*Supported by: Compton WM, Jones CM, Baldwin GT. Relationship between Nonmedical Prescription-Opioid Use and Heroin Use. New England Journal of Medicine. 2016;374(2):154-163.* *Cicero TJ, Ellis MS, Harney J. Shifting Patterns of Prescription Opioid and Heroin Abuse in the United States. New England Journal of Medicine. 2015;373(18):1789-1790.*
39	3	Methods: Overall, the eligibility criteria, search strategies, and analysis methods are appropriate and well described.	*No action needed.*
40	3	Results: Overall, the results are clearly described and summarized. I am not aware of any studies that were overlooked or incorrectly included/excluded.	*No action needed.*

41	3	Comment: Table 2 uses “opioid,” “opiate” and “narcotic.” This may be a purposeful choice to use terms from the original studies. If not, it would be best to stick with “opioid.”	*Yes, this was a purposeful choice to use terms from the original studies*
42	3	Discussion: In general, the key messages are broader than seems appropriate for this narrowly focused evidence review and go well beyond the findings. For example, #6 seems to be opinion-based and is not supported by citations. I recommend keeping key recommendations more focused on the research findings and gaps identified.	*Moved #6, potential barriers to implementation, to the Future Research section.*
43	3	I found the future research section to be rather confusing overall. It seems to call for research with potentially limited clinical, practice, or policy relevance. Reducing opioid use is not a clinical outcome. Pain, pain related function, quality of life, overdose deaths, and opioid harm events are clinical outcomes. Do we really want clinical studies designed to determine CIH effectiveness for reducing opioids? Or do we want studies designed to determine CIH effectiveness for treatment of common clinical pain conditions to also assess possible secondary effects on opioid consumption or prescribing? Perhaps reducing opioid prescribing may be more appropriately considered a policy relevant outcome. In that case, studies of CIH access/coverage policies that can look effects on opioid prescribing practices and ultimately opioid harm outcomes may be indicated.	*Agree that we want studies that evaluate a complete set of key outcomes. Revised to: “There is a need for more research assessing CIH interventions’ value in addressing the opioid epidemic by simultaneously evaluating a complete set of key outcomes, including their impact on pain, pain-related function, quality of life, harms, and on new or ongoing opioid use or stopping opioids entirely.”*
44	3	The future research section provides very specific recommendations for how opioid use (consumption in this case) should be assessed (i.e., daily patient reports), but does not provide any citations to support the recommendations.	*Changed to: “Patient self-report methods for measuring measure opioid use varied substantially across studies, generally without providing a rationale for how methods were selected: recall periods ranging from multiple times daily up to monthly, proportion of patients with any use, daily, or less than daily use, and number of weekly doses. To determine how to select and strengthen patient self-report methods for measuring opioid use, we suggest considering use of well-validated processes, optimized question response formats and recall periods, taking steps to address social desirability concerns, avoiding interview-based assessments, and accounting for self-report challenges such as cognitive functioning, burden, and setting.[Stirratt 2015]”*

45	4	I have rated the report as fair - not because of the quality of the evidence review, background, discussion, or other sections, but rather for the paucity of useful information it contains. Hardly any of the key questions could be addressed, so the reader is left with more questions than answers. Probably the most useful conclusion that can be made is that which was made on p 22 (**a lot** of research is needed about the effectiveness of CIH interventions as they relate to opioid use). I agree this is an important avenue for future work in pain management. Thank you for the opportunity to review.	*No action needed.*
46	4	ES: The text in lines 11-14 appears to be in conflict with text lines 19-42. If the evidence base regarding effectiveness of select CIH interventions is so limited, how can one come to any conclusion regarding their relative effectiveness to that of opioid	*The sections noted relate to different outcomes. Lines 11-14 relate to CIH's effects on pain; whereas, lines 19-42 relate to CIH's effects on opioid use. Regardless, we tempered our statements about the comparative efficacy of opioids and CIH on pain to better reflect the indirectness of the evidence base.*
47	4	Table ES1, row 1: Needs clarification - I do not understand what "up to 8 times 50mg daily means" Does it mean "up to 400mg daily"?	*Yes, changed.*
48	4	Table ES1, row 2, opioid type: I understand this to mean: that the opioid is unknown, and that the unknown opioid was only given at average of one-half dose per week? If I am correct I do not understand how a valid comparison or degree of influence could be made with such sketchy information.	*Agree this is a major deficiency and have called for future studies to report opioid type, dose, and frequency.*
49	4	Table ES1, row 2: How was QOL measured	*Added measurement method of SF-36 physical component*
50	4	Table ES1, row 3: NMP could mean almost any type of acute or chronic pain Dose is defined as mg/wk, then expressed below as mg/DAY (for REA and SEA) - should be consistent - which should it be?	*Yes, study did not specify pain types. But added that it was chronic pain. Corrected mg/wk to mg/d*
51	4	Page 4, line 37: While codeine is indeed a Sch II opioid it is rarely used in that manner - it is usually combined with acetaminophen (and is then no longer a CII). I would suggest substituting morphine here.	*Changed to morphine*
52	4	Page 4, line 54: On page 2, line 24, a range of 80-100 was stated - seems like the ranges used should be consistent, as they are all related to risk for opioid OD death. Later on page 7 line 17 another range of 80-120 is quoted.	*Removed ranges. See response to comment #32.*
53	4	Page 5, line 21: "importance"	*Corrected*
54	4	Page 5, line 34: Consider listing a few or these co-morbidities, especially those that might respond to CIH interventions	*Added: patient demographics and comorbidities (e.g., alcohol or substance use and other mental health and medical disorders)*

55	4	Page 5, line 39: Perhaps this sentence should read "Developing EB guidance for USE OF OPIOIDS for chronic non-cancer pain management is difficult..." Also bear in mind that consensus guidance often is about what is NOT recommended as well as what is recommended, so negative studies can be used as well as positive ones.	*Revised as suggested.*
56	4	Page 5, line 47: Was it Nuckols et al. who decided which of the guidelines were of "fair-to-good" quality? If so, may want to re-phrase. "According to Nuckols et al., nine fair to good-quality quidelines...."	*Changed to "According to Nuckols et al., nine fair to good-quality quidelines...."*
57	4	Page 5, line 57: The unintended consequence is actually increased incidence/rates of opioid use disorder - the increased rate of heroin use is a result of this	*Changed to "the emergence of withdrawal symptoms that may lead to aberrant opioid-seeking behaviors that may result in use of illicit opioids;[Ballantyne 2012]*
58	4	Page 6, line 5: There is a lot of work done and in progress within VA to determine what are risk factors and who is at risk of opioid OD or serious opioid-related resp depression. There is more to it than dose of opioid - this is hinted at in the text with reference to SUD, psychiatric illness, etc.. See Zedler et al. Pain Medicine 2015; 16: 1566-1579, Park et al BMJ 2015; doi: 10.1136/bmj.h2698 + other publications by Bohnert's group: PMID: 26807540 and 26761386,	*Added: "In Veterans receiving opioids, receipt of benzodiazepines has been associated with an increased risk of overdose death[Park 2015] and mental health disorders, pharmacotherapy, impaired drug metabolism or excretion, pulmonary disorders, specific opioid characteristics, and recent hospital visits have been associated with serious opioid-induced respiratory depression.[Zedler 2015]"* *Added PMID 26807540 (Bohnert 2016) to support statement that evidence has not yet identified a clear dose "threshold" for overdose risk* *Added PMID 26761386 (Ilgen 2016) as citation for link between high opioid dose and suicide.*
59	4	Page 6, line 39: The CDC Guidelines were published on March 15 and, as far as I can tell, only CDC recommendation #1 addressed non-pharmacological therapies, and then only mentioned PT, weight loss, and CBT. Based on this new information - this sentence should be re-worked. The 'non-mention' of CIH modalities in the CDC guidance reinforces what was said in the preceding paragraph, lines 23-33	*Added CDC guideline.*
60	4	Page 6, line 52-29: If direct comparisons between opioids and CIH are lacking, how can one conclude that CIH interventions are a reasonable alternative to opioid therapy OR that magnitude of pain reduction between CIH and opioids is comparable?	*Yes, we tempered our statements about the comparative efficacy of opioids and CIH on pain to better reflect the indirectness of the evidence base.*

61	4	Page 7, line 10: If a more rigorous analysis of the evidence for CIH in pain is to come, then possibly some of the statements earlier in this paragraph are premature?	*Yes, we tempered our statements about the comparative efficacy of opioids and CIH on pain to better reflect the indirectness of the evidence base.*
62	4	Page 7, line 16: I would say the main goal should be more patient centric: to achieve or maintain pain relief; to improve function, to reduce side effects/risk. If stopping opioid helps to achieve one or more of those goals, then OK See Berna et al. Tapering Long-Term Opioid Therapy in CNCP Mayo Clinic Proceedings 2015; 90(6) 828-42.	*Changed to: "The goal of reducing opioid use is to reduce risk of overdose deaths, dependence, misuse and other serious complications. In some cases, this means stopping opioids entirely."*
63	4	Page 7, line 25: Again - the risk of reducing opioid dose/use is the emergence of OUD-behaviors - use of illegal narcotics is the end-result. See Ballantyne et al. edit Arch Int Med 172 (17): Sept 24, 2012 pages 1342-3	*Changed to "the emergence of withdrawal symptoms that may lead to aberrant opioid-seeking behaviors that may result in use of illicit opioids;[Ballantyne 2012]*
64	4	Page 21, line 9-11: with so little comparative data how can this statement be made?	*Changed to: "Limited evidence suggests that select CIH interventions may be reasonable non-opioid treatment options in general because, compared to usual care, magnitude of pain reduction for CIH is potentially comparable to opioids, but without serious side effects"*
65	4	Page 21, line 9: "increase" or refine?	*Changed to 'clarify'*
66	5	I found Table ES1 somewhat difficult to interpret, including information provided in the last three columns. Perhaps the authors could consider editing for improved clarity.	*Yes, we edited to improve clarity.*
67	6	Apparently this is the first of a number of planned reviews of alternatives to opioid therapy in preparation for a Nov conference sponsored by the VAHSR&D. The select things covered in this report will hopefully be supplemented by evidence on chiropractic, behavioral therapies like cognitive-behavioral therapy, and others. It would be useful in the background to briefly describe what all will be ultimately included. The terminology (CHI) throws you off a little since it does not include all of the alternatives that are promising.	*Defining the scope of additional work is a key goal of the April 2016 SOTA planning meeting.*
68	6	The three articles on acupuncture are actually not classic acupuncture but electrical stimulation through acupuncture needles, or electro-acupuncture, which is considered quite different from classic acupuncture. The report should call this out, and should make the point that what is being reported here is NOT the impact of classic acupuncture on opioid dose.	*Added this clarification.*
69	6	The 2015 WA opioid guideline includes a new section on non-pharmacological alternatives to opioids-this should perhaps be referenced since it is the only major guideline to date to address this: http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf	*Added.*
70	7	Please make sure to define all abbreviations.	*Done*

71	7	please avoid the use of "opioid users" and use "patients prescribed opioids" throughout the text	*Done*
72	7	Table ES1: what is REA and SEA? PST, EA and CO also need to be explained in the notes section	*Added.*
73	7	Page 5, line 10: what is drug substitution? do you mean medication assisted treatment?	*This is a term used by King 2014. It seems to mean that people with a substance use disorder may substitute prescription opioids for illicit drugs.*
74	7	Page 5, line 13: define SES	*Done*
75	7	Page 5, line 16: are you saying that these things caused more deaths? Usually we say that they mitigate death.	*Yes, this is a summary of the King et al systematic review published in American Journal of Public Health in 2014 that identified these factors as potentially linked to increased risk of opioid-related mortality.*
76	7	Page 6, line 40: The CDC guideline is now published. This should be updated.	*Added.*
77	7	Page 12, line 43: opioid use - or opioid dose?	*Our point here was to identify the studies that measured opioid use versus those that evaluated overall analgesic use.*
78	7	Page 13, line 11: would look into the Cleveland Clinic's work (Ed Covington) or Seddon Savage at Dartmouth's Silver Hill Hospital. To my knowledge, they both use meditation to help with opioid dose reduction and reduced reliance on medication. Also, the Standford program with Beth Darnall might have some data.	*Changed to: "We are also aware of programs that routinely use multidisciplinary approaches to help reduce reliance on pharmacological treatments for pain.[Silver Hill Hospital, the Cleveland Clinic and the Stanford Pain Management Center] But, we were unable to identify clear descriptions of their approaches to using specific CIH interventions or data on their effectiveness."*
79	7	Page 14, line 43: would you translate this to daily dose? A weekly MED doesn't really have much meaning.	*Done*
80	7	Page 15, line 40: again, better if this is tranlsated to MED per day	*Done.*

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