INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Cognitive and Mind-Body Therapies for Chronic Low Back and Neck Pain: Effectiveness and Value

Evidence Report

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The findings contained within this report are current as of the date of publication. Readers should be aware that new evidence may emerge following the publication of this report that could potentially influence the results. ICER may revisit its analyses in a formal update to this report in the future.

In the development of this report, ICER's researchers consulted with several clinical experts, patients, and other stakeholders. The following clinical experts provided input that helped guide the ICER team as we shaped our scope and report. None of these individuals is responsible for the final contents of this report or should be assumed to support any part of this report, which is solely the work of the ICER team and its affiliated researchers.

For a complete list of stakeholders from whom we requested input, please visit:
https://icer-review.org/material/back-and-neck-pain-stakeholders/

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List of Acronyms Used in this Report

AAPM	American Academy of Pain Medicine
AHRQ	Agency for Healthcare Research and Quality
ACP	American College of Physicians
AMSTAR	A Measurement Tool to Assess Systematic Reviews
APS	American Pain Society
CBT	Cognitive Behavioral Therapy
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
CPGS	Chronic Pain Grade Scale
FFbHR	Functional questionnaire Hannover for everyday diagnosis of functional impairment by back pain
GAD-2	Generalized anxiety disorder scale
HADS	Hospital Anxiety and Depression Scale
ICSI	Institute for Clinical Systems Improvement
MBSR	Mindfulness-based stress reduction
MCS	Mental component score
NDI	Neck Disability Index
NICE	National Institute for Health and Care Excellence
NPQ	Northwick Park Neck Pain Questionnaire
NSAID	Non-steroidal anti-inflammatory drugs
ODI	Oswestry Disability Index
OMPSQ	Örebro Musculoskeletal Pain Screening Questionnaire
PCS	Physical component score
PHQ-8	Patient Health Questionnaire-8
POM	Pain on movement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSS	Perceived Stress Scale
QALY	Quality adjusted life year
RMDQ	Roland Morris Back Pain Disability Questionnaire
SMD	Standardized Mean Difference
TENS	Transcutaneous electrical nerve stimulation
UK	United Kingdom
US	United States
USPSTF	United States Preventive Services Task Force
VAS	Visual analog scale
WMD	Weighted Mean Difference

Executive Summary

Background

Low back and neck pain are two of the most common reasons for patient visits to physicians in the United States. The estimated total cost for low back and neck pain in the United States (US) was $88 billion in 2013, third highest after heart disease and diabetes.[1] Total cost for low back and neck pain has increased faster than any other group of diagnoses, from $30.4 billion in 1996 to $87.6 billion in 2013. This does not include the indirect costs related to missed work and disability.

A wide range of non-invasive therapies have been evaluated for chronic pain. This review focuses on five cognitive and mind-body therapies for chronic low back pain and chronic neck pain: acupuncture, cognitive behavioral therapy (CBT), mindfulness-based stress reduction (MBSR), yoga, and tai chi.

The Topic in Context

Most people experience low back and/or neck pain during their lives. In the 2015 Global Burden of Disease study, low back and neck pain was the leading cause of disability in most countries.[2] Because low back pain often occurs in younger individuals, it is a common cause of missed work and reduced productivity resulting in high indirect costs.[3]

Low back and neck pain are typically classified by duration of symptoms as acute (<4 weeks), subacute (4-12 weeks), and chronic (>12 weeks) phases. Most acute pain resolves quickly and patients are able to return to work.[4] Patients with chronic back and neck pain tend to have fluctuating levels of pain and disability that rarely resolve.[4] Most of the disability and cost associated with back and neck pain are in patients with chronic pain.[3,5]

Chronic pain, which is the focus of this review, is considered to be qualitatively different from the other two phases. There is ongoing pain generation in the tissue, but the patient's perception of the pain is out of proportion to the level of damage.

There are many treatment interventions for chronic low back and neck pain including surgical, pharmacologic, and nonpharmacologic. For many of these interventions, such as chronic opioid therapy, the benefits are modest and the harms substantial. Safer, more effective alternatives are needed.

As noted above, chronic pain is hypothesized to be, in part, a cognitive issue. Thus, cognitive and mind-body interventions may be particularly efficacious in the treatment of chronic pain. However, they are often not covered by insurance in typical health plans and thus access to such treatments is limited and often involves out of pocket payments by patients.[6] Given the interest in promoting effective alternatives to both opioid therapy and invasive options for chronic pain, we thought it timely to evaluate evidence on the effectiveness of cognitive and mind-body therapies for chronic low back and neck pain.

During the initial phase of this review, the American College of Physicians (ACP) released a new clinical practice guideline[7] based on an exhaustive systematic review of non-invasive interventions for low back pain performed by the Agency for Healthcare Research and Quality (AHRQ).[8-10] We elected to use the relevant parts of their review as the basis for our own evidence review for chronic low back pain, supplemented by new randomized trials published since their search was performed. We also adopted their approach in our evidence review of cognitive and mind-body therapies for chronic neck pain.

Comparative Clinical Effectiveness

We abstracted data on the interventions considered in this review from the AHRQ systematic review of therapies for low back pain and from subsequent randomized trials of the same interventions for patients with chronic low back pain. Evidence on intervention effectiveness focused on studies of at least six months' duration or studies of more limited duration with outcomes assessed at least four weeks after the cessation of active therapy. Similarly, we abstracted data from systematic reviews of these same five interventions for chronic neck pain and from subsequent randomized trials for the same indication. Following the approach of the AHRQ review, we qualitatively synthesized information from the systematic reviews and randomized trials. Qualitative assessments were based on the consistency of the direction and magnitude of the effect size.

Clinical Benefits

The most important benefit to patients is improvement in function (i.e., a greater ability to work and do their desired daily activities) even if they still have pain. The next most important benefit is a reduction in pain. If achieved, these should translate into improved quality of life.

Chronic Low Back Pain

Acupuncture

The evidence for the effectiveness of acupuncture for the treatment of chronic low back pain is complex. The majority of trials and meta-analyses confirm small to moderate improvements in function and pain compared with usual care immediately following the completion of therapy. However, the differences in outcomes are smaller and often non-significant clinically when compared to sham acupuncture, suggesting that much of the benefit may be from the placebo effect. For example, the largest and longest randomized trial reported that 60% of patients treated with individualized acupuncture, standardized acupuncture, or sham acupuncture had clinically meaningful improvements in function compared with only 39% of patients in the usual care group ($p<0.001$).[11]

Cognitive Behavioral Therapy

The evidence for the effectiveness of CBT for the treatment of chronic low back pain is based on fewer trials than acupuncture, but they were larger and longer. The majority of trials and meta-analyses confirmed small to moderate improvements in function and pain compared with usual care immediately following the completion of therapy. In the most recent trial, the benefits were small, but sustained at one and two years of follow-up. There were additional benefits in terms of reduced depression and improved quality of life.

Mindfulness-Based Stress Reduction

The evidence for the effectiveness of MBSR for the treatment of chronic low back pain is similar to that for CBT. The trial demonstrating sustained benefits for CBT found equivalent benefits for MBSR. As in the evidence base for CBT, the majority of trials and meta-analyses confirmed small to moderate improvements in function and pain compared with usual care immediately following the completion of therapy. In the most recent trial, the benefits were small, but sustained at one and two years of follow-up. The additional benefits observed for CBT (reduced depression and improved quality of life) were smaller and not significant for MBSR.

Yoga

The AHRQ review concluded that yoga had small to moderate benefits compared with education and usual care, but with low strength of evidence. We identified an additional four randomized trials with longer follow-up that support the effectiveness of yoga for low back pain, though the magnitude of the benefits was smaller with longer follow-up.

Tai Chi

There was substantially less evidence for the effectiveness of tai chi for low back pain. On the basis of two fair-quality trials, the AHRQ review concluded that tai chi had a moderate effect on pain and a small effect on function with low strength of evidence. We did not identify any additional randomized trials.

Chronic Neck Pain

Acupuncture

The evidence for the effectiveness of acupuncture for the treatment of chronic neck pain is similar to that for chronic low back pain. The majority of trials and meta-analyses confirmed small to moderate improvements in function and pain compared with usual care immediately following the completion of therapy.

Cognitive Behavioral Therapy

The evidence for the effectiveness of CBT for the treatment of chronic neck pain is less robust than the evidence for low back pain. The majority of trials are short term and equivocal in terms of significant reductions in disability and pain beyond the active treatment period.

Mindfulness-Based Stress Reduction

We did not identify any randomized trials of MBSR for chronic neck pain that reported outcomes at least four weeks after the end of active treatment or that lasted six months.

Yoga

We did not identify any randomized trials of yoga for chronic neck pain that reported outcomes at least four weeks after the end of active treatment or that lasted six months.

Tai Chi

We identified one small trial of tai chi for chronic neck pain. Only 38 patients were randomized to the tai chi arm. The trial was open label with the comparison group, a wait list, potentially susceptible to the nocebo effect due to disappointment from not being randomized to the active group. The effect size on function (7 points on the 100-point NDI) and pain (1 point on a 10-point VAS) were small and potentially exaggerated by the lack of blinding. There were no differences comparing tai chi to neck exercises.

Harms

These five interventions were well-tolerated for both back and neck pain. No serious adverse events that were thought to be related to the intervention were reported in the trials. Commonly-reported adverse events included bleeding and pain at the site of acupuncture needles, and strains and joint aches in patients receiving the MBSR, yoga, tai chi interventions. An increase in back and neck pain for up to one month was sometimes reported. No adverse events were reported with CBT.

Controversies and Uncertainties

There are a number of issues that are important to consider when assessing the evidence base for the cognitive and mind-body interventions. First, each of the categories of interventions considered represents a range of possible interventions. There are many different approaches to acupuncture, different kinds of CBT, and there many different schools of yoga and tai chi and different poses and breathing techniques that could be used within each school. It may be that there is one form of yoga that is particularly effective at managing chronic low back pain, but that form of yoga has not been identified in trials to date. The number and quality of the studies is not sufficiently high to identify a particular sub-genre of any of the mind body therapies as most effective. The heterogeneity within each mind-body intervention is further complicated by variation in the skill level of the therapist teaching patients each of the interventions. MBSR is the one intervention with an agreed upon standard approach to teaching the intervention and training the teachers.

There is also significant heterogeneity within each disease category. There are many different causes for chronic low back and neck pain. Low back pain and neck pain can be sub-divided into those with and without radicular symptoms. Chronic neck pain caused by whiplash is one common subtype. Some patients are being treated with chronic opioid therapies and some suffer from concomitant depression. There may be mind-body interventions that are particularly effective in one of these subtypes of low back and neck pain, but to date the evidence base is not sufficiently robust to identify any variation in effectiveness for any of the therapies we examine.

Some studies found that sham acupuncture was almost as effective as traditional acupuncture or structured acupuncture, but that both were significantly more effective at improving function and decreasing pain compared with usual care. The differences in outcomes between acupuncture and sham acupuncture were less than the differences between them and usual care. This suggests that a significant proportion of the benefit from acupuncture is the placebo effect. Some argue that this is a useful employment of the placebo effect, while others argue that it is unethical to recommend such treatment.

Finally, it is difficult to interpret the clinical significance of average changes in continuous measures of function, quality of life, and pain. Categorical measures reporting the proportion of patients achieving a clinically meaningful improvement in function, quality of life, and pain are more useful and should be reported in addition to average group changes.

Summary and Comment

As discussed above, the evidence from the clinical trials suggest that the five cognitive and mind-body interventions evaluated in this assessment have no important harms. Thus, the conclusions above on clinical benefits drive our judgments on the net health benefits for these interventions. The following tables reflect those judgments.

Chronic Low Back Pain

Table ES1. Comparative Clinical Effectiveness for Mind-Body Interventions for Chronic Low Back Pain Added to Usual Care Versus Usual Care Alone Over the Long Term

Intervention	Net Health Benefit	Level of Certainty	ICER Evidence Rating
Acupuncture	Small	Moderate	C+: Comparable or better
CBT	Small	Moderate	C+: Comparable or better
MBSR	Small	Moderate	C+: Comparable or better
Yoga	Small	Moderate	C+: Comparable or better
Tai Chi	Small	Low	P/I: Promising, but inconclusive

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction

Chronic Neck Pain

Table ES2. Comparative Clinical Effectiveness for Mind-Body Interventions for Chronic Neck Pain Added to Usual Care Versus Usual Care Alone Over the Long Term

Intervention	Net Health Benefit	Level of Certainty	ICER Evidence Rating
Acupuncture	Small	Low	P/I: Promising, but inconclusive
CBT	Small to none	Low	I: Insufficient
MBSR	Unknown	Low	I: Insufficient
Yoga	Unknown	Low	I: Insufficient
Tai Chi	Small to none	Low	I: Insufficient

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction

Comparative Value

Overview

The aim of this analysis was to estimate the cost-effectiveness of the cognitive and mind-body interventions considered in this review for the treatment of chronic low back pain. We did not model the use of any of the nonpharmacologic interventions for chronic neck pain due to a lack of published evidence on key clinical inputs required for the model, such as intervention-related efficacy estimates and quality of life estimates associated with chronic neck pain and improved pain status following interventions. Each of the interventions (acupuncture, CBT, MBSR, yoga, and tai chi) was compared to usual care, which was defined as self-care guidance and educational information on stretching, strengthening, exercise, and lifestyle modifications. Intervention frequency was based on trial data (Table ES3). The modeled population was patients with chronic low back pain who were untreated or had not been previously treated with any of the included interventions, and the population was 60% female with a mean age of 47 years, similar to the populations seen in clinical trials.[12,13] We estimated the total costs, quality-adjusted life years (QALYs) gained, incremental cost per case of clinically-significant pain improvement (i.e., intervention success), and incremental cost-effectiveness ratios relative to usual care, using a health care system perspective over a five-year time horizon. Uncertainty in data inputs and assumptions was evaluated through sensitivity and scenario analyses.

Table ES3. Frequency of Interventions to Treat Chronic Low Back Pain

Intervention	Frequency	Source
Acupuncture	Two sessions/week for three weeks followed by one session/week for four weeks	Cherkin et al., 2009[11]
CBT	Two sessions/week for eight weeks	Cherkin et al., 2016[12]
MBSR	Two sessions/week for eight weeks	Cherkin et al., 2016[12]
Yoga	One session/week for 12 weeks	Sherman et al., 2011[13]
Tai Chi	Two sessions/week for eight weeks followed by one session/week for two weeks	Hall et al., 2011[14]

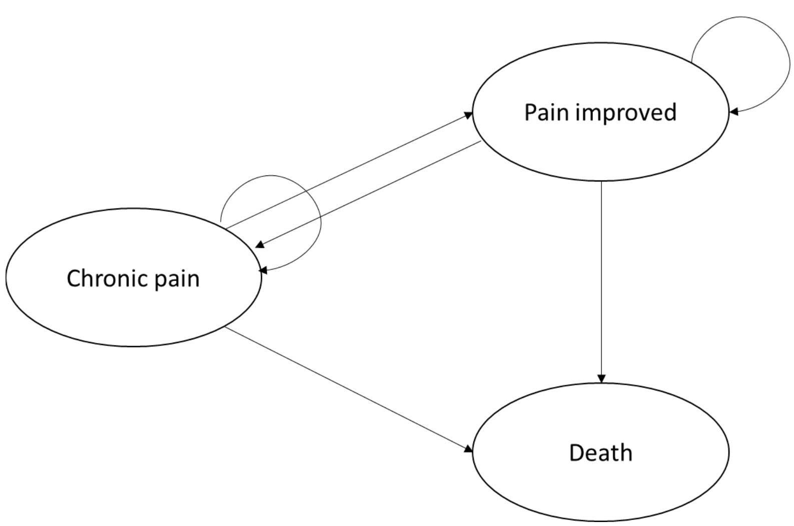
CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction

Methods

We built a *de novo* Markov model that consisted of three health states: “chronic pain,” “pain improved,” and “death,” as depicted in Figure ES1. Patients entered the model in the chronic pain health state, and could remain in that health state or transition to a pain improved state or death at the beginning of each cycle. Patients transitioned between health states during six-month cycles over a five-year time horizon. The model used a 3% discount rate for costs and health outcomes, and costs were converted to 2016 US dollars.

The base-case analysis was conducted from a health care system perspective, and thus focused on all direct intervention costs and medical care costs.

Figure ES1. Markov Model Structure for Chronic Low Back Pain Patients



The model was informed by several assumptions.

- Intervention effectiveness data was sourced from multiple trials due to a lack of head-to-head comparisons.
- Due to a lack of published evidence, no subsequent lines of therapies were modeled for those who failed or intervention or relapsed after initial success. In addition, our objective was to assess the value of different interventions and not intervention pathways.
- All interventions except tai chi were awarded the same measure of effectiveness due to similarity in this estimate across trials.
- We did not model the health or economic outcomes of adverse events due to a lack of published evidence on such adverse events.
- Chronic pain recurrence was assumed to be the same each year and the same across all interventions and usual care.
- Beyond the first cycle of the model, the probability of pain improvement was assumed spontaneous and to be the same as that of usual care.

A detailed description of key model assumptions can be found in Table 5.1 of the full report.

Model Inputs

Transition probabilities for chronic low back pain were based on the percentage of patients who had a clinically-meaningful improvement in pain on the RMDQ (i.e., a ≥ 30% improvement in RMDQ score). We assumed that all interventions except for tai chi had the same probability of pain improvement per cycle (0.6) because clinical trial data suggested similar efficacy for these interventions; the probability of pain improvement for tai chi was 0.5. The transition probabilities associated with usual care for pain improvement and with relapse to chronic pain following any intervention or usual care were 0.441 and 0.259, respectively.

Health state utility point estimates for chronic pain and improved pain were 0.66 and 0.75, respectively, and were obtained from trial data.[15]

Costs included all direct costs of care, including intervention and usual care costs for chronic low back pain as well as background health care costs. As several of these interventions may not currently be covered by payers, we included out-of-pocket prices reported in the grey literature as part of direct costs. Intervention costs were applied once during the first model cycle, and a fee for a 15- or 25-minute doctor's office visit was applied to the cost of each intervention or usual care, respectively. Since usual care consisted of self-care, no additional costs beyond background health care costs were added to this arm. All intervention costs listed in Table ES4 are per-session costs, based on sessions provided in a group format, except for acupuncture and usual care, which are provided to patients on an individual basis.

Background health care costs included additional office visits, hospital stays, laboratory tests, and pharmacologic therapy, and differed based on health state.[16] All costs were inflated to 2016 US dollars using the medical care component of the US Consumer Price Index.[17]

Table ES4. Cost Inputs

Service	Cost	Source
Acupuncture (per session)	$104*	Zhang, 2014[18]
CBT (per session)	$106	Gore et al., 2012[19]
Yoga (per session)	$60	Thumbtack[20]
MBSR (per session)	$77	UMass Medical School Center for Mindfulness in Medicine[21]
Tai Chi (per session)	$18	The Tai Chi Center[22]
Office Visit Costs for Active Intervention†	$52	Centers for Medicare & Medicaid Services[23]
Usual Care Costs (total)‡	$109*	Centers for Medicare & Medicaid Services[23]
Background Care Costs per Patient per Cycle		
Chronic Pain	$701	Fritz et al., 2012[16]; Gore et al., 2012[24]
Improved Pain§	$301	

*One-on-one session

† Assumed to be one office visit pertaining to referral to active intervention, using CPT code 99213 for an established patient visit for a 15-minute duration.

‡Assumed to be one office visit pertaining to obtaining patient education book on self-care, using CPT code 99214 for an established patient visit for a 25-minute duration.

§Assumed 43% of costs seen in patients with chronic pain, derived from Gore et al., 2012, comparing health care costs for patients with chronic low back pain and population without chronic low back pain.

Base-Case Results

Each of the nonpharmacologic interventions resulted in increased costs and QALYs compared to usual care over the five-year time horizon (Tables ES5 and ES6). Since we assumed the same transition probabilities for all active interventions except tai chi, QALY gains were the same for all remaining interventions, with very small incremental gains compared to usual care (0.010). Tai chi had an even smaller incremental QALY gain of 0.004 relative to usual care. All interventions except CBT were estimated to fall within the upper bound of the commonly-cited threshold of $150,000 per QALY gained relative to usual care, with yoga being the most cost-effective at approximately $58,000 per QALY gained.

Because we used the same utility estimates for all interventions, the same response rate to therapy for all interventions except tai chi, and the same relapse rate for all interventions, the variation in the incremental cost-effectiveness ratios across interventions is primarily driven by the differences in individual intervention costs.

Table ES5. Base-Case Deterministic Results

Therapy	Costs	QALYs
Acupuncture	$5,657	3.2875
CBT	$6,316	3.2875
MBSR	$5,852	3.2875
Yoga	$5,342	3.2875
Tai Chi	$4,992	3.2813
Usual Care	$4,767	3.2776

CBT: cognitive-behavioral therapy, MBSR: mindfulness-based stress reduction, QALY: quality-adjusted life year

Table ES6. Base-Case Deterministic Incremental Results Versus Usual Care

Therapy	Incremental Costs	Incremental QALYs	Incremental Cost-Effectiveness Ratio vs. Usual Care (Cost per QALY Gained)
Acupuncture	$891	0.0099	$89,888
CBT	$1,549	0.0099	$156,331
MBSR	$1,085	0.0099	$109,486
Yoga	$575	0.0099	$58,017
Tai Chi	$225	0.0037	$61,265
Usual Care	--	--	--

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction, QALY: quality-adjusted life year

Among the five interventions, the incremental cost of achieving one case of improved pain over the five-year time horizon relative to usual care ranged from approximately $6,200 for tai chi to approximately $15,800 for CBT. Because each intervention's benefit (i.e., pain improvement) occurred within the first two cycles of the model and subsequent benefit was spontaneous and non-intervention related, we used the number of cases with improved pain at the end of one year of treatment.

Table ES7. Incremental Cost per Successful Treatment (Pain Improvement) Versus Usual Care

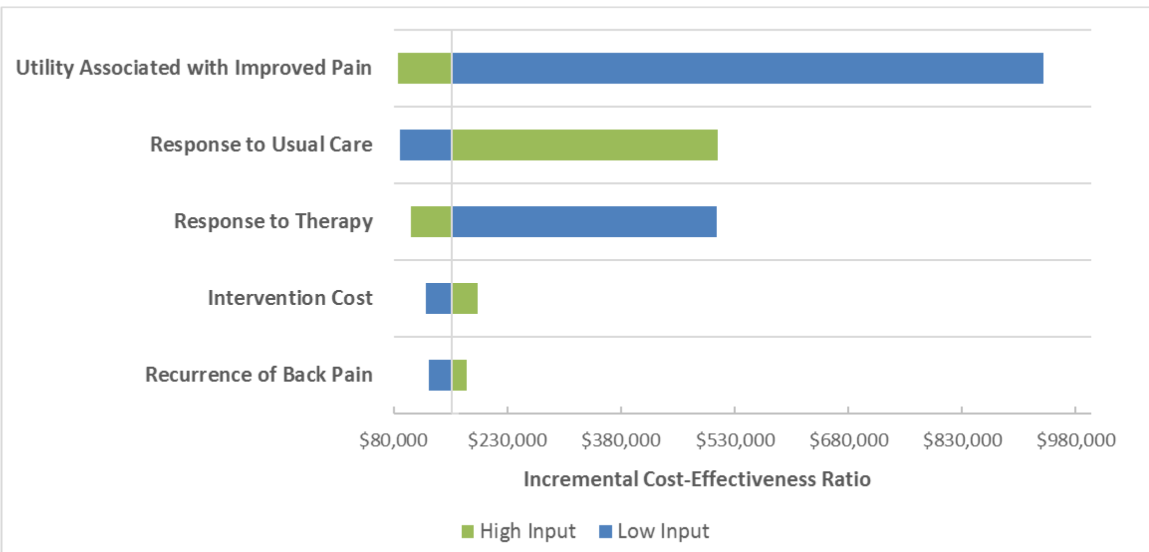
Therapy	Costs
Acupuncture	$9,067
CBT	$15,770
MBSR	$11,044
Yoga	$5,852
Tai Chi	$6,180

CBT: cognitive-behavioral therapy, MBSR: mindfulness-based stress reduction, QALY: quality-adjusted life year

One-Way Sensitivity Analyses

One-way sensitivity analyses were conducted for each intervention by varying key model parameters. As an example, we have presented results for the one-way sensitivity analysis for CBT, the least cost-effective intervention in our analysis, in Figure ES2 and Table ES8. Results of one-way sensitivity analyses for the other interventions are available in Appendix Tables E5-E8 and Figures E1-E4. The health-state utility associated with improved pain had the largest impact on incremental cost-effectiveness for each of the interventions relative to usual care except for tai chi, where results were most sensitive to response to therapy. Results were also sensitive to response to usual care (i.e., probability of pain improvement associated with usual care), response to therapy, and to individual intervention costs. Intervention costs were not the most sensitive variable because they were incurred only once in the first model cycle.

Figure ES2. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Cognitive Behavioral Therapy Versus Usual Care



Base-case ICER: $156,331 per QALY gained

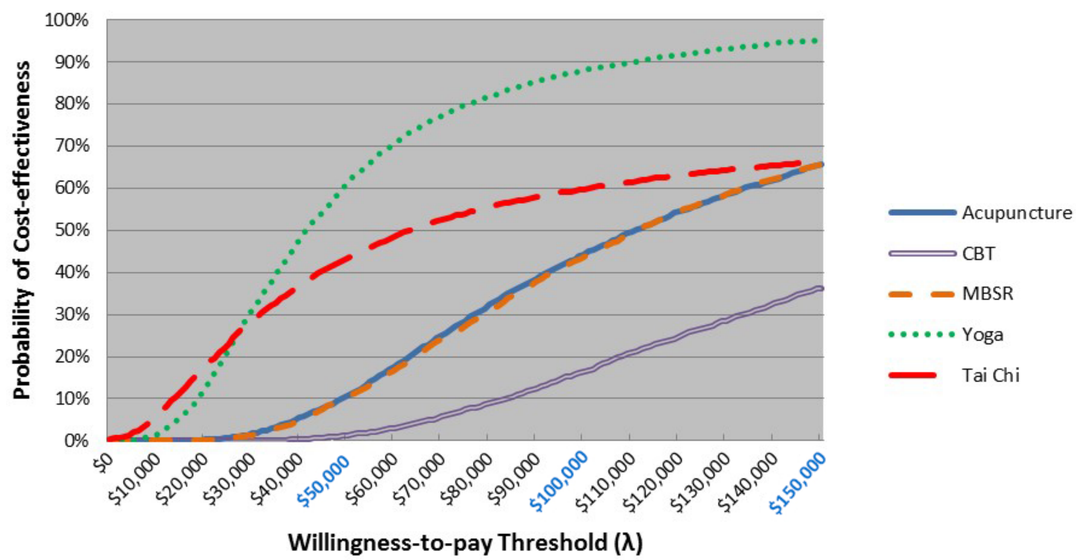
Table ES8. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Cognitive Behavioral Therapy Versus Usual Care

	Low Input	High Input	Low Value	High Value	Range
Intervention Cost	$84.71	$127.06	$122,136	$190,526	$68,390
Response to Therapy	0.492	0.676	$506,202	$102,899	$403,303
Response to Usual Care	0.359	0.542	$87,671	$507,829	$420,157
Recurrence of Back Pain	0.126	0.356	$125,802	$176,386	$50,584
Utility Associated with Improved Pain	0.675	0.825	$937,987	$85,272	$852,715

Probabilistic Sensitivity Analysis Results

We also conducted a probabilistic sensitivity analysis, jointly varying model inputs over 5,000 simulations. Incremental cost-effectiveness ratios (ICERs) for CBT were lower than the commonly-cited cost-effectiveness threshold of $150,000 per QALY in approximately 36% of simulations, while ICERs for yoga were lower than the threshold in approximately 95% of simulations.

Figure ES3. Cost-Effectiveness Acceptability Curves for the Cognitive and Mind-Body Therapies Compared to Usual Care



Note: the curves for acupuncture and MBSR overlapped across the range of willingness to pay thresholds

Scenario Analyses

Shortening the model time horizon to one and three years resulted in higher incremental cost-effectiveness results compared to the base-case. For the one-year time horizon, all interventions exceeded the commonly cited threshold of $150,000 per QALY gained, ranging from approximately $179,000 per QALY gained for yoga to approximately $456,000 per QALY gained for CBT. Using a three-year time horizon, results ranged from approximately $58,000 per QALY gained for yoga to approximately $157,000 per QALY gained for CBT.

A modified societal perspective that included the costs associated with lost productivity in patients with chronic pain resulted in incremental cost-effectiveness ratios very similar to the base-case results, ranging from approximately $54,800 per QALY gained for yoga to approximately $153,100 per QALY gained for CBT, relative to usual care over the five-year time-horizon.

Model Validation

Model validation followed standard practices in the field. Two modelers tested the mathematical functions in the model as well as therapy-specific inputs and corresponding outputs. We also compared the ICER model to previously published models. Our model had higher incremental cost-effectiveness ratios due to differences between model inputs such as sources for intervention-specific probability of response to chronic pain, the quality of life associated with chronic pain and improved pain, and costs of care, as well as structural differences such as assumptions around the frequency of intervention use beyond the first cycle of the model, relapse to chronic pain in subsequent model cycles, and model time-horizons. Additional detail regarding model comparisons can be found in the full report.

Value-Based Benchmark Prices

Our value-based benchmark prices for the five cognitive and mind-body therapies for low back pain are presented in Table ES9. As the literature did not point to a single, consistent price estimate for any of these interventions we have presented the discounts from the assumed base case price per session that would be required to achieve the two cost-effectiveness thresholds.   While the per-session costs may vary, the total cost of each intervention at each threshold would be equal for all interventions except tai chi, as these interventions were awarded the same probability of effectiveness in the model. Discounts would be required for CBT and MBSR to meet the $100,000 per QALY gained threshold price. Threshold prices for acupuncture, yoga, and tai chi (and the price at the $150,000 per QALY threshold for mindfulness-based stress reduction) were higher than the base-case price estimates.

Table ES9. Value-Based Benchmark Prices per Session of Cognitive and Mind-Body Therapies for Chronic Low Back Pain

Intervention	Cost per Session	Price to Achieve $100,000 per QALY	Price to Achieve $150,000 per QALY	Discount/Premium from Current Cost to Reach Thresholds
Acupuncture	$103.58	$113.60	$163.15	+10% to +58%
CBT	$105.89	$71.00	$101.97	4% to 33%
MBSR	$76.88	$71.00	$101.97	8% to +33%
Yoga	$60	$94.67	$135.95	+58% to +127%
Tai Chi	$17.50	$25.41	$35.63	+45% to +104%

CE: cost-effectiveness, QALY: quality-adjusted life year
"+" Indicates premium

Potential Budget Impact

We used results from the same model employed for the cost-effectiveness analyses to estimate total potential budget impact. Potential budget impact was defined as the total differential cost of using the specific low back pain interventions rather than usual care for the treated population, calculated as differential health care costs minus any offsets in these costs from averted health care events.

We derived the number of eligible patients with chronic low back pain for a hypothetical cohort of 1 million members of a managed care organization. With a point prevalence of 13.1%, based on The National Health and Nutrition Examination Survey (NHANES, 2009–2010), applied to the hypothetical cohort of 1 million members, the number of patients with chronic low back pain was estimated to be 131,000.[25] According to a survey by the American Physical Therapy Association (APTA), only 63% of all patients with low back pain seek professional help for pain relief.[26] Applying this percentage to the estimated population with chronic low back pain resulted in an eligible population of 16,506 patients each year, for a total of 82,530 patients over all five years.

We included only MBSR, yoga, and tai chi in the budget impact analysis, deriving the potential budget impact of each of these interventions relative to usual care. We did not include the other interventions, as evidence suggests that some payers currently cover them (see Section 3.1 of the full report).

We modeled the three interventions against usual care, varying their uptake over five years to 10%, 25% and 50% of the eligible population. In addition to reporting the results for each intervention over five years, we have also reported the per member per month (PMPM) cost for each intervention relative to usual care. The PMPM cost is the total monthly spending on a pool of insured members of a plan divided by the total number of plan members.

Yoga

Annual potential budget impact ranged from approximately $966,000 to approximately $4.8 million when treating 10% (2% per year) to 50% (10% per year) of the eligible cohort with yoga relative to usual care. The average potential budget impact over the five-year period was $274 per patient (Table ES10). The PMPM cost ranged from $0.08 to $0.40 when treating 10% to 50% of the eligible cohort with yoga (Figure ES4).

Mindfulness-Based Stress Reduction

Annual potential budget impact ranged from approximately $1.8 million to approximately $9 million when treating 10% to 50% of the eligible cohort with MBSR relative to usual care. The average potential budget impact over the five-year period was $507 per patient (Table ES10). The PMPM cost ranged from $0.15 to $0.75 when treating 10% to 50% of the eligible cohort with MBSR (Figure ES4).

Tai Chi

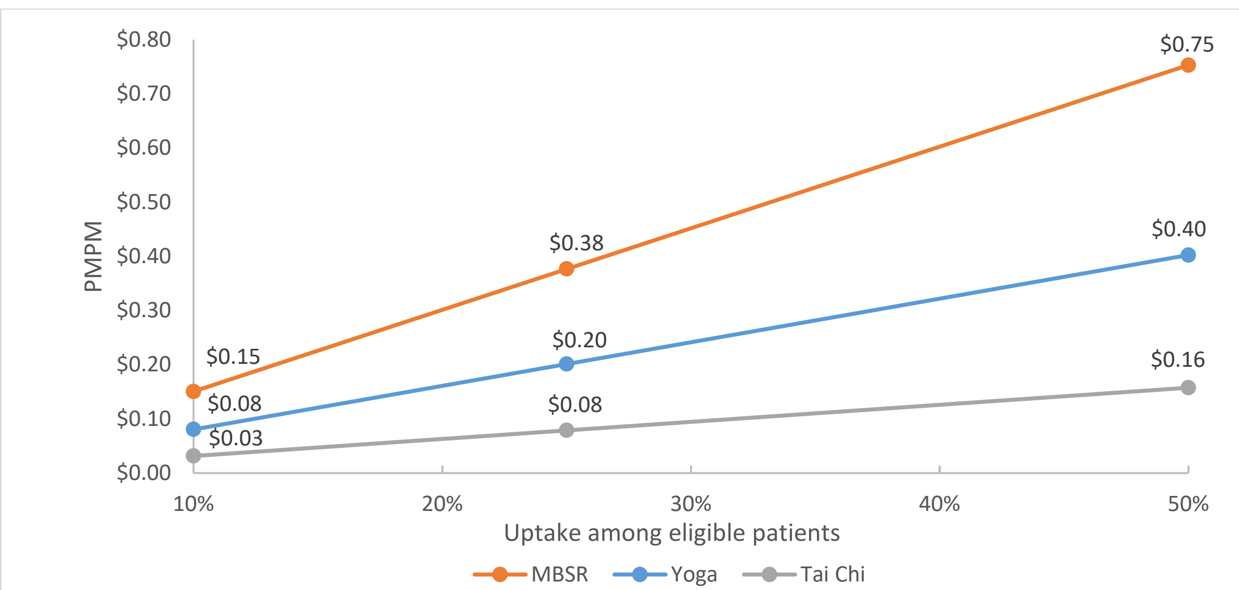
Annual potential budget impact ranged from approximately $378,000 to approximately $1.9 million when treating 10% to 50% of the eligible cohort with tai chi relative to usual care. The average potential budget impact over the five-year period was $107 per patient (Table ES10). The PMPM cost ranged from $0.03 to $0.16 when treating between 10% and 50% of the eligible cohort with tai chi (Figure ES4).

Table ES10. Annualized Per Patient Potential Budget Impact Calculations Over a Five-Year Time Horizon

	Average Annualized Per-Patient Budget Impact			
	Yoga	MBSR	Tai Chi	Usual Care
Per-Patient Budget Impact	$1,426	$1,659	$1,259	$1,152
Difference (Intervention – Usual Care)	$274	$507	$107	--

MBSR: mindfulness-based stress reduction

Figure ES4. Per-Member Per-Month Cost for Yoga, MBSR, and Tai Chi at Varying Percentages of Treatment Uptake Among the Eligible Cohort



By way of comparison, Express Scripts estimates that its 2017 expenditures for medications to treat pain and inflammation, including mostly generic NSAIDs, gamma-aminobutyric acid (GABA) analogs, and opioids, will total $4.46 PMPM.[27] Our highest budget impact estimate ($0.75 PMPM if 50% of the eligible population were treated with MBSR) would represent only 17% of this PMPM spend.

Summary and Comment

We estimated the cost-effectiveness of acupuncture, CBT, MBSR, yoga, and tai chi compared to usual care for patients with chronic low back pain. We did not model chronic neck pain for any of the interventions due to a lack of published evidence on key model inputs. The cost per additional QALY ranged from approximately $58,000 for yoga to approximately $156,000 for CBT over a five-year time horizon. The findings were most sensitive to the health state utility associated with an improvement in pain, patient response to usual care, and intervention costs. The findings were also sensitive to time horizon, with a shorter time horizon resulting in higher incremental cost-effectiveness ratios relative to usual care. A scenario analysis using a modified societal perspective produced results similar to those in the base-case analysis.

Our model had several limitations. First, we did not model varying treatment effectiveness over time due to availability of only short-term trial data. We assumed that the effectiveness of the intervention, defined by the probability of transitioning to improved pain from a chronic pain state for that specific intervention, occurred only in the first cycle when patients receive an intervention, after which improvement in pain status mirrored that of improvement seen with usual care. Second, we did not model subsequent lines of intervention (and resulting pain improvement) for individuals who experienced a recurrence of low back pain due to a lack of published evidence on this estimate. Third, the background health care costs for those with improved pain were derived from a claims analysis by Gore et al., which consisted of a control cohort *without* back pain (i.e., not with "improved pain"). Fourth, we assumed 100% adherence to each intervention, which would not occur in actual practice. Finally, our base-case cost and cost-effectiveness results for the nonpharmacologic interventions reflect current evidence available on average intervention costs, which may vary widely by region and level of insurance coverage.

We examined the budget impact of three interventions, MBSR, yoga, and tai chi, that are not routinely covered by insurance. Our analysis looked at different levels of uptake, and at a high rate of uptake of 50% for the most expensive of the three interventions (MBSR), the additional PMPM cost would be $0.75. For comparison, this is approximately 17% of the estimated PMPM medication costs for treating pain/inflammation at a large national pharmacy benefits management company.

Other Benefits and Contextual Considerations

Our reviews seek to provide information on other benefits or disadvantages offered by the intervention to the individual patient, caregivers, the delivery system, other patients, or the public that would not have been considered as part of the evidence on comparative clinical effectiveness. These elements are listed in Tables ES11-12.

Table ES11. Potential Other Benefits

Potential Other Benefits	Description
This intervention provides significant direct patient health benefits that are not adequately captured by the QALY.	None
This intervention offers reduced complexity that will significantly improve patient outcomes.	We do not think that these interventions reduce complexity. Many of them require sustained behavior change for ongoing effectiveness.
This intervention will reduce important health disparities across racial, ethnic, gender, socio-economic, or regional categories.	None
This intervention will significantly reduce caregiver or broader family burden.	Chronic pain has impacts on everyone that the patient touches. Improved management of chronic pain will likely reduce caregiver / family burden.
This intervention offers a novel mechanism of action or approach that will allow successful treatment of many patients who have failed other available treatments.	Not applicable
This intervention will have a significant impact on improving return to work and/or overall productivity.	Chronic low back pain, in particular, is a major cause of both short- and long-term disability. The benefits of the mind-body interventions are modest at best, but may help some patients return to work or be more productive at their job.
Other important benefits or disadvantages that should have an important role in judgments of the value of this intervention.	One potential benefit that has not been adequately studied would be to reduce or avoid the use of opioid medications for chronic pain. As noted above, a disadvantage is that most of these interventions require ongoing behavior change, which is often difficult to maintain.

Table ES12. Potential Contextual Considerations

Contextual Consideration	Description
This intervention is intended for the care of individuals with a condition of particularly high severity in terms of impact on length of life and/or quality of life.	As noted in the topic in context section, chronic back and neck pain are common and lead to significant reductions in productivity including patients requiring long-term disability.
This intervention is intended for the care of individuals with a condition that represents a particularly high lifetime burden of illness.	Same as above.
This intervention is the first to offer any improvement for patients with this condition.	No
Compared to usual care, there is significant uncertainty about the long-term risk of serious side effects of this intervention.	There may be advantages compared to long-term opioid therapy given the known harms associated with opioid therapy. However, there is a lack of evidence about whether the mind-body interventions can prevent initiation of opioid therapy or facilitate tapering opioid therapy.
Compared to usual care, there is significant uncertainty about the magnitude or durability of the long-term benefits of this intervention.	Yes. As noted under controversies and uncertainties, there is evidence of waning benefit with time and few trials reported outcomes at one year, much less over a longer time period.
There are additional contextual considerations that should have an important role in judgments of the value of this intervention.	None

1. Background

1.1 Introduction

Background

Low back and neck pain are two of the most common reasons for patient visits to physicians in the United States. The estimated total cost for low back and neck pain in the United States (US) was $88 billion in 2013, third highest after heart disease and diabetes.[1] Total cost for low back and neck pain has increased faster than any other group of diagnoses, from $30.4 billion in 1996 to $87.6 billion in 2013. This does not include the indirect costs related to missed work and disability.

A wide range of non-invasive therapies have been evaluated for chronic low back pain and chronic neck pain including pharmacologic therapies (e.g., non-steroidal anti-inflammatory drugs [NSAIDs], opioids, tricyclic antidepressants, anti-epileptic medications), physical therapies (e.g., physical therapy, exercise therapy, high- and low-velocity manipulation), and mind-body therapies (e.g., yoga, tai chi, cognitive behavioral therapy [CBT], mindfulness-based stress reduction [MBSR], acupuncture). These different types of therapies are not mutually exclusive and at times are offered in conjunction with other forms of treatment. However, there are few studies evaluating combined therapy or sequencing of therapies. Patients are less often referred for mind-body therapies than for other non-invasive therapies, and it is uncertain whether this reflects limited clinician awareness of the value of these therapies, appropriate judgments about their relative effectiveness, local availability of these therapies, and/or coverage by insurance of these therapies.[6]

In addition, physicians frequently treat patients suffering from chronic pain with opioids.[28] Appropriate use of effective nonpharmacologic therapy has the potential to reduce the use of opioids in the management of such patients, which may be important given the epidemic of opioid abuse in the US.

Because chronic pain is often a life-long issue, we focused this review on intermediate (at least four weeks after the end of therapy or six months of follow-up) and long-term improvements in function, pain, and quality of life. We placed greater emphasis on functional outcomes, as these matter the most to patients.

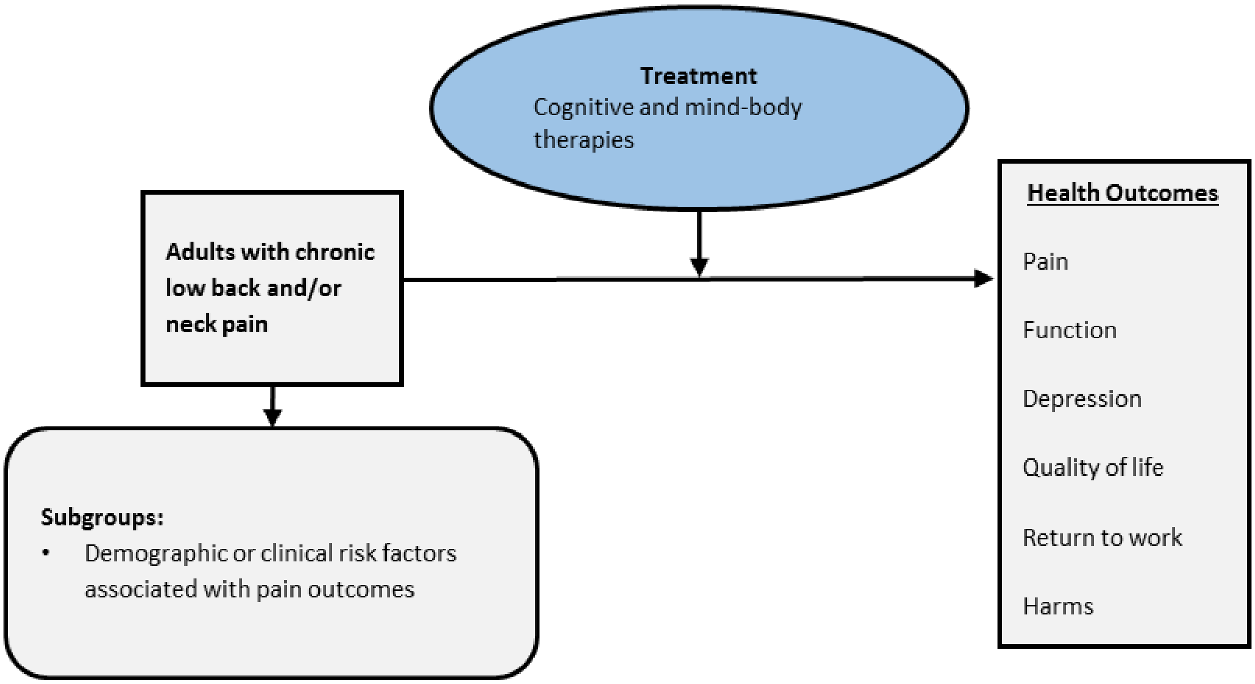
Scope of the Assessment

The scope for this assessment is described on the following pages using the PICOTS (Population, Intervention, Comparators, Outcomes, Timing, and Settings) framework. Evidence was abstracted from systematic reviews and randomized controlled trials. For chronic low back pain, our review is based in part on the recent Agency for Healthcare Research and Quality (AHRQ) review performed to support the updated American College of Physicians (ACP) guidelines on low back pain.[7,98] We performed our own review, analogous to that performed by AHRQ, for chronic neck pain. Our evidence review also includes input from patients and patient advocacy organizations.

Analytic Framework

The analytic framework for this assessment is depicted in Figure 1.1.

Figure 1.1. Analytic Framework:



Populations

The population for the review is adults 18 years of age and older suffering from chronic low back or neck pain that is not due to cancer, infection, inflammatory arthropathy, high-velocity trauma, fracture, and pregnancy, and that is not associated with progressive neurologic deficits; patients with whiplash were included. Chronic pain is defined by the presence of symptoms for at least 12 weeks. The interventions are evaluated separately for patients with chronic low back pain and for patients with chronic neck pain.

Interventions

The list of interventions was developed with input from patient organizations, clinicians, and insurers on which treatments to include. The full list of interventions is as follows:

- Acupuncture
- CBT
- MBSR
- Yoga
- Tai chi

Comparators

The primary comparison for each of these interventions was usual care or a sham/placebo intervention.

Outcomes

The primary goal of treatment is to improve function and reduce pain to allow patients to return to their usual daily activities including work. Improving function is the most important outcome. We also assessed harms associated with therapy as well as patient reported quality of life.

Primary Outcomes

- Pain (e.g. visual analog scale)
- Function (e.g. Oswestry Disability Index, Roland Morris Disability Questionnaire)
- Depression (e.g. Patient Health Questionnaire 9; Center for Epidemiologic Studies Depression Scale)
- Return to work / disability
- Quality of life (e.g. Short Form 36)
- Harms (e.g. musculoskeletal injuries)

Timing

Evidence on intervention effectiveness focused on studies of at least six months' duration or studies of more limited duration with outcomes assessed at least four weeks after the cessation of active therapy (intermediate term), but trials with long-term outcomes (one or more years) were preferred.

Settings

All relevant settings were considered, with a focus on outpatient settings in the United States.

2. The Topic in Context

Most people experience low back and/or neck pain during their lives. In the 2015 Global Burden of Disease study, low back and neck pain was the leading cause of disability in most countries.[2] Because low back pain often occurs in younger individuals, it is a common cause of missed work and reduced productivity resulting in high indirect costs.[3]

Low back and neck pain are typically classified by duration of symptoms as acute (<4 weeks), subacute (4-12 weeks), and chronic (>12 weeks) phases. Most acute pain resolves quickly and patients are able to return to work.[4] Patients with chronic back and neck pain tend to have fluctuating levels of pain and disability that rarely resolve.[4] Most of the disability and cost associated with back and neck pain are in patients with chronic pain.[3,5] Patients with poor coping strategies, mental health diagnoses, and poor overall health are more likely to transition from acute low back and neck pain to chronic pain.[29]

Chronic pain, which is the focus of this review, is considered to be qualitatively different from the other two phases. In acute pain, there is tissue damage and inflammation with activation of the pain centers of the brain.[30] With the transition to chronic pain, the pain centers remain activated, but there are significantly higher levels of activation of the emotional circuits and central sensitization amplifies the patient's perception of pain and other physical symptoms.[30,31] There is ongoing pain generation in the tissue, but the patient's perception of the pain is out of proportion to the level of damage.

There are numerous causes for low back and neck pain including degenerative disc disease, arthritis, disc herniation, and spinal stenosis, but these are often present in patients without low back or neck pain. It is often difficult to know if the pain experienced by a patient is due to one of these specific diagnoses.

There are many treatment interventions for chronic low back and neck pain. These interventions include those that are invasive (epidural injections, discectomy, laminectomy, spinal fusion, neurostimulation, implantable pumps), pharmacologic (non-steroidal anti-inflammatory drugs, corticosteroids, tricyclic anti-depressants, serotonin-norepinephrine reuptake inhibitors, muscle relaxants, anti-seizure medications, and opioids), and nonpharmacologic (physical therapy, ultrasound, nerve stimulation, spinal manipulation, acupuncture, CBT, MBSR, yoga, and tai chi).

As noted above, chronic pain causes the greatest proportion of human and economic burden from back and neck pain.[3,5] Typically, patients with chronic pain have already unsuccessfully attempted treatment with the standard interventions used for acute low back and neck (rest, ice or heat, physical therapy, medications, and surgery where appropriate). In addition, chronic pain is hypothesized to be, in part, a cognitive issue. Thus, cognitive and mind-body interventions may be particularly efficacious in the treatment of chronic pain. However, they are often not covered by insurance in typical health plans and thus access to such treatments is limited and often involves out of pocket payments by patients.[6] Given the interest in promoting effective alternatives to both opioid therapy and invasive options for chronic pain, we thought it timely to evaluate evidence on the effectiveness of cognitive and mind-body therapies for chronic low back and neck pain.

During the initial phase of this review, the ACP released a new clinical practice guideline[7] based on an exhaustive systematic review of non-invasive interventions for low back pain performed by AHRQ.[8-10] We elected to use the relevant parts of their review as the basis for our own evidence review for chronic low back pain, supplemented by new randomized trials published since their search was performed. We also adopted their approach in our evidence review of cognitive and mind-body therapies for chronic neck pain.

Cognitive and Mind-Body Therapies

Acupuncture

Acupuncture is one element of traditional Chinese medicine in which thin needles are inserted into the skin at specific points in the body in order to influence the flow of qi, or energy, through meridians in the body. In western culture, acupuncture is sometimes described as placing needles in the body according to current understanding of the body's structure and function.[32] Typically, between five and 20 needles are inserted and left in place for up to 20 minutes. Electroacupuncture is a modern variant of acupuncture in which the needles are attached to a source of continuous electric current. Acupuncture is used for many indications, but most commonly to treat pain.[33] Modern acupuncture is done by trained, licensed providers using sterile, single use needles. Potential harms include pain, infections and rarely pneumothorax.[33]

Cognitive Behavioral Therapy

Cognitive behavioral therapy (CBT) is a category of psychotherapy typically delivered by a trained therapist. It focuses on helping individuals to develop their own coping strategies to manage the problem being addressed and to change unhealthy patterns of thoughts, emotions, and behaviors. CBT focuses on a patient's current situation, rather than the influences of the past. It was originally developed to treat depression, but is now used for many indications including pain. The focus and content of CBT is different for each indication. Typically, CBT is delivered weekly in six to 18 hour-long sessions sometimes followed by maintenance sessions one to three months following the completion of the primary treatment.[34] The therapists typically prescribe some form of homework for the patient to do in between sessions. CBT-based coping skills education may also be delivered in small group settings. When used for pain, CBT includes both pain education and specific pain management skills. CBT is generally thought to have minimal or no potential harms.

Mindfulness-Based Stress Reduction

Mindfulness-based stress reduction (MBSR) uses a combination of mindfulness meditation, body awareness, and yoga to manage stress, pain, and improve quality of life. It was developed at the University of Massachusetts Medical Center in the 1970s by Dr. Jon Kabat-Zinn. It is typically taught by certified trainers in a group setting during eight weekly two-hour sessions and a one-day, six-hour retreat. The training also involves daily practicing of mindfulness for 45 minutes. MBSR is generally thought to have minimal or no potential harms.

Yoga

Yoga is a group of physical, mental, and spiritual practices with origins in India. There are a number of different yoga traditions. When used as a form of medical therapy, yoga primarily refers to the use of a series of physical poses, breathing techniques, and meditation or relaxation aimed at restoring balance and improving well-being. Yoga is typically taught and practiced in group classes that last between 45 and 90 minutes. The primary harms are musculoskeletal injuries.[35] The most common tradition that is taught in the United States is hatha yoga, which includes Iyengar, Ashtanga, Vini, Kundalini, and Bikram yoga.

Tai Chi

Tai chi is a form of Chinese martial art. Like yoga, there are a number of different traditional forms of tai chi. The form popular in the United States and commonly adapted for promoting health is practiced with slow movements, deep breathing, relaxation, mindfulness, and meditation. Tai chi is supposed to balance the two opposing life forces in Chinese philosophy, yin and yang, that govern health. It may be practiced individually or in groups and is typically taught in group classes. Typical harms of tai chi include muscle soreness and foot or knee pain.

Definitions

Chronic back and neck pain can be categorized by duration, location, intensity and functional impact. Several of the common approaches to classification are defined below. There is no consensus on what change in the measures of pain and function is clinically meaningful, but the commonly cited recommendations are described below.

Table 2.1. Classification of Low Back or Neck Pain by Duration

Classification	Duration
Acute	< 4 weeks
Subacute	4-12 weeks
Chronic	12 weeks

Radicular Pain: extremity pain, numbness, weakness due to irritation of a spinal nerve root.

Visual Analog Scale (VAS) for Pain Intensity: A self-reported pain intensity or severity scale from 0 to 10 or 0 to 100, with 0 being no pain and higher numbers representing worse pain. For consistency, we report all results on a 10-point scale (scores using a 100-point scale are divided by 10). A 1.5- to 2-point change in pain is usually considered clinically important, with some evidence that larger changes are needed for patients with more severe pain at initial assessment. A 30% change from baseline is also considered clinically significant.[36]

Visual Analog Scale (VAS) for Pain Bothersomeness: A self-reported pain scale from 0 to 10 or 0 to 100, with 0 being no bothersomeness from pain over the past week and higher numbers representing worse bothersomeness. For consistency, we report all results on a 10-point scale (scores using a 100-point scale are divided by 10). A 1.5- to 2-point change in pain is usually considered clinically important, with some evidence that larger changes are needed for patients with more severe pain at initial assessment. A 30% change from baseline is also considered clinically significant.[36]

Roland Morris Back Pain Disability Questionnaire (RMDQ): A self-reported questionnaire with 24 items that takes less than five minutes to complete. The score ranges from 0 to 24, with 0 representing no disability and 24 representing maximal disability. A common modification excludes one question and reports scores ranging from 0 to 23. A change of at least 5 points is considered clinically important. A 30% change from baseline is also considered clinically significant.[36]

Oswestry Disability Index (ODI): A self-reported questionnaire for low back pain that includes 10 sections assessing limitations on different activities of daily living. The questionnaire is scaled to 100 and takes less than five minutes to complete; higher scores represent greater disability. A change of at least 10 points is considered clinically important. A 30% change from baseline is also considered clinically significant.[36]

Neck Disability Index (NDI): The NDI is a modification of the ODI for neck pain. Like the ODI, it is a self-reported questionnaire for neck pain assessing limitations on different activities of daily living that is scaled to 100 and takes less than five minutes to complete. Higher scores represent greater disability. A change of at least 10 points is considered clinically important. A 30% change from baseline is also considered clinically significant.[36]

Northwick Park Neck Pain Questionnaire (NPQ): The NPQ is a nine-item questionnaire with each item scored from 0 to 4, and higher responses reflecting greater pain or disability.[37] The questionnaire is scored by adding up the responses and dividing by 36, and is reported as a percentage ranging from 0 to 100%. The higher the percentage, the greater the pain and disability. Follow-up questionnaires add an additional question asking about their global assessment of change on a five-point scale ranging from “much worse” to “much better.” A 25% reduction from baseline is considered clinically significant as long as the patient reports at least "better" on the global rating of change question.[38]

Medical Outcomes Study Short-Form 36 (SF-36): A self-reported 36-item questionnaire that measures health-related quality of life across eight domains including both physical and emotional domains. It is scored from 0 to 100 with higher scores representing lower quality of life. Despite wide-spread use, the minimally important clinical difference is not established, though 5-10 points is often cited as clinically meaningful.

EuroQoL (EQ-5D): A self-reported questionnaire to assess health related quality of life in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression plus a visual analog scale rating their overall health state. The minimally important clinical difference has not been established, despite the questionnaire's widespread use in estimating patient utilities.

Standardized Mean Difference (SMD): The SMD is the mean (average) difference between two groups divided by the standard deviation. If the two groups represent a treatment group and a control group, the SMD is the number of standard deviations of the outcome measure due to the intervention. The scale is the number of standard deviations. This allows meta-analyses to estimate summary statistics combining results from studies that used different instruments to measure the same concept. For instance, results from the RMDQ and the ODI can be combined using the SMD.

Weighted Mean Difference (WMD): The weighted mean difference, on the other hand, is a summary using the scale of the measurement instrument. It assumes that the same scale was used in all of the trials that are combined in the meta-analysis. The individual trial estimates are usually weighted by the inverse of the variance when combining the trial results. For example, in a meta-analysis combining the results of trials of a therapy to reduce blood pressure, the WMD would be the pooled estimate of the change in blood pressure measured in millimeters of mercury (mm Hg).

Insights Gained from Discussions with Patients and Patient Groups

Patients and patient advocacy organizations emphasized that chronic low back and neck pain can be life-changing events that force many patients to limit or stop their normal daily activities. Patients with chronic pain report feelings of anger, depression, and guilt related to their pain and its impact on their functioning, which can control all aspects of their life. A diagnosis of chronic pain poses similar challenges to family members who must modify their activities and expend considerable emotional energy to care for a family member in pain. One patient advocate told us the only difference between a family member and the person in pain is that the family member does not feel the pain, but they experience the anger, frustration, and guilt. Pain controls their life as well.

With regards to cognitive and mind-body therapies, we heard that access is a widespread problem for patients. Many of the therapies are not covered by patients' insurance plans, so patients have to pay out of pocket, which is challenging for individuals who are often limited in their ability to work due to pain. In addition, there are many areas of the country with little access to providers of cognitive and mind-body therapies.

The most important outcome to patients is improving their ability to function. They want to return to doing their usual activities of daily living. A second important aspect of great importance to patients is to relieve their sense of suffering. Patients want to be able to do the things that they used to enjoy. Examples included the ability to drive their car again or to go out to dinner at a restaurant without pain overwhelming their enjoyment of the experience.

3. Summary of Coverage Policies and Clinical Guidelines

3.1 Coverage Policies

To understand the insurance landscape for cognitive and mind-body therapies for chronic low back and neck pain, we reviewed publicly-available coverage policies from the Centers of Medicare and Medicaid Services (CMS), California Department of Health Care Services (DHCS), and from regional and national commercial insurers (Aetna, Anthem, Blue Shield of California [BSCA], Cigna, Health Net, Humana, Kaiser Permanente, and United HealthCare [UHC]).

CMS has a longstanding National Coverage Determination (NCD) regarding acupuncture and does not currently consider the treatment to be medically necessary.[39] We were unable to locate any NCDs or Local Coverage Determinations (LCDs) for CBT, MBSR, yoga, or tai chi. California's DHCS covers acupuncture and electroacupuncture for members with chronic pain resulting from a recognized medical condition. However, DHCS requires acupuncture to be sought through a Medi-Service reservation, which limits members to two total visits per month across a combination of several services (acupuncture, audiology, chiropractic, occupational therapy, podiatry, and speech therapy).[40] We were unable to locate any information from DHCS pertaining to the coverage of the other treatment modalities included in this review.

Six of the eight commercial plans (Aetna, BSCA, Cigna, Health Net, Kaiser Permanente, and Humana) cover acupuncture for the treatment of chronic low back and neck pain, although three insurers (Aetna, Cigna, and BSCA) note that some plans may exclude the coverage of acupuncture.[41-47] Anthem was the only payer included in our search that did not consider the treatment to be medically necessary.[48] We were unable to locate any determinations on the coverage of any of the interventions of interest from UHC.

Each of the payers that cover acupuncture require that it be provided by a licensed professional and cover a specific number of visits, which may vary across the plans offered by a given payer (Table 3.1). Kaiser Permanente requires prior authorization before coverage will be authorized, and Cigna requires a treatment plan that includes the frequency and duration of treatment. Three of the insurers (Aetna, Health Net, and Humana) require an evaluation of whether acupuncture has improved pain after several weeks to determine whether continued treatment will be authorized. Two of those plans (Aetna and Humana) allow continued treatment only if acupuncture has proven effective for the patient. Health Net allows for two additional months of treatment if acupuncture proves effective, but does not consider further treatment to be medically necessary. Four of the insurers (Aetna, Cigna, Health Net, Humana) do not cover acupuncture for maintenance care.

CBT is typically covered under the behavioral/mental health benefit (i.e., patients with depression as a result of chronic pain can be referred to a mental health practitioner who may include CBT in a treatment plan), but we were unable to locate any policies specific to the treatment of chronic low back or neck pain. With one exception, we were also unable to locate any publicly-available utilization management policies by any of the commercial insurers regarding MBSR, tai chi, or yoga, reflecting a lack of coverage for these services across payers. Cigna explicitly does not cover yoga for any indication.[49] Many insurers include these treatments in their wellness plans, either by offering discounts for these services to members, by providing educational material to inform individuals that these treatments may help with chronic pain, or, in one case, by offering classes open to members and non-members.

Among the insurers that offer wellness programs, two insurers (BSCA and Health Net) provide discounts for members seeking acupuncture outside of their standard coverage.[50,51] BSCA also provides an online portal through which members may purchase yoga and tai chi courses and materials. Kaiser Permanente was the only surveyed payer that offered wellness program services specifically addressing chronic pain. We were unable to find any information on how the other insurers' wellness programs incorporate these treatments for chronic low back and neck pain.

Kaiser Permanente offers courses to members and non-members as a branch of their wellness program.[52] Courses include mindfulness meditation, which includes gentle yoga aimed at coping with pain, and tai chi to reduce pain.[53,54] Both are offered to members and non-members for a fee, with the fee for non-members being slightly greater. Other courses, such as "Managing Chronic Pain" are available only to plan members.[55]

Table 3.1. Representative Public and Private Payer Policies for Acupuncture

Criteria	Medi-Cal	Aetna	Anthem	Cigna	Humana	UHC	BSCA	Health Net	Kaiser Permanente
Covered?	Yes	Yes	No	Some plans	Yes	--	Some plans	Yes	Yes
Prior Authorization?	No	No	No	No	No	--	No	No	Yes
Number and/or Timeframe of Allowed Sessions	Two services per month	Four weeks, reauthorization for additional visits if effective	--	Varies between plans	Five treatments, reauthorization for additional visits if effective	--	Varies between plans	Six treatments over one month, reauthorization for six additional visits over subsequent 2 months if effective	--

BSCA: Blue Shield of California, UHC: United HealthCare

3.2 Clinical Guidelines

To better understand the perspective of clinical specialty societies on the appropriate use of cognitive and mind-body therapies for chronic low back and neck pain, we reviewed guideline statements issued by selected US and ex-US organizations. For the purposes of this report, we have focused on statements pertaining to the five included interventions.

The American College of Physicians (ACP) / American Pain Society (APS), 2007, 2017[7,56]

The American College of Physicians (ACP) and American Pain Society (APS) Joint Recommendation in 2007 summarized the available evidence for management of acute, subacute, and chronic pain. In 2017, the ACP issued an update to these guidelines that was determined by the results of a systematic review conducted by the AHRQ.

Nonpharmacologic treatments including but not limited to acupuncture, CBT, MBSR, yoga, and tai chi are recommended as first-line treatments for patients with non-specific chronic low back pain, although there are no head to head comparisons of these interventions with pharmacologic therapy. The ACP considered the strength of this recommendation to be "strong," meaning that the "benefits clearly outweigh risks and burden, or risks and burden clearly outweigh benefits." The recommendation for MBSR was informed by a moderate-quality evidence base, while tai chi, yoga, acupuncture, and CBT were supported by low-quality evidence.

Clinicians may recommend the use of NSAIDs for patients who have an inadequate response to nonpharmacologic therapy, though they should recommend the lowest effective does for the shortest time period possible given NSAIDs' potential gastrointestinal and renal risks. Tramadol, an opioid, or duloxetine are to be considered only for patients who have unsuccessfully attempted treatment with nonpharmacologic therapy and for whom the potential benefits outweigh the considerable risks. Other opioids should only be considered the last treatment option in patients for whom other therapies have not proved successful.

American Academy of Pain Medicine (AAPM), 2009[57]

The AAPM lists the Chronic Pain Medical Treatment Guidelines by the Division of Worker's Compensation through California's Department of Industrial Relations as recommended guidelines for the treatment of chronic pain.

The guidelines recommend using a biopsychosocial model for chronic pain conditions, which includes an evaluation of potential psychosocial factors of chronic pain in addition to historical and physical patient evaluation.

Behavioral interventions are recommended for the treatment of general chronic pain. Patients should be screened for fear avoidance beliefs and other factors that leave them "at risk" for delayed recovery. Exercise treatments with CBT components should be prioritized for these at-risk patients instead of exercise alone, and clinicians should consider a separate referral to CBT if patients do not experience improvement in pain and disability after four weeks. In general, it is recommended that clinicians follow a stepped care approach to incorporating CBT into treatment regimens for chronic pain, starting with patient education for self-management of pain with MBSR, potential referral to group or individual treatment with a CBT specialist, and finally intensive care in a multidisciplinary setting. Biofeedback is also recommended as a complement to CBT programs.

The guidelines also recommend psychological therapies as complementary to opioid treatment; mindfulness meditation is suggested along with relaxation, acceptance, and distraction as tools to increase self-management of pain simultaneous to opioid use.

Yoga is recommended only as an option for a subset of patients who are identified as highly-motivated. The guidelines recommend approval where yoga is requested by a specific patient, as outcomes of depression and disability are dependent on motivation level of patient.

Acupuncture and electroacupuncture should be used as a treatment either alone or in conjunction with physical rehabilitation, post-surgical intervention, or a decrease in pain medication.

Centers for Disease Control and Prevention (CDC), 2016[58]

The CDC developed a guideline for safe and effective opioid prescription that states increased coverage for nonpharmacologic treatments could be one tool in improving patient health and safety surrounding chronic pain and the opioid crisis. The CDC recommends the first-line use of nonpharmacologic and non-opioid pharmacologic (NSAIDs, acetaminophen, etc.) treatments in comparison to long-term opioid therapy, particularly given their relative reduction in harms, for patients with general chronic pain. While nonpharmacologic therapies are a first-line treatment option for patients with chronic low back pain, the CDC stresses that adherence to a stepwise approach of nonpharmacologic therapies, then non-opioid pharmacologic interventions, followed by opioids is not mandatory. Clinicians should weigh the risks and benefits of these three treatment options when devising a treatment plan and prevent patients from having to use an ineffective treatment method for a prolonged period of time. Nonpharmacologic interventions can also be useful in conjunction with tapering opioid doses.

Institute for Clinical Systems Improvement (ICSI), 2016[59]

The set of guidelines from the Institute for Clinical Systems Improvement (ICSI) was established by consensus of a working group using the best available evidence.

ICSI recommends that patients presenting with chronic pain be evaluated with a behavioral health assessment, hopefully improving treatment selection and outcomes. In addition, ICSI suggests measuring and documenting the patient’s functional status, quality-of-life, and pain intensity along with whether the patient has had previous opioid exposure and their history or current experiences with substance use disorders.

For patients with chronic pain, a multidisciplinary approach is recommended whenever possible, as ICSI believes that chronic pain is best treated with a biopsychosocial approach. ICSI also recommends psychotherapy, particularly CBT or MBSR, within or separate from a multidisciplinary setting for all patients with chronic pain. Patients should engage in active physical rehabilitation (exercise), with passive modalities such as massage or spinal manipulation only as adjunct to such a treatment plan.

National Institute for Health and Care Excellence (NICE), United Kingdom, 2017[60]

For individuals ages 16 and over with chronic pain, NICE recommends providing advice and basic education, including encouragement to continue with regular activity and pain self-management. NICE also encourages consideration of a group exercise regimen (including mind-body programs), particularly for patients with a specific flare-up of pain and taking into account patient's exercise preferences. Clinicians can also consider manual therapy in conjunction with exercise, with or without additional psychological therapy.

For pharmacologic interventions, NICE recommends oral NSAIDs for managing low back pain, although they do not recommend offering opioids for managing chronic low back pain. In patients with chronic low back pain, combined physical and psychological programs are recommended, particularly CBT programs in group settings. CBT and other psychological therapies are not recommended without concurrent exercise. Acupuncture is explicitly not recommended for managing low back pain.

4. Comparative Clinical Effectiveness

4.1 Overview

We abstracted data on the interventions considered in this review from the AHRQ systematic review of therapies for low back pain and from subsequent randomized trials of the same interventions for patients with chronic low back pain. We focused primarily on changes in function, pain, and quality of life that persist beyond the initial treatment period by at least four weeks, but ideally for a year or more. Similarly, we abstracted data from systematic reviews of the same five interventions for chronic neck pain and from subsequent randomized trials for the same indication. Following the approach of the AHRQ review, we qualitatively synthesized information from the systematic reviews and randomized trials. Qualitative assessments were based on the consistency of the direction and magnitude of the effect size.

4.2 Methods

Data Sources and Searches

Procedures for the systematic literature review assessing the evidence on cognitive and mind-body therapies for chronic low back and neck pain followed established best methods.[61,62] The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[63] The PRISMA guidelines include a list of 27 checklist items, which are described further in Appendix Table A1.

We searched MEDLINE/PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials for relevant studies. The search was limited to English-language studies of human subjects and focused on trials of at least six month's duration or outcomes measured at least four weeks after the end of active therapy; articles indexed as guidelines, letters, editorials, narrative reviews, or news items were excluded.

The search strategies included a combination of indexing terms (MeSH terms in MEDLINE/PubMed and EMTREE terms in EMBASE), as well as free-text terms, and are presented in Appendix Tables A2-A5. In order to supplement the above searches and ensure optimal and complete literature retrieval, we performed a manual check of the references of recent relevant systematic reviews and meta-analyses. We also contacted specialty societies and patient advocacy organizations to ensure that we captured all of the relevant literature.

Study Selection

After the literature search and removal of duplicate citations using both online and local software tools (DistillerSR and Endnote X8.0.2), study selection was performed using two levels of screening, at the abstract and full-text level. Three reviewers screened the titles and abstracts of all publications identified through electronic searches per the inclusion and exclusion criteria defined by the PICOTS elements; a fourth reviewer worked with the initial three reviewers to resolve any issues of disagreement through consensus. No study was excluded at abstract-level screening due to insufficient information. For example, an abstract that did not report an outcome of interest in the abstract would be accepted for further review in full text.

Citations accepted during abstract-level screening were retrieved in full text for review. In the full text screening stage, four reviewers screened all publications using the same inclusion and exclusion criteria, and a fifth reviewer resolved any conflicts that resulted. Reasons for exclusion were categorized according to the PICOTS elements during both title/abstract and full-text review.

Key inclusion criteria included studies of at least six months' duration or that reported outcomes at least four weeks after the end of active treatment. We required that studies report pain and/or function outcomes for adults of at least 18 years of age with chronic back or neck pain treated with at least one of the interventions of interest (acupuncture, CBT, MBSR, yoga, tai chi) compared to usual care, sham therapy, or other active therapy.

Data Extraction and Quality Assessment

For the systematic literature review, each publication was abstracted by a single reviewer, and the abstracted data was then validated for quality assurance by a different reviewer. Five total reviewers participated in data abstraction.

Information from the accepted studies was extracted into data extraction forms and summarized in Appendix Tables D3-D10.

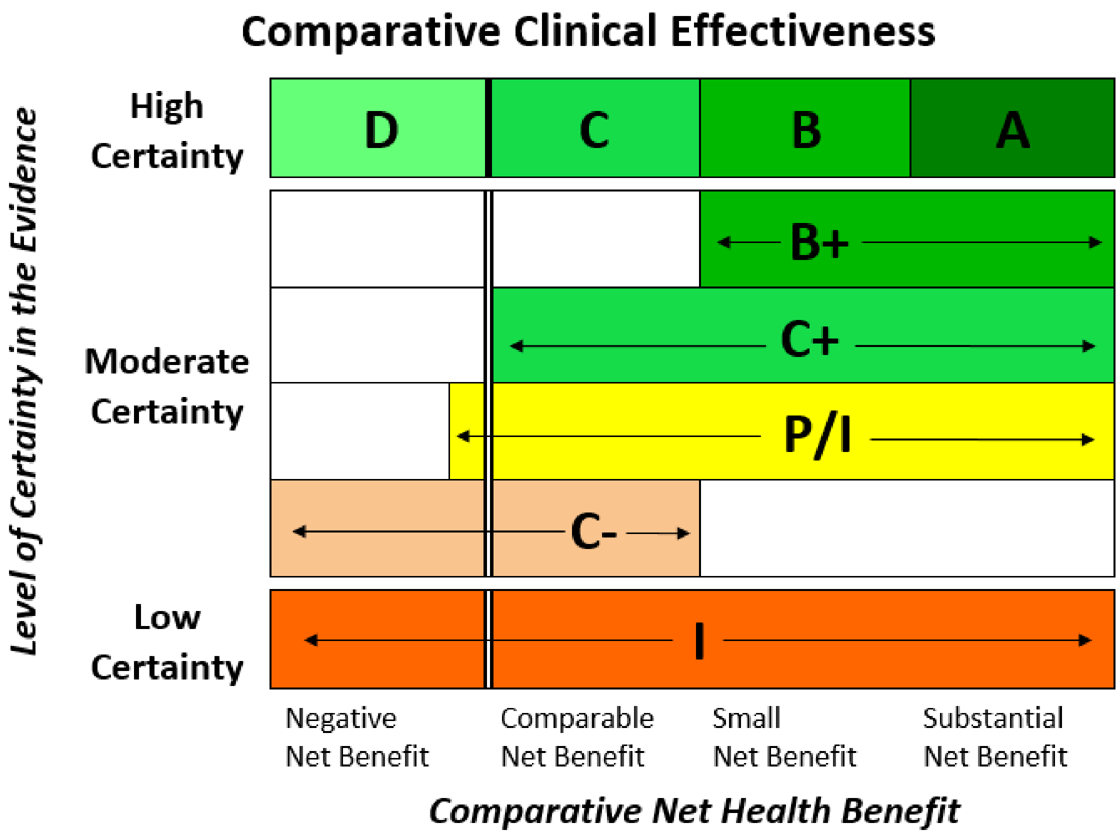
Quality assessment of randomized trials follows the AHRQ implementation of the USPSTF criteria.[64] Quality assessment of systematic reviews follows the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) guidelines.[65]

Assessment of Level of Certainty in Evidence

We used the ICER Evidence Rating Matrix (see Figure 4.1) to evaluate the evidence for a variety of outcomes. The evidence rating reflects a joint judgment of two critical components:

a) The **magnitude** of the difference between a therapeutic agent and its comparator in "net health benefit" – the balance between clinical benefits and risks and/or adverse effects AND
b) The level of **certainty** in the best point estimate of net health benefit.[66]

Figure 4.1. ICER Evidence Rating Matrix



*A = **"Superior"** - High certainty of a substantial (moderate-large) net health benefit*
*B = **"Incremental"** - High certainty of a small net health benefit*
*C = **"Comparable"**- High certainty of a comparable net health benefit*
*D = **"Negative"**- High certainty of an inferior net health benefit*
*B+ = **"Incremental or Better"** - Moderate certainty of a small or substantial net health benefit, with high certainty of at least a small net health benefit*
*C+ = **"Comparable or Better"** - Moderate certainty of a comparable, small, or substantial net health benefit, with high certainty of at least a comparable net health benefit*
*P/I = **"Promising but Inconclusive"** - Moderate certainty of a comparable, small, or substantial net health benefit, and a small (but nonzero) likelihood of a negative net health benefit*
*C- = **"Comparable or Inferior"** - Moderate certainty that the point estimate for comparative net health benefit is either comparable or inferior*
*I = **"Insufficient"** - Any situation in which the level of certainty in the evidence is low*

Data Synthesis and Statistical Analyses

Data on relevant outcomes were summarized in Appendix Tables D6 and D10, and synthesized qualitatively below.

4.3 Results

The results are presented in the following order: study selection, quality of studies, benefits, harms, controversies and uncertainties, and summary. In each section, we first review chronic low back pain and then chronic neck pain. Within each indication, we evaluated five cognitive and mind-body interventions in the following order: acupuncture, cognitive behavioral therapy, mindfulness based stress reduction, yoga, and tai chi. In the benefits section for each intervention, we begin by summarizing a key trial and then present the summary estimates on key outcomes from systematic reviews and additional randomized trials published after the systematic reviews. Key trials are the larger, higher-quality trials with longer follow-up for each intervention.

Study Selection

The literature search identified 472 citations (Appendix Figure A1). After reviewing the titles and abstracts, 143 full-text articles were evaluated. Of the 36 total references that were included, 24 were systematic reviews and 12 reported on randomized trials. Four systematic reviews of cognitive and mind-body therapies for chronic neck pain were identified to complement the AHRQ review[9] of therapies for low back pain.[67-70] These were the most recent, high-quality reviews for each of the five interventions in the scope of our review. Two of the systematic reviews looked for trials of tai chi and yoga for neck pain and did not identify any randomized trials meeting their inclusion criteria.[68,70] Since our inclusion criteria differed from that of the AHRQ review for chronic low back pain and the four systematic reviews of therapies for chronic neck pain, we reviewed the randomized trials included within these systematic reviews to determine if they met our specifications. Specifically, we only included studies of at least six month's duration or studies of a more limited duration with outcomes assessed at least four weeks after cessation of active therapy. From the AHRQ review,[9] we included 24 studies on acupuncture, CBT, yoga, tai chi and mindfulness. From the systematic reviews identified for chronic neck pain, we included six studies from two reviews on acupuncture and five studies from one review on CBT. The full list of included and excluded studies from these previous systematic reviews is available in Appendix Table D1 and D2.

We identified eight publications describing seven new randomized trials meeting our inclusion criteria for low back pain[12,71-76] that have been published since the search performed for the AHRQ review. We also identified four trials for chronic neck pain[77-80] that met our inclusion criteria and were not included in prior systematic reviews. Details of the studies are summarized in Appendix Tables D3-6.

Quality of Individual Studies

Chronic Low Back Pain

Systematic Review

The AHRQ review of low back pain[9] was a high-quality systematic review. It met all 11 of the AMSTAR criteria.

New Randomized Trials

Six additional randomized trials were identified. There was one pilot trial of a mindfulness intervention with poor comparability of participants at baseline, lack of blinding, and poor reporting of key outcomes.[76] The remaining four trials all evaluated yoga: three were good quality[74,75,81] and one fair quality.[71] The fair quality trial was downgraded for differential loss to follow-up (12% for yoga and 30% for the other two arms).

Chronic Neck Pain

Systematic Reviews

The quality of the systematic reviews of interventions for chronic neck pain were more heterogeneous (Appendix Table D9). The two systematic reviews of acupuncture for neck pain were of high quality, meeting 10 of the 11 AMSTAR criteria, with one review not reporting any assessment for publication bias[69] and one review not stating whether an *a priori* design was used.[70] The systematic review of CBT was also high quality.[67] The systematic review that looked for RCTs of yoga was of low quality and did not find any trials meeting their inclusion and exclusion criteria.[68]

New Randomized Trials

Four additional randomized controlled trials were identified in the chronic neck pain population that met our inclusion criteria. One new study of acupuncture was judged to be of low quality due to significant baseline difference and significant loss to follow-up.[82] The other two new studies of acupuncture were of fair quality.[79,80] One RCT looked at the effect of tai chi compared to conventional neck exercise and waitlist control. While the study was powered to detect differences between the arms, the study was only of fair quality due to low adherence rates in the neck exercise group.[78]

Clinical Benefits

The most important benefit to patients is improvement in function (i.e., a greater ability to work and do their desired daily activities) even if they still have pain. The next most important benefit is a reduction in pain. If achieved, these should translate into improved quality of life. We summarize the magnitude of these effects in the clinical trials using the following table derived from the AHRQ review as a guide.[9] There is no consensus in the literature on the magnitude of a difference in pain or function on these scales that is clinically significant, but one group has made proposals based on a review of the literature.[36]

Table 4.1. Magnitude of Effect Based on Average Between-Group Differences*

Outcome	Slight / Small Improvement	Moderate Improvement	Large / Substantial Improvement
Function	5-10 points on the ODI or NDI 1-2 points on the RMDQ	>10-20 points on the ODI or NDI >2-5 points on the RMDQ	>20 points on the ODI or NDI >5 points on the RMDQ
Pain	0.5-1.0 points on 10-point VAS	>1.0-2.0 points on 10-point VAS	>2.0 points on 10-point VAS
Pain or Function	0.2-0.5 SMD	>0.5-0.8 SMD	>0.8 SMD

ODI =Oswestry Disability Index; NDI = Neck Disability Index; VAS = Visual Analog Scale; SMD = Standardized Mean Difference

*Based on Table 1 in the AHRQ Systematic Review performed for the ACP[9]

Chronic Low Back Pain

Acupuncture

There were no new trials published since the AHRQ review.[9] Their primary findings for the use of acupuncture for chronic low back pain are summarized after the key trial below, emphasizing outcomes assessed at least four weeks after the end of active treatment.

<u>Key Trial: *Cherkin 2009*</u>

Cherkin 2009 was chosen as the key trial representing acupuncture for low back pain because it is the largest trial of acupuncture with the longest follow-up.[11] It provided unique insights because the investigators compared standardized acupuncture not only to sham acupuncture, but also to individualized acupuncture and to usual care. It was a good quality trial with appropriate randomization and allocation concealment, no important differences between groups at baseline, and good follow-up (91%) at the 26- and 52-week follow-up visits with no differential lost to follow-up. The primary outcomes were assessed by telephone interviewers who were unaware of the randomization status of the patients. Finally, a strict intention to treat analysis was performed.

The investigators randomized 638 adults with chronic low back pain to one of four arms: individualized acupuncture, standardized acupuncture, sham acupuncture, and usual care. Participants randomized to real or sham acupuncture were treated twice weekly for three weeks and then weekly for four weeks, for a total of 10 treatments. In the individualized acupuncture group, a diagnostician prescribed treatment at the beginning of each session, with no constraints placed on the number of needles, depth of insertion, or needle manipulation. Participants assigned to standardized acupuncture received a standardized prescription for low back pain that included eight insertion points on the low back and lower leg; acupuncture points were needled for 20 minutes, and needles were twirled at 10 minutes and prior to removal for stimulation. Sham acupuncture followed the same procedure by placing a standard acupuncture needle guide tube against the skin and touching eight standardized acupuncture points with a toothpick. Participants assigned to usual care followed the care their physicians selected, which consisted largely of medication, primary care, and physical therapy; all participants also received a self-care book containing information on management of flare-ups, exercise, and lifestyle modification. The primary outcomes were back-related dysfunction (RMDQ score; range, 0-23) and symptom bothersomeness (0-10 scale).

The participants had a mean age of 47 years, 62% female, and 68% reporting low back pain for more than one year at baseline. At 26 weeks, participants receiving real or sham acupuncture were more likely to experience a clinically-meaningful improvement (≥ 3-point improvement) on the dysfunction scale than those receiving usual care (58-62% vs. 44%; p=0.01; mean score 6.4-6.8 vs. 8.4), although statistical differences were not detected between the individualized, standardized, and sham acupuncture groups. These improvements were maintained at 52 weeks. For both the individualized and standardized acupuncture groups, the average RMDQ score decreased from 10.8 at baseline to 6.0 at 52 weeks; for the sham acupuncture group, the RMDQ score decreased from 9.8 to 6.2 and for the usual care group from 11.0 to 7.9. The average decrease in the RMDQ score compared to usual care was significant at one year (p<0.05) for the individualized and standardized acupuncture, but not for the simulated acupuncture. The reduction in symptom bothersomeness was significantly greater in the standard and simulated acupuncture groups compared to usual care at both 26 and 52 weeks (0.6 points for both at 52 weeks). There was a trend toward a greater reduction in symptom bothersomeness for the individualized acupuncture group that was significant at eight weeks, but no longer significant at 26 and 52 weeks (0.45 points at 52 weeks).

Adverse events were reported by 4% of participants in each of the individualized and standardized acupuncture groups and 0% of the other groups. The adverse events were primarily short-term increases in pain, with one severe increase in pain lasting for a month.

Reduction in Disability / Improvement in Function

The AHRQ review found that acupuncture – whether standardized or sham – was associated with better function (standardized mean difference [SMD] -0.94, 95% confidence interval [CI] -1.4 to -0.47) compared to no acupuncture immediately following treatment. However, the improvement in function was no longer significant after one year of follow-up. There were no significant differences in functional improvements when acupuncture was compared with sham acupuncture.

Acupuncture was associated with better function compared with medications (SMD -0.36, 95% CI -0.67 to -0.04) immediately following treatment, but no long-term follow-up data were available.

Eleven trials in the AHRQ review met our inclusion criteria (outcomes measured at least four weeks after the end of treatment or at least six months of treatment) and six of them reported on function. The change in disability measured by the RMDQ ranged from -0.8 to +2.3 points compared with usual care with positive numbers representing greater improvement. This range of results was overall consistent with the findings of the AHRQ review. One trial reported on changes in disability compared with sham acupuncture; the difference was +0.7 points at 6 months and +1.2 points at one year.

Reduction in Pain

The AHRQ review reported that acupuncture was associated with lower pain intensity (SMD -0.72, 95% CI -0.94 to -0.49) compared to no acupuncture immediately after the intervention. The reduction in pain was no longer significant in the long term (at least one year of follow-up).

Acupuncture also reduced pain more than sham acupuncture immediately after the intervention (WMD -1.7, 95% CI -3.3 to -0.2 on 10-point VAS) and through 12 weeks of follow-up (WMD -0.95, 95% CI -1.6 to -0.3). Acupuncture was also associated with lower pain intensity compared with medications (WMD -1.1, 95% CI -2.0 to -0.10) in the short term.

In the 11 trials meeting our inclusion criteria, the change in pain measured by the 10-point VAS ranged from -0.6 to +3.0 points compared with usual care and -0.1 to +2.4 points at one year compared with sham acupuncture. This range of results was overall consistent with the findings of the AHRQ review.

Other reported benefits

No other benefits were described.

Table 4.2. Key Outcomes from AHRQ Systematic Review of Acupuncture for Chronic Low Back Pain

	Short-Term Function	Short-Term Pain	Long-Term Function	Long-Term Pain
Acupuncture vs. Usual Care	SMD -0.94 (-1.41 to -0.47)	SMD -0.72 (-0.94 to -0.49)	Two trials reported small or no differences	Two trials reported small or no differences
Acupuncture vs. Sham Acupuncture	No difference	WMD -1.7 (-3.3 to -0.02)	No data	No data
Acupuncture vs. Medicines	SMD -0.36 (-0.67 to -0.04)	WMD -1.1 (-2.0 to -0.08)	No data	No data

Cognitive Behavioral Therapy

The AHRQ review included five RCTs from a prior systematic review, two of which met our inclusion criteria. Three studies within the AHRQ review that assessed CBT plus another form of treatment versus the other treatment alone also met our inclusion criteria. One head-to-head study comparing CBT to MBSR and usual care met our criteria. We found one additional publication that reported 24 months follow-up for one of the included trials and is described in detail below.

Key trial: *Cherkin 2016*

Cherkin 2016 was chosen as the key trial representing both cognitive behavioral therapy and mindfulness based stress reduction because it was the largest trial of both with the longest follow-up.[12] It also was the only trial directly comparing two of the interventions of interest in our review. It was a fair quality trial with appropriate randomization, allocation concealment, and no important differences between groups at baseline. Follow-up was acceptable at the 52 week (85%) and 104 week (81%) follow-up visits with greater follow-up in the usual care group (94% at 52 weeks). A strict intention to treat analysis was performed.

In this three-arm interviewer-blind RCT, 342 adults with chronic low back pain were randomized to CBT, MBSR, or usual care.[12] All participants continued to receive medical care that they were otherwise receiving prior to trial enrollment. However, patients in the usual care arm could seek any additional treatment that they desired. Both CBT and MBSR were delivered in group format for two hours per week for eight weeks, with an optional six-hour retreat offered to patients in the MBSR arm. Additionally, patients in the CBT and MBSR arms were given materials and instructions to practice the interventions at home.

The co-primary outcomes were clinically meaningful improvements in the RMDQ score and 10-point pain bothersomeness scores. A 30% reduction in both the RMDQ score and the back pain bothersomeness scale were considered clinically meaningful.

The baseline characteristics were similar in all three arms with a mean age of 49 years, 66% female, and 80% reporting low back pain for more than one year. At 26 weeks, 57.7% of participants reported clinically-meaningful improvement in RMDQ results in the CBT arm, 60.5% in the MBSR group and 44.1% in the usual care group. Similar findings were observed at 52 weeks. The comparison between active treatment and usual care was statistically significant for CBT at 26 weeks only and for MBSR at 26 and 52 weeks. At 104 weeks, the proportion of patients with clinically-meaningful improvement was 62.0% for the CBT group, 55.4% for the MBSR group, and 42% for the usual care group, which was not statistically significant. The average between-group difference in the RMDQ was significant for CBT versus usual care at 104 weeks, but not for MBSR versus usual care or CBT versus MBSR.[72]

For pain bothersomeness, patients in the CBT and MBSR groups had a greater proportion of patients with clinically-meaningful improvements than those receiving usual care at 26 weeks (44.9% CBT, 43.6% MBSR, and 26.6% usual care). At 52 weeks, the between-group comparison was only significant for MBSR (39.6% CBT, 48.5% MBSR, and 31.0% usual care). No significant difference was observed between the three groups at 104 weeks (39.6% CBT, 41.2% MBSR, and 31.1% usual care).

The study evaluated a number of other outcomes in addition to disability and pain bothersomeness. CBT significantly reduced depression compared with usual care at 26 months, but not 52 weeks. CBT also significantly reduced anxiety at 26 weeks compared with both usual care and MBSR. Both CBT and MBSR reduced pain intensity more than usual care at 26 weeks and 52 weeks with no significant differences comparing CBT to MBSR. Finally, CBT significantly improved quality of life assessed by the SF-12 Mental Health Component Score at 26 weeks, but not 52 weeks.

Adherence to CBT and MBSR was low in the trial. Among those randomized to CBT or MBSR 89% attended at least one session, but only 57% of patients randomized to CBT and 51% of patients randomized to MBSR and attended at least six of the eight sessions and only 26% attended the six-hour MBSR retreat. The findings from the study should be interpreted with caution as the extent to which adherence issues adversely impacted the results is unknown. Follow-up for outcomes was higher (85% at 52 weeks and 81% at 104 weeks).

Adverse events were reported by 10% of participants attending at least one CBT session and 29% of patients attending at least one MBSR session. The adverse events were primarily a temporary increase in pain during progressive relaxation for the CBT group and a temporary increase in pain with yoga in the MBSR group. No serious adverse events were reported.

Reduction in Disability / Improvement in Function

Overall, the AHRQ review found that CBT was not associated with improved function based on a prior 2010 Cochrane review. Three trials assessed this outcome and met our inclusion criteria. Two of these trials (including the key trial discussed above) compared CBT to either advice or usual care and reported significant improvements in function on the RMDQ of 1.4 and 1.5 points at six months and 1.3 points in both trials at one year. These results were consistent with the findings of the AHRQ review. In one trial, when CBT was added to physical therapy, the RMDQ was worse in the CBT group at six months (-0.6 points) and at one year (-1.2 points) compared with physical therapy alone.

Reduction in Pain

The AHRQ review found that CBT was associated with lower pain intensity (SMD -0.60, 95% CI -0.94 to -0.49) compared with usual care. However, among the three trials meeting our inclusion criteria, when CBT was added to either relaxation therapy or physical therapy, CBT was associated with higher pain intensity at six months (-0.5 and -1.3 points) and at one year (-0.8 points in both trials). The key trial described above used a pain bothersomeness 10-point scale rather than a pain intensity scale.[12,72] In that trial, there was a greater improvement in pain bothersomeness in the CBT group compared with the usual care group at one year (+0.8), but not at two years (+0.5), which was consistent with the findings of the AHRQ review.

Other reported benefits

No other benefits were described in the AHRQ review, but the key trial reported that patients randomized to CBT had significant reductions in depression on the PHQ-8 and anxiety on the GAD-2 at eight and 26 weeks. Similarly, they reported significant improvements on the Physical Component Score and the Mental Component Score of the SF-12 quality of life instrument at weeks eight and 26. At 52 weeks, only the depression and pain intensity scores remained statistically significant.

Table 4.3. Key Outcomes from AHRQ Systematic Review of CBT for Chronic Low Back Pain

	Short-Term Function	Short-Term Pain	Long-Term Function	Long-Term Pain
CBT vs. Usual Care	No difference	SMD -0.60 (-0.97 to -0.22)	Not reported	Not reported

CBT: cognitive behavioral therapy

Mindfulness-Based Stress Reduction

The AHRQ review included three trials of MBSR for chronic low back pain, but performed no meta-analysis. Our search identified one small, new publication,[76] and a second which reported 24-month follow-up on one of the three trials in the AHRQ review.[72]

Key trial: *Cherkin 2016*

Please refer to the Key Trial in the CBT section above. The trial compared MBSR to CBT and to usual care.[12,72]

Reduction in Disability / Improvement in Function

The key trial described above[12,72] reported a significant improvement in function of 1.4 points on the 24-point RMDQ at 26 weeks compared with usual care that increased to 1.9 points at 52 weeks. This corresponded to 60% of patients in the MBSR group with a clinically-meaningful improvement in function at 26 weeks and 69% at 52 weeks, compared with 44% and 49% respectively in the usual care group. At 104 weeks, the difference was no longer statistically significant (1.3 points, 55% vs. 42%).

The second good-quality trial in the AHRQ review reported significant improvements in function at eight weeks compared to an educational intervention (-1.1 points on RMDQ, 95% CI -2.1 to -0.01), but the difference was no longer significant at six months.[73] The third study in the AHRQ review was a small (n=40), poor quality pilot trial by the same author that reported improvements in function (RMDQ) compared to an educational intervention that were larger at four months follow-up than at the end of the active treatment phase, but did not reach statistical significance.[83]

The new study was a pilot trial that enrolled 35 patients on chronic opioid therapy (average morphine equivalents 148 mg/day) and compared an eight-week MBSR intervention to a wait list usual care control.[76] There were significant baseline differences between the study groups ($p<0.001$ for pain intensity, for example), so the study was of poor quality. There was no significant between-group difference in the ODI at 26 weeks follow-up.

All four studies met our inclusion criteria, but only two reported functional outcomes after six months or longer. At six months, the improvement was 0.4 in one trial and 1.4 in the other, increasing to 1.6 at 12 months, but decreasing to 1.3 at 24 months, which was consistent with the findings of the AHRQ review.

Reduction in Pain

The key trial described above[12,72] reported significant reductions in pain intensity on a 10-point VAS at 26 weeks (-0.64 points) and at 52 weeks (-0.85 points) and in pain bothersomeness at 26 weeks (-1.4 points on a 10-point scale) and 52 weeks (-1.9 points). The other two trials in the AHRQ review did not report significant improvements in pain compared to the control group.[73,83] The poor-quality RCT among patients on high-dose opioid therapy found no significant between-group differences in pain intensity at 26 weeks.[76]

Other Reported Benefits

No other benefits were described in the AHRQ review, but the key trial reported that patients randomized to MBSR had significant reductions in depression on the PHQ-8 and significant improvements on the Mental Component Score of the SF-12 quality of life instrument at eight weeks. These were no longer significant at 26 and 52 weeks and the GAD-2 and SF-12 Physical Component Score were never statistically significant.

Table 4.4. Key Outcomes from AHRQ Systematic Review of MBSR for Chronic Low Back Pain

	Short-Term Function	Short-Term Pain	Long-Term Function	Long-Term Pain
MBSR vs. Usual Care	RMDQ -1.4 (-2.5 to -0.2)	-0.6 (-1.1 to -0.1)	RMDQ -1.9 (-3.1 to -0.6)	-0.8 (-1.4 to -0.3)
MBSR vs. Education	RMDQ -1.1 (-2.1 to -0.01)	No significant difference	No data	No data

MBSR: mindfulness-based stress reduction, RMDQ: Roland Morris Disability Questionnaire

Yoga

The AHRQ review included 14 trials of yoga for chronic low back pain, 10 from a prior systematic review. Eight of the 10 trials in the systematic review were rated as having a low risk of bias and two of the new trials were rated as fair quality and two as good quality. We identified four additional trials with longer-term outcomes.

Key Trial: *Saper 2017*

Saper 2017 was chosen as the key trial representing yoga because it was the largest trial of yoga with the longest follow-up.[74] However, it's quality was rated as poor because of baseline differences between groups, lack of blinding and differential loss to follow-up (physical therapy group had larger loss to follow-up, but yoga and education groups were similar. The final analysis adjusted for baseline differences between groups.

In this three-arm single-blind randomized non-inferiority trial, 320 adults aged 18 to 64 years with non-specific chronic low back pain were enrolled and randomized to yoga, physical therapy, and education in a 2:2:1 ratio.[74] The researchers conducted the study in a large academic safety-net hospital and seven federally-qualified community health centers in racially diverse neighborhoods. The study design consisted of two phases, a 12-week treatment phase and 40-week maintenance phase.

The aim in the treatment phase was to determine if yoga was not inferior to physical therapy for improving function and pain in the lower back. Secondly, Saper and colleagues aimed to determine if yoga and physical therapy were both better at improving function than education. The maintenance phase split the two active arms of yoga and physical therapy into four groups, randomly assigning participants to yoga drop-in classes, yoga at home, physical therapy booster sessions, and physical therapy at home. The education group remained unchanged during this phase. At 52 weeks, the researchers evaluated whether both yoga drop-in classes and physical therapy booster sessions were superior to their respective at-home practices.

The yoga sessions included 12 weekly 75-minute classes, adapted from previous studies and input from yoga experts. Maintenance phase classes had a higher participant-instructor ratio (8:1 as opposed to 5:1 in the treatment phase), but were otherwise structured similarly. Participants in physical therapy attended 15 60-minute appointments for 12 weeks. The protocol consisted of treatment-based classification, graded exercise, and screening for fear-avoidance beliefs. Booster session participants were requested to meet with physical therapist at months four, six, eight, 10, and 12. At-home participants received instructions and supplies and reported the number of exercises performed daily. Education participants received a help book and newsletters previously used by other trials with information on self-management of chronic low back pain. During data collection, entry, and analysis, the assessors were masked. The primary outcomes were change from baseline to 12 weeks in RMDQ scores for function and in pain scores on an 11-point pain scale (0 = no pain and 10 = worst pain).

Participants had a mean age of 46 years and 64% were female. There were baseline differences in RMDQ, sex, and body mass index (p<0.1), which were adjusted for in the analyses. At 12 weeks, the change in the mean RMDQ score was -3.8 for the yoga group [95% CI, -4.6 to -2.9], -3.5 for the physical therapy group [95% CI -4.5 to -2.6]), and -2.5 for the education group (95% CI -3.8 to -1.3). None of the between-group differences were significant. The mean difference in RMDQ scores was -0.26. At 12 weeks, the change in the mean pain score was -1.7 for the yoga group (95% CI, -2.1 to -1.4), -2.3 for the physical therapy group (95% CI -2.7 to -1.9), and -1.4 for the education group (95% CI -3.8 to -1.3). Physical therapy had a significant reduction in pain compared to the education group (-0.84, 95% CI -1.5 to -0.2). The differences in pain reduction between the yoga group and the other two groups were not significant.

The investigators defined a clinically-meaningful responses as a 30% reduction in the score for both the RMDQ and the pain intensity VAS, which mirrored the recommendations of other groups.[36] The proportion of patients who achieved a clinically-meaningful reduction in the RMDQ at 12 weeks was 48% for the yoga group, 37% for the physical therapy group, and 23% for the education group. The proportion of patients achieving a clinically-meaningful reduction in pain at 12 weeks was 35% for the yoga group, 42% for the physical therapy group, and 25% for the education group.

There were no significant differences in function or pain comparing yoga drop-in classes to yoga home practice during the maintenance phase through 52 weeks. Similarly, there were no significant differences in function or pain comparing physical therapy booster sessions to physical therapy home practice during the maintenance phase through 52 weeks. The investigators did not compare outcomes between the yoga, physical therapy, and education groups at 52 weeks in this publication, although they conclude that "the improvements in yoga and PT were maintained at one year."

Secondary outcomes were self-reported pain medication use in previous week, global improvement (seven-point scale from extremely worsened to extremely improved), patient satisfaction with interventions, and health-related quality of life using the SF-36 questionnaire. Yoga and physical therapy participants were 21% and 22% less likely than patients in the education group to use pain medication. The only significantly-important difference observed in self-rated global improvement and satisfaction was between physical therapy and education. There were no significant differences for SF-36 scores between groups. The limitations of this study included low participation rates in all three of the interventions (less than 50% met attendance goals in each) and a disproportionate loss to follow-up within the physical therapy group.

Adverse events were more common in the active treatment groups (yoga 7%, physical therapy 11%, education 2%). The most common were joint pain and increased back pain (21/23 reported events). There was one serious adverse event in the yoga group: hospitalization for wrist swelling at the site of a wrist fracture that had been treated surgically prior to the trial. The patient was diagnosed with cellulitis and treated successfully with antibiotics.

Reduction in Disability / Improvement in Function

One trial in the AHRQ review compared yoga with usual care; yoga was associated with a significant improvement in function at 24 weeks (3 points on the ODI). In five trials compared to exercise, yoga was usually associated with better function, but the differences were small and not always statistically significant. Finally, in five trials compared with education, yoga was associated with better function in the short term (SMD -0.45, 95% CI -0.65 to -0.25) and long term (SMD -0.39, 95% CI -0.66 to -0.11). Among the two trials meeting our inclusion criteria reporting functional outcomes, there was a 0.4 point increase in the RMDQ versus education at three months,[74] but a 2.5 point greater improvement in the RMDQ with yoga compared to usual care at six months.[81]

Reduction in Pain

In the AHRQ review, the only trial that compared yoga with usual care reported a significant reduction in pain at 24 weeks (1.3 points on the VAS). In five trials compared to exercise, yoga was usually associated with decreased pain, but the differences were small and not always statistically significant. Finally, in five trials compared with education, yoga was associated with reduced pain in the short term (SMD -0.45, 95% CI -0.63 to -0.26), but the difference was smaller and not significant with long term follow-up. For the four trials meeting our inclusion criteria, the differences in pain between the yoga and control groups at six months ranged from -0.6 to +0.6 that was overall consistent with the AHRQ review.

Other Reported Benefits

No other benefits were reported except as described in the key trial above.

Table 4.5. Key Outcomes from AHRQ Systematic Review of Yoga for Chronic Low Back Pain

	Short-Term Function	Short-Term Pain	Long-Term Function	Long-Term Pain
Yoga vs. Usual Care	ODI -3, p<0.01	VAS -1.3, p<0.01	Not reported	Not reported
Yoga vs. Exercise	Better function, small difference	Less pain, small difference	Not reported	Not reported
Yoga vs. Education	SMD -0.45 (-0.65 to -0.25)	SMD -0.45 (-0.63 to -0.26)	SMD -0.39 (-0.66 to -0.11)	Not significant

ODI: Oswestry Disability Index, SMD: standardized mean difference, VAS: visual analog scale

Tai Chi

The AHRQ review summarized two fair-quality trials that randomized 480 participants to tai chi or usual care. Our search did not identify any additional trials of tai chi that met our inclusion criteria.

Key Trial: *Weifen 2013*

The key trial is the largest of the two trials of tai chi, but only followed participants for six months.[84] AHRQ rated this as a fair quality trial, though the reporting in the publication did not follow the CONSORT criteria, so assessment of trial quality was challenging. The trial studied a unique population, retired Chinese athletes, who were younger than participants in most of the other trials, so the results may not generalize to Americans with chronic low back pain.

In this double-blind RCT in Fujian, China, 320 patients were randomized to practice tai chi (n=141), backwards walking (n=47), jogging (n=47), swimming (n=38), or no exercise (n=47) for six months. Participants were retired athletes between the ages of 20 and 45 years with non-specific chronic low back pain confined to the lumbar vertebrae of one to five years' duration. Patients' average pain intensity over the last week had to exceed 4 mm on a 10 mm VAS to be eligible for inclusion, and they had to have not participated in any physical treatments in the three months prior to the trial. Patients were instructed to refrain from their regular athletic routines for the duration of the study.

All participants received physical treatment throughout the trial, including electrotherapy, traditional Chinese manipulation, traction, and massage. Additionally, patients received acupuncture and spinal manipulation along with basic advice on healthy lifestyle habits. In the tai chi group, participants were instructed to practice four cycles of the 24-step Chen style tai chi exercises for 45 minutes each day, five days per week. Participants in the jogging, backwards walking, and swimming groups were instructed to practice their respective exercises for 30 minutes each day after a 15-minute warm-up exercise routine, five days per week.

The primary outcome was pain intensity score on a VAS from 0 to 10 mm, assessed at three months and again at six months immediately after cessation of treatment. Medical examinations assessing body mass index, heart rate, blood pressure, and daily sleep habits were also performed at baseline and three and six months.

The groups were comparable at baseline with mean age of 38 years, 40% female, and an average duration of 2.1 years of back pain. At six months, patients in the tai chi group had a mean VAS pain score of 2.2, a 3.0-point improvement from baseline. There was no statistically-significant difference between the tai chi and swimming groups ($p>0.05$). There were significant differences reported for tai chi compared with backwards walking, jogging, and no exercise ($p<0.05$ for each). The between-group difference in pain comparing tai chi to no exercise at six months was 1.0 points ($p<0.01$, no confidence interval given). No functional outcomes or adverse events were reported.

Reduction in Disability / Improvement in Function

Only one of the two trials reported on function. It found a greater improvement in function with tai chi on the RMDQ (2.6 points, 95% CI 1.1 to 3.7) at the end of the 10-week program. The trial did not follow participants beyond 10 weeks, so there are no studies reporting significant long-term improvements in function.

Reduction in Pain

Both studies reported that tai chi reduced pain compared to no active treatment at the end of active treatment: (0.9 and 1.3 points respectively on a 10-point VAS). Only one trial reported outcomes at six months: a reduction of 1.0 points.

Other Reported Benefits

No other benefits were reported.

Table 4.6. Key Outcomes from AHRQ Systematic Review of Tai Chi for Chronic Low Back Pain

	Short-Term Function	Short-Term Pain	Long-Term Function	Long-Term Pain
Tai Chi vs. Wait List	RMDQ -2.6 (-3.7 to -1.1)	VAS -0.9	Not reported	Not reported
Tai Chi vs. No Tai Chi	Not reported	VAS -1.3	Not reported	Not reported

RMDQ: Roland Morris Disability Questionnaire

Chronic Neck Pain

Acupuncture

Our search identified two recent systematic reviews[69,70] of acupuncture for chronic neck pain and three additional randomized trials[79,80,82] not included in the reviews that reported outcomes at least four weeks after the completion of acupuncture treatment or six months or more after initiation of therapy.

Key Trial: *MacPherson 2015*

MacPherson and colleagues randomized 517 patients with chronic neck pain to acupuncture, the Alexander Technique, or usual care. The acupuncture arm received 12 50-minute sessions either weekly or every other week over no more than six months. The Alexander Technique arm received 20 30-minute sessions either weekly or every other week over the same period.[79] The Alexander Technique focuses on improving posture and movement through mindfulness in order to decrease tension in the body. The usual care arm received medications and physical therapy visits consistent with routine clinical practice in a primary care population.[79]

The primary outcome for the study was the score on the Northwick Park Neck Pain Questionnaire (NPQ) at 12 months. The NPQ is a joint measure of both pain and disability that has been validated in the literature.[37] Secondary outcomes included pain intensity on a 0-8 scale collected by text message, the SF-12 physical and mental component scores, self-efficacy collected through the Chronic Pain Self-Efficacy Scale (score 0-8), and preferences and expectations. Adverse events were collected throughout the study.

Overall baseline characteristics were balanced among the arms with a mean age of 53 years, 69% female, and a median duration of neck pain of six years. At 12 months, 442 subjects (85%) provided outcome data with no difference in loss to follow-up between the arms.

At 12 months, the reduction in the NPQ was greater in the acupuncture arm compared to usual care (-3.9 point, 95% CI -6.9 to -1.0). After adjusting for covariates, the difference was slightly greater (-4.0 points, 95% CI -6.7 to -1.4). The mean percentage reduction in the NPQ at one year was 32% for the acupuncture group, 31% for the Alexander Technique group, and 23% for usual care. Comparisons between the acupuncture group and the Alexander Technique group were not reported.

Current pain levels were assessed with a text message system and a pain intensity score of 0-8 (0 equals no pain, 8 equals worst pain). Only 70.6% of study enrollees participated in the text message outcome; there was a greater reduction in pain for the acupuncture group compared with usual care (0.60 points on the 8-point VAS, $p<0.001$). There was no difference between the acupuncture group and the usual care group on the physical component score of the SF-12 at one year, but there was a significant difference in the mental component score (1.8 points, 95% CI 0.1 to 3.4). There were also greater improvements in self-efficacy with acupuncture compared with usual care (-3.3 points, 95% CI -4.4 to -2.3).

Serious adverse events occurred in a similar proportion of patients in each group (5.2% acupuncture, 7.6% Alexander technique, 4.7% usual care). Non-serious adverse events were numerically more common in the acupuncture group (13.9% acupuncture, 10.5% Alexander technique, 4.7% usual care). Adverse events that were classified as possibly related to acupuncture included bruising, swelling, numbness, muscle spasms, pain, and respiratory problems.

Reduction in Disability / Improvement in Function

In the Yuan systematic review, acupuncture was superior to sham acupuncture in disability reduction up to one month after treatment (SMD- 0.42, 95% CI, -0.66 to -0.19).[70] The improvement remained significant at three months (SMD -0.37, 95% CI -0.59 to -0.14).[70] There was no significant reduction in disability compared with sham TENS.[70]

Six studies met our inclusion criteria, but only three reported functional outcomes. The three studies that compared acupuncture to sham acupuncture reported an improvement of 0.4 to 5.6 points on the NPQ at 12 to 24 weeks follow-up, which was consistent with the Yuan review findings. In the small study comparing acupuncture to NSAID therapy, the improvement in disability was greater than that for NSAID therapy (0.7 at seven weeks).[82] When compared to usual care, the reduction in disability at one year was 3.1 points greater with acupuncture.[79]

Reduction in Pain

In the 2015 review by Yuan et al., a meta-analysis of two RCTs showed that up to one month after treatment, acupuncture was superior to sham acupuncture in pain relief (WMD -0.72, 95% CI -1.07 to -0.37).[70] Pain benefit was no longer significant by three months follow-up.

Among the six trials meeting our inclusion criteria, four trials reported a change in pain scores ranging from -1.7 to 2.1 points comparing acupuncture to sham acupuncture, with the overall range consistent with the findings in the Yuan review. Comparing acupuncture to a waitlist control, pain intensity was 2.5 points lower in the acupuncture group at 12 weeks. When acupuncture was compared to NSAIDs, pain intensity decreased more in the acupuncture group (0.8 points at seven weeks).

Other Reported Benefits

Improvements in self-efficacy and mental component scores on the SF-12 in the key trial were greater for acupuncture compared with usual care.[79]

Cognitive Behavioral Therapy

A recent Cochrane review evaluated CBT for both subacute and chronic neck pain.[67] The review included eight studies with a total of 499 patients with chronic neck pain. Five of the eight studies were assessed to have a high risk of bias. Our search did not identify any additional randomized trials with intermediate- to long-term follow-up.

Reduction in Disability / Improvement in Function

The Cochrane review reported that CBT reduced disability in the short term compared with physical therapy (SMD -0.61, 95% CI -1.2 to -0.01) based on two trials (n=89) with a high risk of bias. They also reported that CBT added to other treatments did not reduce disability more than other treatments alone in reducing disability in the short term (SMD -0.10, 95% CI -0.56 to +0.36) based on three trials (n=185).

Among the six trials meeting our inclusion criteria, three trials compared CBT to usual care and reported significant improvements of 3.0 to 4.3 points on the NDI at up to one year of follow-up, which was consistent with the findings of the Cochrane review. Three additional trials reported disability outcomes for CBT in combination with physical therapy (PT) that were worse in the CBT plus PT group compared to PT alone (-0.9 points).

Reduction in Pain

The Cochrane review reported that CBT reduced pain in the short term compared with physical therapy (SMD -0.58, 95% CI -1.0 to -0.2) based on three trials (n=89) with a high risk of bias. They reported that CBT did not reduce pain more than physical therapy in the intermediate term (SMD -0.89, 95% CI -2.7 to +0.94) based on two trials (n=168).

Among the six trials meeting our inclusion criteria, the reduction in pain with CBT compared with usual care ranged from -0.4 to 1.5 points at four to six months and was 0 points in the one trial reporting outcomes at 12 months. This range of findings was consistent with those reported in the Cochrane review. Three trials compared CBT in combination with PT to PT alone: the reduction in pain ranged from 0.3 to 0.7 points at four to six months and 0.5 points at 12 months.

Other Reported Benefits

There were no additional reported benefits.

Mindfulness-Based Stress Reduction

Our search did not identify any systematic reviews or trials of MBSR for the management of chronic neck pain that met our inclusion criteria.

Yoga

Our search did not identify any systematic reviews or trials of yoga for the management of chronic neck pain that met our inclusion criteria.

Tai Chi

Our search identified one systematic review of tai chi for chronic neck pain.[68] That systematic review, published in 2016, did not identify any relevant trials. Our search identified one subsequent trial, also published in 2016, that met our inclusion criteria.[78] It is described below as the key trial.

Key Trial: *Lauche 2016*

Lauche et al. randomized 114 patients with chronic neck pain to tai chi, traditional neck exercises, or a waitlist control and followed patients for 24 weeks (12 weeks of intervention and an additional 12 weeks of follow-up).[78] Those randomized to the tai chi arm (n=38) received 12 weeks of Yang-style tai chi (75- to 90-minute group sessions weekly) using an explicit protocol. Participants were also asked to practice tai chi at home for 15 minutes each day. The neck exercise participants (n=37) were given group classes on a weekly basis for 12 weeks (60-75 minutes each class) and were taught basic exercises (proprioceptive, isometric, dynamic mobilization, stretching, strengthening and core). Neck exercise participants were also asked to practice at home for 15 minutes per day. Wait list participants (n=39) were instructed to continue with usual treatments but not to engage in any new therapy during the 24 weeks of the study. All waitlist participants could receive tai chi or neck exercises at the end of the study.

The groups were comparable at baseline; mean age was 49 years and 80% were female. Pain intensity at 12 weeks was significantly lower in the tai chi group compared with the waitlist group (difference -1.0, 95% CI -2.0 to -0.1) and remained significant at 24 weeks (difference -1.1, 95% CI -2.1 to -0.03). There was no difference in pain intensity between the tai chi arm and neck exercise arm at 12 or 24 weeks.

Patients randomized to the tai chi group had a greater reduction in disability on the NDI compared with the waitlist group at both 12 (difference -7.2, 95% -11.7 to -2.7) and 24 weeks (difference -6.6, 95% CI, -11.6 to -1.6). No differences were found in disability reduction between the tai chi and neck exercise arms.

Adverse events were uncommon. In the tai chi group two patients reported Achilles tendon pain and one reported a migraine that were thought to be possibly related to tai chi. In the neck exercise group one participant reported knee pain that was thought to be related to the neck exercises.

Reduction in Disability / Improvement in Function

There is no additional information beyond that found in the key trial.

Reduction in Pain

There is no additional information beyond that found in the key trial.

Other Reported Benefits

At 24 weeks, average pain on movement scores were lower in the tai chi arm compared to the waitlist arm (-14.3 on a 100-point scale; 95% CI -22.0 to -6.7).[78] Other significant secondary outcomes include improvements in physical quality of life and social role functioning in the tai chi arm compared to the waitlist arm.[78] No significant differences were found in any endpoint at 24 weeks between the tai chi arm and the active neck exercise arm.[78]

Harms

These five interventions were well-tolerated for both back and neck pain. No serious adverse events were reported in the trials that were thought to be related to the intervention. Commonly-reported adverse events included bleeding and pain at the site of acupuncture needles, and strains and joint aches in patients receiving the MBSR, yoga, tai chi interventions. An increase in back and neck pain for up to one month was sometimes reported. No adverse events were reported with CBT.

Controversies and Uncertainties

There are a number of issues that are important to consider when assessing the evidence base for the cognitive and mind-body interventions. First, each of the categories of interventions considered represents a range of possible interventions. There are many different approaches to acupuncture, different kinds of CBT, and there many different schools of yoga and tai chi and different poses and breathing techniques that could be used within each school. It may be that there is one form of yoga that is particularly effective at managing chronic low back pain, but that form of yoga has not been identified in trials to date. The number and quality of the studies is not sufficiently high to identify a particular sub-genre of any of the mind body therapies as most effective. The heterogeneity within each mind-body intervention is further complicated by variation in the skill level of the therapist teaching patients each of the interventions. MBSR is the one intervention with an agreed upon standard approach to teaching the intervention and training the teachers.

There is also significant heterogeneity within each disease category. There are many different causes for chronic low back and neck pain. Low back pain and neck pain can be sub-divided into those with and without radicular symptoms. Chronic neck pain caused by whiplash is one common subtype. Some patients are being treated with chronic opioid therapies and some suffer from concomitant depression. There may be mind-body interventions that are particularly effective in one of these subtypes of low back and neck pain, but to date the evidence base is not sufficiently robust to identify any variation in effectiveness for any of the therapies we examine.

Prior systematic reviews find that the five interventions considered in this review improve pain and function to some degree during the active treatment phase. However, chronic pain is just that – long in duration and often for life. It is essential to evaluate the long-term efficacy of the therapy. We attempted to address this by focusing this evidence review on trials of at least six months duration or those that evaluated pain and function at least four weeks after the end of the active treatment phase. Hearteningly, more recent trials are reporting outcomes after one year of follow-up. This is essential to a robust evaluation of the long-term effects of the interventions on chronic pain, a condition that generally persists for the life of the patient and rarely is cured.

A related issue is adherence to the assigned intervention. All five interventions include requirements for attendance and participation in multiple treatment sessions and all except acupuncture include home therapy as well. As noted in the key trial the evaluated both CBT and MBSR for chronic low back pain, adherence to the randomized intervention was relatively low. Interventions that improve adherence with the initial sessions and ongoing practice of these interventions may increase their effect size in both the short and long term. None of the studies examined the extent to which patients continued to practice their new skills at the time of longer term outcome assessment.

Some studies found that sham acupuncture was almost as effective as traditional acupuncture or structured acupuncture, but that both were significantly more effective at improving function and decreasing pain compared with usual care. The differences in outcomes between acupuncture and sham acupuncture were less than the differences between them and usual care. This suggests that a significant proportion of the benefit from acupuncture is the placebo effect. Some argue that this is a useful employment of the placebo effect, while others argue that it is unethical to recommend such treatment.

It is difficult, if not impossible to blind patients to the receipt of CBT, MBSR, yoga, or tai chi. The primary outcomes of trials in patients with chronic pain are subjective outcomes (function, pain, quality of life), which are most susceptible to placebo/nocebo effects.[85-87] Thus the effect size observed in these trials may be greater than the true treatment effect. Evidence from trials of acupuncture with and without an appropriate sham control support this hypothesis.

Finally, it is difficult to interpret the clinical significance of average changes in continuous measures of function, quality of life, and pain. Categorical measures reporting the proportion of patients achieving a clinically meaningful improvement in function, quality of life, and pain are more useful and should be reported in addition to average group changes.

Summary

Chronic Low Back Pain

Table 4.7. Comparative Clinical Effectiveness for Mind-Body Interventions for Chronic Low Back Pain Added to Usual Care Versus Usual Care Alone Over the Long Term

Intervention	Net Health Benefit	Level of Certainty	ICER Evidence Rating
Acupuncture	Small	Moderate	C+: Comparable or better
CBT	Small	Moderate	C+: Comparable or better
MBSR	Small	Moderate	C+: Comparable or better
Yoga	Small	Moderate	C+: Comparable or better
Tai Chi	Small	Low	P/I: Promising, but inconclusive

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction

Acupuncture

The evidence for the effectiveness of acupuncture for the treatment of chronic low back pain is complex. The majority of trials and meta-analyses confirm small to moderate improvements in function and pain compared with usual care immediately following the completion of therapy. However, the differences in outcomes are smaller and often non-significant clinically when compared to sham acupuncture, suggesting that much of the benefit may be from the placebo effect. Furthermore, the magnitude of the benefits for acupuncture decline with longer follow-up. We placed the greatest weight on the results of studies with at least one year of follow-up. That said, the harms of treatment were uncommon and generally mild. Thus, we assess the net health benefit to be small. The majority of the studies were small and had less than one year of follow-up and there was some inconsistency in the results, so we assessed the level of certainty to be moderate. Therefore, we consider acupuncture to be comparable or better when added to usual care (physician recommendations and educational handouts with oral analgesics and physical therapy) for chronic low back pain (Table 4.7 above).

Cognitive Behavioral Therapy

The evidence for the effectiveness of CBT for the treatment of chronic low back pain is based on fewer trials than acupuncture, but they were larger, longer, and more often focused on chronic pain. The majority of trials and meta-analyses confirmed small to moderate improvements in function and pain compared with usual care immediately following the completion of therapy. In the most recent trial, the benefits were small, but sustained at one and two years of follow-up. There were additional benefits in terms of reduced depression and improved quality of life. The harms of treatment were uncommon and generally mild. Thus, we assess the net health benefit to be small. The studies were of moderate size, not blinded, and there was some inconsistency in the results, so we assessed the level of certainty to be moderate. Therefore, we consider CBT to be comparable or better when added to usual care for chronic low back pain.

Mindfulness-Based Stress Reduction

The evidence for the effectiveness of MBSR for the treatment of chronic low back pain is similar to that for CBT. The key trial demonstrating sustained benefits for CBT found equivalent benefits for MBSR. As in the evidence base for CBT, the majority of trials and meta-analyses confirmed small to moderate improvements in function and pain compared with usual care immediately following the completion of therapy. In the most recent trial, the benefits were small, but sustained at one and two years of follow-up. The additional benefits observed for CBT (reduced depression and improved quality of life) were smaller and not significant for MBSR. The harms of treatment are uncommon and generally mild. Thus, we assess the net health benefit to be small. The studies were of moderate size, not blinded, and there was some inconsistency in the results, so we assess the level of certainty to be moderate. Therefore, we consider MBSR to be comparable or better when added to usual care for chronic low back pain.

Yoga

The AHRQ review, which included 14 RCTs, concluded that yoga had small to moderate benefits compared with education and usual care, but with low strength of evidence. We identified an additional four randomized trials with longer follow-up that support the effectiveness of yoga for low back pain, though the magnitude of the benefits was smaller with longer follow-up. As with the other therapies, the harms of yoga were mild, so we assess the net heath benefit to be small. The studies were of small to moderate size, not blinded, and there was some inconsistency in the results, so we assess the level of certainty to be moderate. Therefore, we consider yoga to be comparable or better when added to usual care for chronic low back pain.

Tai Chi

There was substantially less evidence for the effectiveness of tai chi for low back pain. On the basis of two fair-quality trials, the AHRQ review concluded that tai chi had a moderate effect on pain and a small effect on function with low strength of evidence. We did not identify any additional randomized trials. We assessed the net health benefit to be small with a low level of certainty because of the paucity of trials and the lack of trials with follow-up beyond six months. Therefore, we consider that the evidence for the effectiveness of tai chi for chronic low back pain to be promising, but inconclusive compared to usual care.

Chronic Neck Pain

Table 4.8. Comparative Clinical Effectiveness for Mind-Body Interventions for Chronic Neck Pain Added to Usual Care Versus Usual Care Alone Over the Long Term

Intervention	Net Health Benefit	Level of Certainty	ICER Evidence Rating
Acupuncture	Small	Low	P/I: Promising, but inconclusive
CBT	Small to none	Low	I: Insufficient
MBSR	Unknown	Low	I: Insufficient
Yoga	Unknown	Low	I: Insufficient
Tai Chi	Small to none	Low	I: Insufficient

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction

Acupuncture

The evidence for the effectiveness of acupuncture for the treatment of chronic neck pain is similar to that for chronic low back pain. The majority of trials and meta-analyses confirmed small to moderate improvements in function and pain compared with usual care immediately following the completion of therapy. The harms of treatment are uncommon and generally mild. Thus, we assess the net health benefit to be small. The majority of the studies were small and had less than one year of follow-up and there was some inconsistency in the results, so we assess the level of certainty to be low. Therefore, we consider the evidence for acupuncture to be promising, but inconclusive when added to usual care for chronic neck pain.

Cognitive Behavioral Therapy

The evidence for the effectiveness of CBT for the treatment of chronic neck pain is less robust than the evidence for low back pain. The majority of trials are short term and equivocal in terms of significant reductions in disability and pain beyond the active treatment period. The harms of treatment were uncommon and generally mild. Thus, we assess the net health benefit to be small to none. The studies were sparse, small, not blinded, and there was some inconsistency in the results, so we assessed the level of certainty to be low. Therefore, we consider the evidence for CBT to be insufficient (I) to assess its value when added to usual care for chronic neck pain.

Mindfulness-Based Stress Reduction

We did not identify any randomized trials of MBSR for chronic neck pain that reported outcomes at least four weeks after the end of active treatment or that lasted six months. The net health benefits are unknown and the level of certainty is low. Therefore, we consider the evidence for MBSR for chronic neck pain to be insufficient (I).

Yoga

We did not identify any randomized trials of yoga for chronic neck pain that reported outcomes at least four weeks after the end of active treatment or that lasted six months. The net health benefits are unknown and the level of certainty is low. Therefore, we consider the evidence for yoga for chronic neck pain to be insufficient (I).

Tai Chi

We identified one small trial of tai chi for chronic neck pain. Only 38 patients were randomized to the tai chi arm. The trial was open label with the comparison group, a wait list, potentially susceptible to the nocebo effect due to disappointment from not being randomized to the active group. The effect size on function (7 points on the 100-point NDI) and pain (1 point on a 10-point VAS) were small and potentially exaggerated by the lack of blinding. There were no differences comparing tai chi to neck exercises. The potential harms were uncommon and mild, but we still judge the net health benefit to be small to none based on this one trial. The level of certainty is low. Therefore, we consider the evidence for tai chi used for patients with chronic neck pain to be insufficient (I) compared to usual care.

5. Economic Analyses

5.1 Long-Term Cost Effectiveness

Overview

The aim of this analysis was to estimate the cost-effectiveness of the nonpharmacologic interventions considered in this review for the treatment of chronic low back pain. We did not model the use of any of the nonpharmacologic interventions for chronic neck pain due to a lack of published evidence on key clinical inputs required for the model, such as clinically meaningful response to each intervention of interest, quality of life estimates associated with chronic neck pain, improvement of neck pain after intervention, and length of treatment with each intervention. Each of the interventions (acupuncture, CBT, MBSR, yoga, and tai chi) was compared to usual care, which was defined as self-care guidance and educational information on stretching, strengthening, exercise, and lifestyle modifications. Model parameters were obtained from the published literature. We estimated the total costs, quality-adjusted life years (QALYs) gained, incremental cost per case of clinically-significant pain improvement (i.e., intervention success), and incremental cost-effectiveness ratios relative to usual care, using a health care system perspective over a five-year time horizon. Uncertainty in data inputs and assumptions was evaluated through sensitivity and scenario analyses.

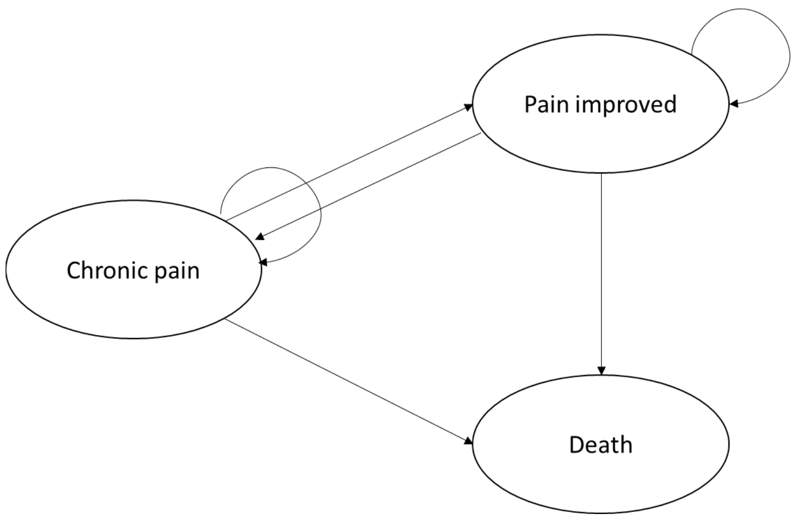
Cost-Effectiveness Model: Methods

Model Structure

We built a *de novo* Markov model in Microsoft Excel, as depicted in Figure 5.1. The model structure is based partly on prior published models that evaluated interventions to treat chronic low back pain.[88,89] A representative cohort of patients with chronic low back pain, defined as low back pain lasting for at least three months,[90] entered the model. Patients transitioned between health states during six-month cycles over a five-year time horizon. We did not use a lifetime horizon because of the short duration of the interventions (12 weeks or less), a lack of data regarding durability of treatment effects beyond one year, and an absence of data on subsequent lines of therapy following intervention failure. The model used a 3% discount rate for costs and health outcomes, and costs were converted to 2016 US dollars.

The model consisted of three health states: chronic pain, pain improved, and death. Patients entered the model in the chronic pain health state, and could remain in that health state or transition to a pain improved state or death at the beginning of each cycle. Patients in the pain improved health state remained there until they either relapsed to chronic pain or died from other causes (i.e., background mortality). Patients with no improvement in pain after initial therapy were assumed to cease treatment and returned to receiving usual care. In subsequent cycles, they either remained in a state of chronic pain or experienced spontaneous improvement in pain, which was assumed to occur at the same rate as pain improvement associated with usual care. Because none of the treatments were assumed to have any effect on mortality, deaths were modeled using age-specific all-cause mortality rates alone.

Figure 5.1. Markov Model Structure for Chronic Low Back Pain Patients



Target Population

The modeled population was patients with chronic low back pain who were untreated or had not previously been treated with any of the included interventions. Chronic back pain excluded back pain due to cancer, infection, inflammatory arthropathy, high-velocity trauma, fracture, or pregnancy, and that is not associated with progressive neurological deficits. The mean age of the population in the model was 47 years, and 60% of patients were female, based on the compositions of populations seen in trial data.[12,13]

Key Model Characteristics

The base-case analysis was conducted from a health care system perspective, and thus focused on all direct intervention costs and medical care costs. For a more detailed description of the types of impacts included in this analysis from a health care system perspective, see the impact inventory in Appendix Table E1. All future costs and outcomes were discounted at 3% per year.

Key Model Assumptions

The model was informed by several assumptions, as listed in Table 5.1.

Table 5.1. Key Model Assumptions

Assumption	Rationale
The model utilized data from multiple trials and observational studies to derive effectiveness estimates for each intervention.	Given the paucity of head-to-head comparisons, we did not utilize any formal indirect treatment comparison methods.
The model did not assume subsequent lines of therapy for those who had not improved or had a relapse of pain.	We did not find any evidence on the relative effectiveness of chronic back pain therapies following prior treatment failure. Additionally, the objective of this analysis was to model different treatment alternatives for low back pain and not different treatment pathways.
We assumed the same probability of treatment response for all active interventions except tai chi.	Our evidence review of the trial data concluded that the four other interventions had similar efficacy, with very small differences seen between interventions.
We have not modeled adverse events related to any of the included interventions.	Based on the clinical trials and observational data reviewed, we found no mention of specific adverse events severe enough to accrue costs or disutilities associated with any of the therapies included.
Spontaneous improvement in pain following unsuccessful treatment with any of the listed interventions is assumed to be the same as pain improvement with usual care.	We have not found any published literature on spontaneous pain improvement following intervention failure.
Those with pain improvement and without relapse (whether via usual care or any intervention) were assumed to have constant quality of life, without any deterioration over time.	We found no evidence on declining efficacy of interventions over time, or any evidence on utilities or effectiveness beyond the first year of treatment. Trial follow-up periods lasted no longer than 52 weeks from initiation of intervention.
Recurrence (relapse) of chronic back pain was not assumed to be intervention-specific; the same estimate has been applied to all interventions and comparators.	No published evidence on intervention-specific recurrence was available.
Patients with relapsed pain following an intervention accrued costs (background care costs) and QALYs associated with chronic pain.	Due to a lack of published evidence, we assumed patients would revert to their baseline level of chronic pain.

QALY: quality-adjusted life year

Treatment Strategies

The interventions included in the model were the same as those in the clinical evidence review (acupuncture, CBT, MBSR, yoga and tai chi). All interventions except acupuncture were assumed to be offered in a group format, in keeping with the clinical trials.[12-14] We compared each intervention to usual care, which included self-care guidance and educational information on stretching, strengthening, exercise, and lifestyle modifications. As described in the key assumptions table, both interventions and usual care were assumed to be initiated with a one-time doctor's office visit lasting 15 minutes and 25 minutes, respectively. We assumed that the 15-minute visit would primarily involve referral to one of the interventions of interest, while the longer 25-minute visit would include discussion between the patient and doctor about usual care for chronic low back pain. As described above, all interventions were assumed to be completed during the first six-month cycle of the model, and we did not model subsequent lines of therapy when patients were unsuccessfully treated with an intervention or relapsed following therapy.

Table 5.2. Frequency of Interventions to Treat Chronic Low Back Pain

Intervention	Frequency	Source
Acupuncture	Two sessions/week for three weeks followed by one session/week for four weeks	Cherkin et al., 2009[11]
CBT	Two sessions/week for eight weeks	Cherkin et al., 2016[12]
MBSR	Two sessions/week for eight weeks	Cherkin et al., 2016[12]
Yoga	One session/week for 12 weeks	Sherman et al., 2011[13]
Tai Chi	Two sessions/week for eight weeks followed by one session/week for two weeks	Hall et al., 2011[14]

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction

Clinical Inputs

Transition probabilities between chronic pain and pain improved health states for each intervention were derived using a rounded average from relevant clinical trials (Table 5.3). Transition probabilities for chronic low back pain were based on the percentage of patients who had a clinically meaningful improvement in pain on the RMDQ. A clinically-meaningful improvement in pain was defined as a ≥ 30% decrease in RMDQ score from baseline.[74,91] Given the six-month cycle length of the model, we used the percentage of patients with a clinically meaningful improvement in RMDQ reported at 26 weeks in the trials for all interventions except tai chi. The longest reported follow-up with tai chi was only 10 weeks after baseline, so we assumed that the percentage of patients with clinically meaningful improvement in pain at 10 weeks was the same at 26 weeks.

As mentioned earlier in the model assumptions section, we assumed the same transition probability of moving from a chronic pain health state to an improved pain health state for all active interventions except tai chi. This was because the likelihood of clinical improvement in separate trials for each intervention varied over only a very narrow range (acupuncture: 0.58 – yoga: 0.66), and there were a paucity of data directly comparing these interventions. We nevertheless used summary estimates specific to each intervention in sensitivity analyses.

The transition probability for recurrence of pain (i.e., relapse) was derived from a previously published cost-effectiveness model of chronic low back pain. The model, by Norton et al., included an annual rate of recurrence based on observational data, which we converted to a six-month probability (formula in Appendix Table E2).[88] Patients also had a probability of death from all causes, which was derived using age- and gender-adjusted US general population mortality rates.[92]

As mentioned in the assumptions table, the interventions included here were assumed to have no effect on mortality.

Table 5.3. Transition Probabilities for Pain Improvement or Recurrence

	Mean	Lower Range	Upper Range	Source
Acupuncture	0.600*	0.480†	0.720†	Cherkin et al., 2009[11]
CBT	0.600*	0.492	0.676	Cherkin et al., 2016[12]
MBSR	0.600*	0.520	0.703	Cherkin et al., 2016[12]
Yoga	0.600*	0.560	0.780	Sherman et al., 2011[13]
Tai Chi	0.500	0.450‡	0.600†	Hall et al., 2011[14]
Usual Care	0.441	0.359	0.542§	Cherkin et al., 2016[12]
Recurrence	0.259	0.126	0.346	Calculation, Norton et al., 2015[88]

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction

All transition probabilities are six-month probabilities.

*Average of transition probabilities for acupuncture, CBT, mindfulness therapy and yoga reported in studies.

†Assumed range of 20% around the point estimate.

‡Does not represent a 20% lower-end range. Assumed to be greater than the mean estimate of effectiveness associated with usual care in the one-way sensitivity analysis.

§Assumed to be lower than the mean estimate of effectiveness in the one-way sensitivity analysis for tai chi.

Quality of Life Inputs

Health state utilities were obtained from trial data and applied to the chronic pain and pain improved health states (Table 5.4).[15] The trial was conducted in a sample of 234 patients with chronic low back pain in the UK, randomized to receive either a community-based CBT program (two hours per week for eight weeks) or general practitioner care. Utilities were measured using the EuroQoL (EQ-5D) instrument at baseline and followed up at different time points up to 15 months from baseline. We assumed that utility values for the same health states did not vary across interventions in the model, and also assumed that the health state utilities did not vary across interventions after patients relapsed to back or neck chronic pain states.

Table 5.4. Health State Utilities

	Base Case	Lower Range	Upper Range	Std. Dev	Source
Chronic Pain (Baseline) – Low back	0.66	--	--	0.22	Johnson et al., 2007[15]
Pain Improved – Low Back	0.75	0.675	0.825	0.24	Johnson et al., 2007[15] Ranges Assumed
Death	0	0	0	--	Convention

Std. Dev: standard deviation

Cost Inputs

Costs included all direct costs of care, including intervention and usual care costs for chronic low back as well as background health care costs. As several of these interventions may not currently be covered by payers, we included out-of-pocket prices reported in the grey literature as part of direct costs. Intervention costs are one-time costs that were applied in the first cycle of the model. The fee for a one-time doctor's office visit lasting either 15 minutes or 25 minutes was added to the cost of each intervention or usual care, respectively. Since usual care consisted of self-care, no additional costs (except background health care costs) were added to this arm. All intervention costs listed in Table 5.5 are per-session costs, based on sessions provided in a group format, except for acupuncture and usual care, which are provided to patients on an individual basis.

Background health care costs included additional office visits, hospital stays, laboratory tests, and pharmacologic therapy, and differed based on health state.[16] Those in the pain improved state were assumed to have only 43% of background health care costs of those in the chronic pain state, as reported in a matched healthcare claims analysis of patients with and without a diagnosis of chronic low back pain.[24]

All costs were inflated to 2016 US dollars using the medical care component of the US Consumer Price Index.[17]

Table 5.5. Cost Inputs

Service	Cost		Source
Acupuncture (per session)	$104*		Zhang, 2014[18]
CBT (per session)	$106		Gore et al., 2012[19]
Yoga (per session)	$60		Thumbtack[20]
MBSR (per session)	$77		UMass Medical School Center for Mindfulness in Medicine[21]
Tai Chi (per session)	$18		The Tai Chi Center[22]
Office Visit Costs for Active Intervention†	$52		Centers for Medicare & Medicaid Services[23]
Usual Care Costs (total)‡	$109*		Centers for Medicare & Medicaid Services[23]
Background Care Costs per Patient per Cycle	**Chronic Pain**	**Improved Pain§**	**Source**
Physician Visits	$78	$34	Fritz et al., 2012;[16] Gore et al., 2012[24]
Emergency Room Visits	$7	$3	
Prescription Medication	$39	$17	
Imaging Procedures	$108	$47	
Inpatient Non-Surgical Procedures	$30	$13	
Injection/Surgical Procedures	$275	$119	
Other Pain-Related Costs	$163	$71	

*One-on-one session

†Assumed to be one office visit pertaining to referral to active intervention, using CPT code 99213 for an established patient visit for a 15-minute duration.

‡Assumed to be one office visit pertaining to obtaining patient education book on self-care, using CPT code 99214 for an established patient visit for a 25-minute duration.

§Assumed 43% of costs seen in patients with chronic pain, derived from Gore et al., 2012, comparing health care costs for patients with chronic low back pain and population without chronic low back pain.

Adverse Events

We found no mention of specific adverse events severe enough to accrue costs or disutilities associated with any of the therapies included here, and therefore did not include adverse events in the model.

Mortality

None of the interventions included had a mortality effect. Only background all-cause mortality, obtained from age- and gender-adjusted US general population mortality rates, was included in the model.[92]

Sensitivity Analyses

We ran one-way sensitivity analyses to identify the key drivers of model outcomes. We also ran probabilistic sensitivity analyses comparing each intervention to usual care by simultaneously varying key model inputs using appropriate distributions over 5,000 simulations, then calculating the probability of each intervention being cost-effective at three commonly-cited cost-effectiveness thresholds. Relevant scenario analyses were also conducted where adequate data were available, including varying time horizons to one or three years, using a modified societal perspective including productivity loss, and using point estimates for effectiveness of each of the interventions as reported in the trials.

Cost-Effectiveness Model: Results

Base-Case Results

Each of the nonpharmacologic interventions resulted in increased costs and QALYs compared to usual care over the five-year time horizon. Total costs over five years ranged from approximately $5,000 for tai chi to approximately $6,300 for CBT (Table 5.6). Incremental costs compared to usual care ranged from approximately $200 for tai chi to approximately $1,600 for CBT (Table 5.7). Since we assumed the same transition probabilities for all active interventions except tai chi, QALY gains were the same for all remaining interventions, with very small incremental gains compared to usual care (0.010). Tai chi had an even smaller incremental QALY gain of 0.004 relative to usual care. All interventions except CBT were estimated to fall within the upper bound of the commonly-cited threshold of $150,000 per QALY gained relative to usual care, with yoga being most cost-effective at approximately $58,000 per QALY gained.

Because we used the same utility estimates for all interventions, the same response rate to therapy for all interventions except tai chi, and the same relapse rate for all interventions, the variation in the incremental cost-effectiveness ratios across interventions is primarily driven by the differences in individual intervention costs.

Table 5.6. Base-Case Deterministic Results

Therapy	Costs	QALYs
Acupuncture	$5,657	3.2875
CBT	$6,316	3.2875
MBSR	$5,852	3.2875
Yoga	$5,342	3.2875
Tai Chi	$4,992	3.2813
Usual Care	$4,767	3.2776

CBT: cognitive-behavioral therapy, MBSR: mindfulness-based stress reduction, QALY: quality-adjusted life year

Table 5.7. Base-Case Deterministic Incremental Results Versus Usual Care

Therapy	Incremental Costs	Incremental QALYs	Incremental Cost-Effectiveness Ratio vs. Usual Care (Cost per QALY Gained)
Acupuncture	$891	0.0099	$89,888
CBT	$1,549	0.0099	$156,331
MBSR	$1,085	0.0099	$109,486
Yoga	$575	0.0099	$58,017
Tai Chi	$225	0.0037	$61,265
Usual Care	--	--	--

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction, QALY: quality-adjusted life year

Among the five interventions, the incremental cost of achieving one case of improved pain over the five-year time horizon relative to usual care ranged from approximately $6,200 for tai chi to approximately $15,800 for CBT (Table 5.8). Because each intervention's benefit (i.e., pain improvement) occurred within the first two cycles of the model and subsequent benefit was spontaneous and non-intervention related, we used the number of cases with improved pain at the end of one year of treatment.

Table 5.8. Incremental Cost per Successful Treatment (Pain Improvement) Versus Usual Care

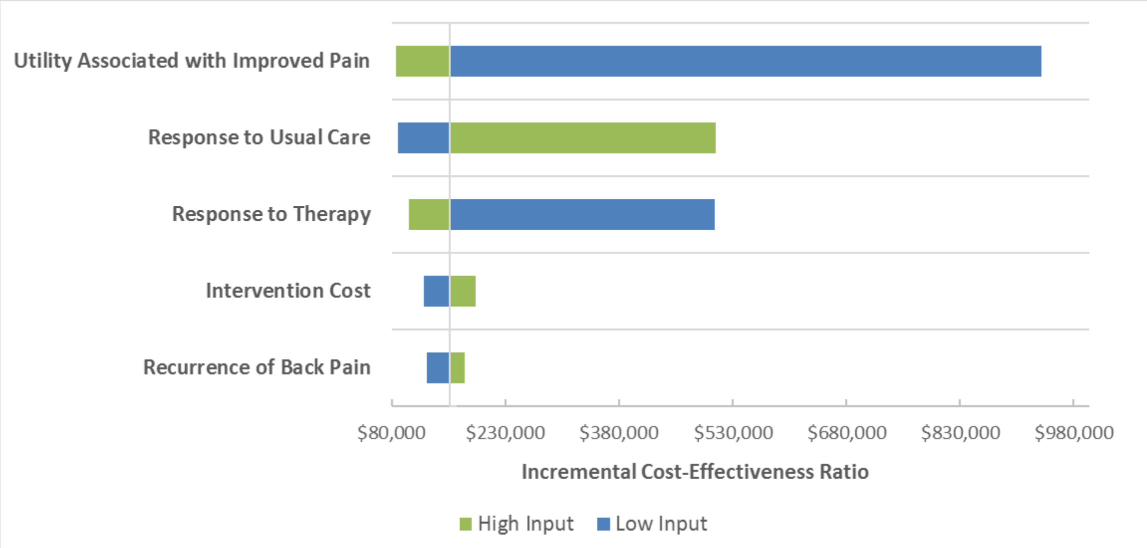
Therapy	Costs
Acupuncture	$9,067
CBT	$15,770
MBSR	$11,044
Yoga	$5,852
Tai Chi	$6,180

CBT: cognitive-behavioral therapy, MBSR: mindfulness-based stress reduction, QALY: quality-adjusted life year

One-Way Sensitivity Analyses

One-way sensitivity analyses were conducted for each intervention by varying key model parameters. As an example, we have presented the results for the one-way sensitivity analysis for CBT in Figure 5.2 and Table 5.9. We chose to present the results of CBT in the report since it was the least cost-effective intervention in our analysis. Results of one-way sensitivity analyses for the other interventions are available in Appendix Tables E4-E8 and Figures E1-E4. The health-state utility associated with improved pain had the largest impact on incremental cost-effectiveness for each of the interventions relative to usual care, except in tai chi where results were most sensitive to response to the intervention. Results were also sensitive to response to usual care (i.e., probability of pain improvement associated with usual care) and to individual intervention costs. Intervention costs were not the most sensitive variable because they were incurred only once, in the first model cycle. Results were least sensitive to the probability of back pain recurrence.

Figure 5.2. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Cognitive Behavioral Therapy Versus Usual Care



Base-case ICER: $156,331 per QALY gained

Table 5.9. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Cognitive Behavioral Therapy Versus Usual Care

	Low Input	High Input	Low Value	High Value	Range
Intervention Cost	$84.71	$127.06	$122,136	$190,526	$68,390
Response to Therapy	0.492	0.676	$506,202	$102,899	$403,303
Response to Usual Care	0.359	0.542	$87,671	$507,829	$420,157
Recurrence of Back Pain	0.126	0.356	$125,802	$176,386	$50,584
Utility Associated with Improved Pain	0.675	0.825	$937,987	$85,272	$852,715

Probabilistic Sensitivity Analysis Results

We also conducted a probabilistic sensitivity analysis, jointly varying model inputs over 5,000 simulations. Incremental cost-effectiveness ratios (ICERs) for CBT were lower than the commonly-cited cost-effectiveness threshold of $150,000 per QALY in approximately 36% of simulations, while ICERs for yoga were lower than the threshold in approximately 95% of simulations. These incremental cost-effectiveness ratios were under the threshold in approximately 65% of all simulations for acupuncture and MBSR, and in approximately 66% of all simulations for tai chi. The probabilistic sensitivity analysis results are shown in Appendix Table E8 and Figures E5-14.

Scenario Analyses - Results

Time Horizon

Shortening the model time-horizon to one and three years increased the incremental cost-effectiveness results for all interventions relative to usual care, with all interventions showing levels of cost-effectiveness greater than the commonly-cited threshold of $150,000 per QALY. Using a one-year time horizon, the results ranged from approximately $179,000 per QALY gained for yoga to approximately $456,000 per QALY gained for CBT. These results are driven by the small QALY gain for each intervention relative to usual care, along with the fact that all intervention costs occur in the first year. Using a three-year time-horizon, incremental cost-effectiveness results were very similar to the results seen in the base-case analysis, ranging from approximately $58,000 per QALY gained for yoga to approximately $157,000 per QALY gained for CBT. Incremental cost-effectiveness results for each intervention at the one- and three-year time horizon are available in Appendix Table E3.

Modified Societal Perspective

In this scenario analysis, we included costs associated with lost productivity in patients with chronic low back pain in the model. According to the Bureau of Labor Statistics, approximately 80% of the population in the 25- to 54-year age group fell under the category of civilian labor force participation, which is the percentage of population that is currently employed or seeking employment.[17] Applying this percentage to the per-person productivity loss reported in a study by the Integrated Benefits Institute, and inflating to 2016 dollars resulted in a per-person productivity loss of approximately $146 over six months (the model cycle length).[93,94] We did not include costs associated with productivity loss to care-givers due to a lack of published evidence specific to low back pain. Including productivity losses produced incremental cost-effectiveness results very similar to those seen in the base-case, ranging from approximately $54,800 per QALY gained for yoga to approximately $153,100 per QALY gained for CBT, relative to usual care over the five-year time-horizon. Incremental cost effectiveness results for each intervention relative to usual care can be found in Appendix Table E4.

Trial-reported Intervention Effectiveness Estimates

In this scenario analysis, we used the estimates for clinically-meaningful response to therapy as reported in the trials instead of the average used in the base-case analysis. The input for tai chi did not differ from the base-case model, which already used a trial result. Compared to the base case results, incremental cost-effectiveness results for all interventions except yoga were greater, with results ranging from approximately $39,700 per QALY gained for yoga to approximately $184,300 per QALY gained for CBT over five years.

Table 5.10. Incremental Cost Effectiveness Results Versus Usual Care Using Trial-Reported Intervention Effectiveness Estimates

Therapy	Incremental Cost-Effectiveness Ratio vs. Usual Care (Cost per QALY Gained)
Acupuncture	$104,100
CBT	$184,272
MBSR	$105,877
Yoga	$39,688
Tai Chi	$61,265*
Usual Care	--

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction, QALY: quality-adjusted life year
*Same as base-case result

Threshold Analysis

For each intervention, prices per session that would achieve commonly-cited cost-effectiveness thresholds ranging from $50,000 to $150,000 per QALY gained are presented in Table 5.11, along with the base-case cost per session. The price per session at the three cost-effectiveness thresholds for cognitive behavioral therapy and mindfulness-based stress reduction are equal since both interventions have the same number of sessions and the same rate treatment efficacy.

Table 5.11. Threshold Analysis of Cognitive and Mind-Body Therapies for Chronic Low Back Pain

Intervention	Base-Case Cost per Session	Price to Achieve $50,000 per QALY	Price to Achieve $100,000 per QALY	Price to Achieve $150,000 per QALY
Acupuncture	$103.58	$64.06	$113.60	$163.15
CBT	$105.89	$40.03	$71.00	$101.97
MBSR	$76.88	$40.03	$71.00	$101.97
Yoga	$60.00	$53.38	$94.67	$135.95
Tai Chi	$17.50	$15.20	$25.41	$35.63

Model Validation and Prior Published Evidence on Costs and Cost-Effectiveness

Model validation followed standard practices in the field. We tested all mathematical functions in the model to ensure they were consistent with the report. We also conducted sensitivity analyses with null input values to ensure the model produced findings consistent with expectations. Two modelers tested the mathematical functions in the model as well as therapy-specific inputs and corresponding outputs.

We also compared the ICER model to previously published models. We searched the literature to identify models that were similar to ours, with comparable populations, setting, perspective and treatments.

Norton et al. developed a cost-utility model comparing CBT to active exercise in patients with chronic low back pain from a US commercial payer perspective.[88] They reported incremental cost-effectiveness results that were much lower than in the ICER model ($7,197 vs. $156,331 per QALY gained). Although the ICER model used the same probability of back pain recurrence as in the Norton et al. model, the contrasting results can be attributed to several other differences between the two models. First, a longer time horizon (10 years) was used in the Norton et al. model than in the ICER model (five years). Second, a lower probability of transition (0.31) to an improved pain state for usual care was used in the Norton model compared to the ICER model (0.441). Third, the Norton model used the initial transition probability of pain improvement resulting from CBT (0.59) but with a 20% decrement in each subsequent cycle, whereas in the ICER model treatment benefit of CBT was applied only to the first cycle, after which pain improvement was assumed to occur only spontaneously.

Kim et al. developed a Markov model for low back pain in patients in South Korea over a five-year time horizon from a societal perspective.[89] Patients entered the model with acute low back pain and could transition between no pain and/or chronic low back pain health states. This model compared acupuncture to usual medical care. Although this model had similar baseline utility estimates for chronic pain (0.65), the Kim et al. model accrued higher QALYs (4.24) relative to the ICER model (3.29), predominantly due to higher utility estimates for the pain improved state (Kim et al.: 0.96 vs. ICER: 0.75). In other respects, the Kim et al. model is not comparable to the ICER model (i.e., differences in perspective, setting, modeled health states and costs).

A cost-utility analysis by Thomas et al. compared acupuncture to usual care using clinical evidence from a randomized controlled trial set in three acupuncture clinics in the United Kingdom.[95] Patients' quality-of-life was measured using the SF-6D and EQ-5D questionnaires. Patient sample sizes in the model were reduced to reflect the number of individuals who responded to the questionnaires in the trial. Among a total of 123 patients with follow-up at 24 months in the acupuncture group, 78 patients completed the SF-6D questionnaire and 85 patients completed the EQ-5D questionnaire. There was a statistically-significant difference in mean costs between the acupuncture and usual care group, but the mean difference in QALYs using the EQ-5D was not statistically significant, with a 95% confidence interval ranging from -0.036 to 0.178 (mean difference = 0.071). Using a National Health Service perspective, the authors reported an incremental cost-effectiveness ratio of £4,241 ($11,304[i]) per QALY gained using SF-6D (mapped

[i] In this section, British pounds were converted to US dollar amounts using the annual average exchange rate from the year of comparator study analysis, and inflating the exchanged US dollar amount using the medical care CPI from the year of study analysis to the 2017 six-month average medical care CPI.[96]

from SF-36) and £3,598 ($9,590) per QALY gained using EQ-5D over a two-year time-horizon. The ICER model estimated a substantially higher cost-utility ratio for acupuncture (at $89,888 per QALY gained). Key methodological differences between the two models may contribute to the difference in results. The ICER model allowed for worsening pain and associated cost as well as disutility, whereas the Thomas et al. model focused only on utility improvement at a single point in time. Thomas et al. modeled treatment efficacy and subsequent outcomes only for the duration of the trial using utility data directly from the trial, whereas the ICER model estimates intervention efficacy and cost outcomes beyond trials' duration, extending to a period of five years, by making assumptions around intervention efficacy (i.e., no additional intervention-related efficacy following the first cycle of the ICER model) The increase in quality of life from chronic pain to pain improvement with acupuncture was also higher in the Thomas et al. model than in the ICER model (i.e., 0.202 using EQ-5D vs. 0.09). Finally, our assumed costs of acupuncture were significantly higher than those estimated in the UK model ($1,036 vs. £214 [$570] in the ICER and UK models respectively), and other background costs were much higher as well.

We adjusted our model structure to mimic that of the Thomas model. Assuming no pain recurrence and sustained intervention efficacy through the time-horizon of our model resulted in an incremental cost-effectiveness ratio of $29,885 per QALY gained, which is lower than the upper-end range of cost-effectiveness reported by Thomas et al. (£28,026 [$74,698] using SF-6D and £22,149 [$59,034] using EQ-5D).

5.2 Value-Based Benchmark Prices

Our value-based benchmark prices for the five cognitive and mind-body therapies for low back pain are presented in Table 5.12. As noted in the ICER methods document,[97] the value-based benchmark prices for a drug (or non-drug intervention) are defined as the prices that would achieve incremental cost-effectiveness ratios of $100,000 and $150,000 per QALY gained. As none of these interventions have a single, consistent price reported in the literature, we have presented the discounts from the assumed base case price per session that would be required to achieve the three cost-effectiveness thresholds. Note that while the per-session costs may vary, the total cost of each intervention at each threshold would be equal for all interventions except tai chi, as these interventions were awarded the same probability of effectiveness in the model. Threshold prices for cognitive behavioral therapy would require discounts from the base-case price, as would the price to reach the $100,000 per QALY threshold for mindfulness-based stress reduction. Threshold prices for acupuncture, yoga and tai chi (and the price at the $150,000 per QALY threshold for mindfulness-based stress reduction) were higher than the base-case price estimates.

Table 5.12. Value-Based Benchmark Prices per Session of Cognitive and Mind-Body Therapies for Chronic Low Back Pain

Intervention	Cost per Session	Price to Achieve $100,000 per QALY	Price to Achieve $150,000 per QALY	Discount/Premium from Current Cost to Reach Thresholds
Acupuncture	$103.58	$113.60	$163.15	+10% to +58%
CBT	$105.89	$71.00	$101.97	4% to 33%
MBSR	$76.88	$71.00	$101.97	8% to +33%
Yoga	$60	$94.67	$135.95	+58% to +127%
Tai Chi	$17.50	$25.41	$35.63	+45% to +104%

CE: cost-effectiveness, QALY: quality-adjusted life year
"+" Indicates premium

5.3 Potential Budget Impact

Potential Budget Impact Model: Methods

We used results from the same model employed for the cost-effectiveness analyses to estimate total potential budget impact. Potential budget impact was defined as the total differential cost of using the specific low back pain interventions rather than usual care for the treated population, calculated as differential health care costs minus any offsets in these costs from averted health care events. All costs were undiscounted and estimated over one- and five-year time horizons. The five-year timeframe was of primary interest, given the potential for cost offsets to accrue over time and to allow a more realistic impact on the number of patients treated with the therapies not covered by payers.

The potential budget impact analysis included a hypothetical candidate population for treatment that consisted of adults with chronic low back pain for at least three months with pain not due to cancer, infection, inflammatory arthropathy, high-velocity trauma, fracture, or pregnancy, and that is not associated with progressive neurological deficits. We derived the number of eligible patients with chronic low back pain for a hypothetical cohort of 1 million members of a managed care organization. With a point prevalence of 13.1%, based on The National Health and Nutrition Examination Survey (NHANES, 2009–2010), applied to the hypothetical cohort of 1 million members, the number of patients with chronic low back pain was estimated to be 131,000.[25] According to a survey by the American Physical Therapy Association (APTA), only 63% of all patients with low back pain seek professional help for pain relief.[26] Applying this percentage to the estimated population with chronic low back pain resulted in an eligible population of 16,506 patients each year, for a total of 82,530 patients over all five years.

We included only MBSR, yoga, and tai chi in the budget impact analysis, deriving the budget impact of each of these interventions relative to usual care. We did not include the other interventions, as evidence suggests that some payers currently cover them (Section 3.1). We modeled these interventions against usual care, varying their uptake over five years to 10%, 25% and 50% of the eligible population. In addition to reporting the results for each intervention over five years, we have also reported the per member per month (PMPM) cost for each intervention relative to usual care. The PMPM cost is the total monthly spending on a pool of insured members of a plan divided by the total number of plan members. ICER's methods for estimating potential budget impact are described in detail elsewhere and have recently been updated.[97]

Potential Budget Impact Model: Results

Yoga

Annual potential budget impact ranged from approximately $966,000 to approximately $4.8 million when treating 10% (2% per year) to 50% (10% per year) of the eligible cohort with yoga relative to usual care. The average potential budget impact over the five-year period was $274 per patient (Table 5.13). The per member per month (PMPM) cost ranged from $0.08 to $0.40 when treating 10% to 50% of the eligible cohort with yoga (Figure 5.3).

Mindfulness-Based Stress Reduction

Annual potential budget impact ranged from approximately $1.8 million to approximately $9 million when treating 10% to 50% of the eligible cohort with MBSR relative to usual care. The average potential budget impact over the five-year period was $507 per patient (Table 5.13). The PMPM cost ranged from $0.15 to $0.75 when treating 10% to 50% of the eligible cohort with MBSR (Figure 5.3).

Tai Chi

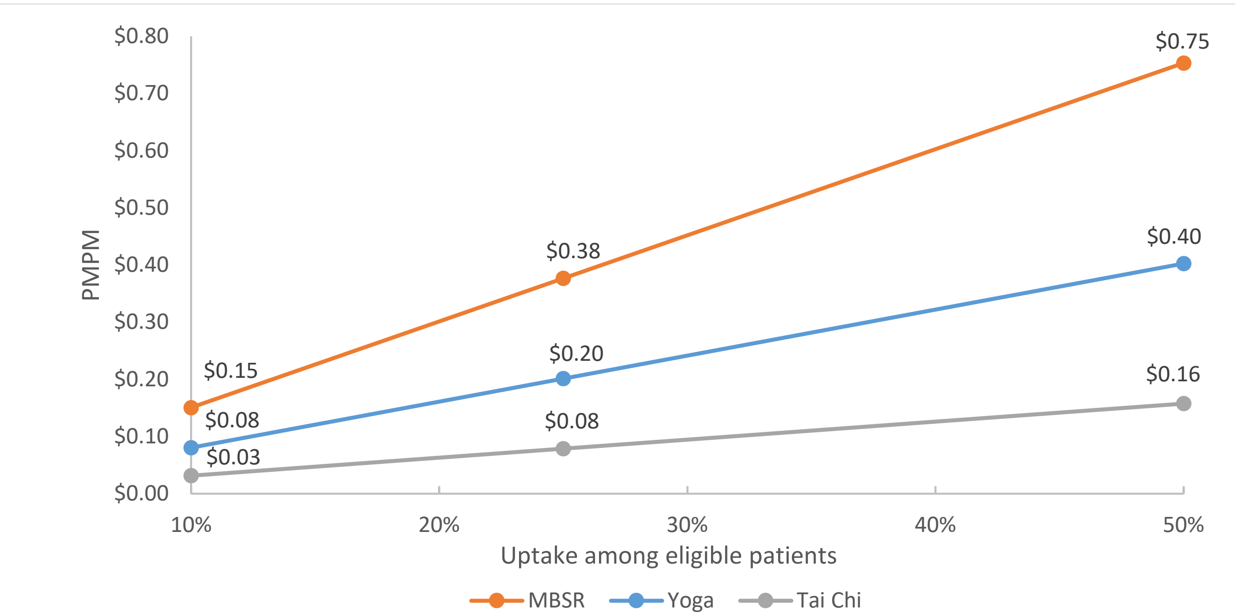
Annual potential budget impact ranged from approximately $378,000 to approximately $1.9 million when treating 10% to 50% of the eligible cohort with tai chi relative to usual care. The average potential budget impact over the five-year period was $107 per patient (Table 5.13). The per-member per-month cost ranged from $0.03 to $0.16 when treating between 10% and 50% of the eligible cohort with tai chi (Figure 5.3).

Table 5.13. Annualized Per Patient Potential Budget Impact Calculations Over a Five-Year Time Horizon

	Average Annualized Per-Patient Budget Impact			
	Yoga	MBSR	Tai Chi	Usual Care
Per-Patient Budget Impact	$1,426	$1,659	$1,259	$1,152
Difference (Intervention – Usual Care)	$274	$507	$107	--

MBSR: mindfulness-based stress reduction

Figure 5.3. Per-Member Per-Month Cost for Yoga, MBSR, and Tai Chi at Varying Percentages of Treatment Uptake Among the Eligible Cohort



By way of comparison, Express Scripts estimates that its 2017 expenditures for medications to treat pain and inflammation, including mostly generic NSAIDs, gamma-aminobutyric acid (GABA) analogs, and opioids, will total $4.46 PMPM.[27] Our highest budget impact estimate ($0.75 PMPM if 50% of the eligible population were treated with MBSR) would represent only 17% of this PMPM spend.

5.4 Summary and Comment: Long-Term Cost Effectiveness and Potential Budget Impact

We estimated the cost-effectiveness of acupuncture, CBT, MBSR, yoga, and tai chi compared to usual care for patients with chronic low back pain. We did not model chronic neck pain for any of the nonpharmacologic interventions due to a lack of published evidence on key model inputs. The cost per additional QALY ranged from approximately $58,000 for yoga to approximately $156,000 for CBT over a five-year time horizon. The findings were most sensitive to the health state utility associated with an improvement in pain, patient response to usual care, and intervention costs. The findings were also sensitive to time horizon, with a shorter time horizon resulting in increased incremental cost-effectiveness results relative to usual care. A scenario analysis using a modified societal perspective produced results similar to those in the base-case analysis.

Our model had several limitations. First, we did not model varying treatment effectiveness over time due to availability of only short-term trial data. We assumed that effectiveness of the intervention occurred only in the first cycle when patients receive an intervention, after which improvement in pain status mirrored that of improvement seen with usual care. Second, we did not model subsequent lines of intervention (and resulting pain improvement) for individuals who experienced a recurrence of low back pain due to a lack of published evidence on this estimate. The objective of this analysis was to model different treatment alternatives for low back pain and not different treatment pathways. We assumed that pain improvement after recurrence would only occur as spontaneous pain improvement, which was assumed to have the same probability of pain improvement as usual care. Third, the background health care costs for those with improved pain were derived from a claims analysis by Gore et al., which consisted of a control cohort *without* back pain (i.e., not with "improved pain"). Fourth, we assumed 100% adherence to each intervention, which would not necessarily occur in actual practice. Finally, our base-case cost and cost-effectiveness results for the nonpharmacologic interventions reflect current evidence available on average intervention costs, which may vary widely by region and level of insurance coverage.

We examined the budget impact of three interventions, MBSR, yoga, and tai chi, that are not routinely covered by insurance. Our analysis looked at different levels of uptake, and at a high rate of uptake of 50% for the most expensive of the three interventions (MBSR), the additional PMPM cost would be $0.75. For comparison, this is approximately 17% of the estimated PMPM medication costs for treating pain/inflammation at a large national pharmacy benefits management company.

6. Other Benefits and Contextual Considerations

Our reviews seek to provide information on other benefits or disadvantages offered by the intervention to the individual patient, caregivers, the delivery system, other patients, or the public that would not have been considered as part of the evidence on comparative clinical effectiveness. These elements are listed in the table below.

Table 6.1. Potential Other Benefits or Contextual Considerations

Potential Other Benefits
This intervention provides significant direct patient health benefits that are not adequately captured by the QALY.
This intervention offers reduced complexity that will significantly improve patient outcomes.
This intervention will reduce important health disparities across racial, ethnic, gender, socio-economic, or regional categories.
This intervention will significantly reduce caregiver or broader family burden.
This intervention offers a novel mechanism of action or approach that will allow successful treatment of many patients who have failed other available treatments.
This intervention will have a significant impact on improving return to work and/or overall productivity.
Other important benefits or disadvantages that should have an important role in judgments of the value of this intervention.
Potential Other Contextual Considerations
This intervention is intended for the care of individuals with a condition of particularly high severity in terms of impact on length of life and/or quality of life.
This intervention is intended for the care of individuals with a condition that represents a particularly high lifetime burden of illness.
This intervention is the first to offer any improvement for patients with this condition.
Compared to surveillance with no maintenance chemotherapy, there is significant uncertainty about the long-term risk of serious side effects of this intervention.
Compared to surveillance with no maintenance chemotherapy, there is significant uncertainty about the magnitude or durability of the long-term benefits of this intervention.
There are additional contextual considerations that should have an important role in judgments of the value of this intervention.

Although uncertainty remains about the impact of cognitive and mind-body therapies on long-term management of chronic low back and neck pain, these therapies may provide additional benefits that are not adequately captured in the clinical literature. For example, chronic pain has impacts on everyone that the patient touches. Improved management of chronic pain will likely reduce caregiver / family burden. Chronic low back pain, in particular, is a major cause of both short- and long-term disability. The benefits of the mind-body interventions are modest at best, but may help some patients return to work or be more productive at their job. In addition, they may allow some patients to reduce or stop taking daily opioid therapy to manage their pain, thus reducing the risk for the harms associated with opioid therapy.

As noted in the topic in context section, chronic back and neck pain are common and lead to significant reductions in productivity including patients requiring long-term disability. They are often life-long conditions, so small improvements in function and pain can have a substantial impact on quality of life over many years.

Conversely, the majority of the clinical trials of cognitive and mind-body interventions for chronic pain followed patients for less than a year and no studies evaluated their impact beyond two years. Continued benefits may require ongoing behavior change, for example with ongoing practice of mindfulness, yoga, or tai chi. Long-term behavior change is challenging. Thus, there remains considerable uncertainty about their long-term benefits, although they are unlikely to have any long-term harms.

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This is the first CTAF review of cognitive and mind-body therapies for chronic low back and neck pain.

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APPENDICES

Appendix A. Search Strategies and Results

Table A1. PRISMA 2009 Checklist

	#	Checklist Item
TITLE		
Title	1	Identify the report as a systematic review, meta-analysis, or both.
ABSTRACT		
Structured Summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
INTRODUCTION		
Rationale	3	Describe the rationale for the review in the context of what is already known.
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).
METHODS		
Protocol and Registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.
Eligibility Criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.
Information Sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
Study Selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).
Data Collection Process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.
Data Items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.
Risk of Bias in Individual Studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.

Summary Measures	13	State the principal summary measures (e.g., risk ratio, difference in means).
Synthesis of Results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.
Risk of Bias Across Studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional Analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
RESULTS		
Study Selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.
Study Characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
Risk of Bias within Studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).
Results of Individual Studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of Results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of Bias Across Studies	22	Present results of any assessment of risk of bias across studies (see Item 15).
Additional Analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).
DISCUSSION		
Summary of Evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
FUNDING		
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.

From: Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Table A2. Cochrane Central Register of Controlled Trials Search, June 3, 2017 (via Ovid)

1	Exp low back pain/
2	back pain or lumbago
3	tai chi
4	acupunture
5	Exp tai ji/
6	Exp cognitive therapy/
7	Exp mindfulness/
8	mindfulness
9	(1 or 2) and (3 or 4 or 5 or 6 or 7 or 8)
10	Exp neck pain/
11	cervicalgia or cervicodynia
12	(10 or 11) and (3 or 4 or 5 or 6 or 7 or 8)

Table A3. Chronic Low Back Pain Since ACP/AHRQ Review: PubMed, June 5, 2017

#1	((("Low Back Pain"[Mesh] OR ("low back" AND pain) OR "spinal stenosis"[mh] OR "spinal stenosis" OR "spinal stenoses" OR "radiculopathy"[mh] OR radiculopathy OR radicular OR "back injuries"[mh] OR "back injury" OR "back injuries" OR "spinal injuries"[mh] OR "spinal injury" OR "spinal injuries")
#2	#1 AND ("Cognitive therapy"[mh] OR "cognition therapy" OR "Cognition Therapies" OR "Cognitive Behavior Therapy" OR "Cognitive Psychotherapy" OR "Cognitive Psychotherapies" OR "Cognitive Behavior Therapies" OR "Cognitive Behavioral Therapy" OR "Cognitive Behavioral Therapies" OR "yoga"[mh] OR yoga[tiab] OR "Tai Ji"[Mesh] OR Tai-ji OR Tai Chi OR Tai Ji Quan OR Taiji OR Taijiquan OR T'ai Chi OR Tai Chi Chuan OR "Acupuncture Therapy"[mh] OR "Acupuncture"[mh] OR acupuncture[tiab] OR Pharmacoacupuncture OR Pharmacopuncture))
#3	("2015/04/27"[PDat] : "3000/12/31"[PDat])) AND (randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]))
#4	#2 AND #3

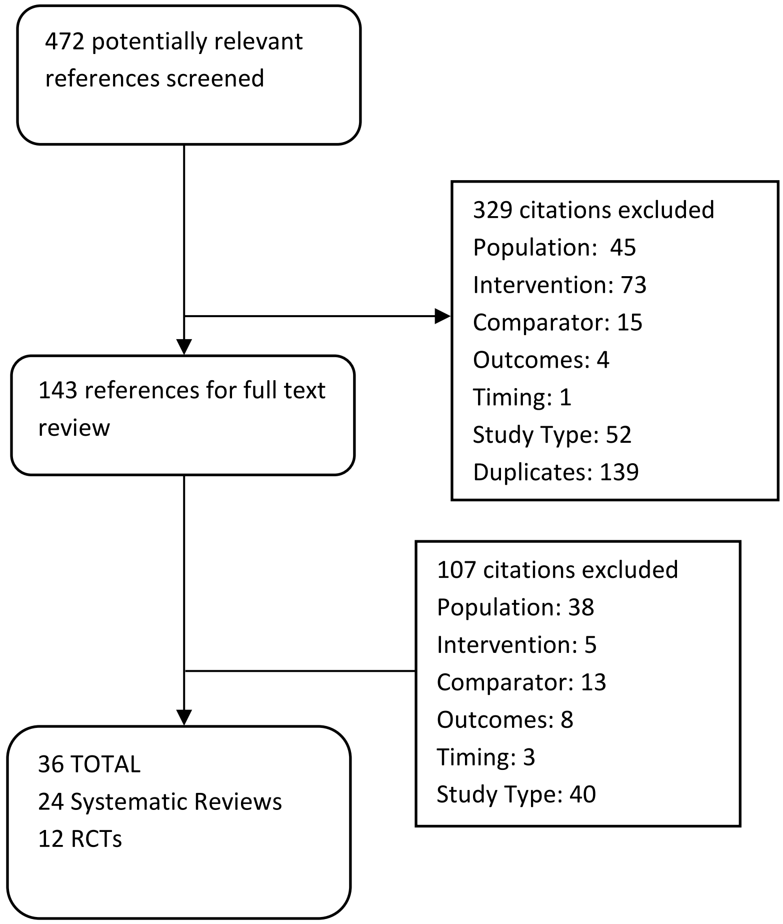
Table A4. Systematic Reviews of Chronic Neck Pain: PubMed, June 5, 2017

#1	systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]
#2	clinical guideline [tw] AND management [tw]
#3	(evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)
#4	(systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence)
#5	#1 OR #2 OR #3 OR #4
#6	literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook
#7	#5 AND #6
#8	(letter [pt] OR newspaper article [pt])
#9	#7 NOT #8
#10	“Neck Pain”[mh] OR “Neck Pains” OR “Neck Ache” OR “Neck Aches” OR “Cervicalgia” OR “Cervicalgias” OR “Cervicodynia” OR “Cervicodynias” OR “Neckache” OR “Neckaches” OR “Cervical Pain” OR “Cervical Pains”
#11	“Cognitive therapy”[mh] OR “cognition therapy” OR “Cognition Therapies” OR “Cognitive Behavior Therapy” OR “Cognitive Psychotherapy” OR “Cognitive Psychotherapies” OR “Cognitive Behavior Therapies” OR “Cognitive Behavioral Therapy” OR “Cognitive Behavioral Therapies” OR “yoga”[mh] OR yoga[tiab] OR "Tai Ji"[Mesh] OR Tai-ji OR Tai Chi OR Tai Ji Quan OR Taiji OR Taijiquan OR T'ai Chi OR Tai Chi Chuan OR “Acupuncture Therapy”[mh] OR “Acupuncture”[mh] OR acupuncture[tiab] OR Pharmacoacupuncture OR Pharmacopuncture
#12	#10 AND #11
#13	#9 AND #12

Table A5. Embase, July 2, 2017

#1	'low back pain'/exp OR (('low back' OR 'lumbosacral region'/exp) AND 'chronic pain'/exp) OR 'pain'/exp OR pain OR 'lumbar spinal stenosis'/exp OR 'spinal stenosis'/exp OR 'spinal stenosis' OR 'spinal stenoses' OR 'radiculopathy'/exp OR radiculopathy OR radicular OR ('musculoskeletal injury'/exp AND 'lumbar region'/exp) OR 'back injury'/exp OR 'back injury' OR 'back injuries'/exp OR 'back injuries' OR 'spinal injury'/exp OR 'spinal injury' OR 'spinal injuries'/exp OR 'spinal injuries'
#2	'cognitive behavioral therapy'/exp OR ‘cognition therapy’ OR 'Cognitive Behavior Therapy’ OR ‘Cognitive Psychotherapy’ OR ‘Cognitive Psychotherapies’ OR ‘Cognitive Behavior Therapies’ OR ‘Cognitive Behavioral Therapy’ OR ‘Cognitive Behavioral Therapies’
#3	‘mindfulness’/exp OR mindfulness OR ‘stress reduction’ OR ‘psychotherapy’/exp OR psychotherapy
#4	‘yoga’/exp OR ‘yoga’:ab,ti
#5	‘Tai Chi’/exp OR Tai-ji OR ‘Tai Chi’ OR ‘Tai Ji Quan’ OR Taiji OR Taijiquan OR ‘Tai Chi Chuan’
#6	‘acupuncture’/exp OR ‘acupunctur’:ab,ti
#7	Pharmacoacupuncture OR Pharmacopuncture OR ‘alternative medicine’/exp OR ‘Complementary Medicine’ OR ‘Alternative Medicine’ OR ‘Alternative Therapies’ OR CAM
#8	#2 OR #3 OR #4 OR #5 OR #6 OR #7
#9	#1 AND #8
#10	[2015-2017]/py
#11	([controlled clinical trial]/lim OR [randomized controlled trial]/lim)
#12	#10 AND #11
#13	#9 AND #12

Figure A1. PRISMA Flow Chart Showing Results of Literature Search for Cognitive and Mind-Body Therapies for Chronic Low Back and Neck Pain



Appendix B. Health Technology Assessments

CADTH[98-100]

CADTH has produced multiple reviews of guidelines on treating chronic pain, including the use of behavioral and psychological therapies. A review on the clinical and economic evidence surrounding multidisciplinary biopsychosocial treatment for chronic pain[98] found that the clinical benefit was moderate, with statistically significant differences compared with controls. However, the treatment effect was not consistent across outcomes. No economic reviews were identified.

CADTH reviewed the clinical evidence for the optimal frequency of acupuncture used to treat chronic shoulder and lower back pain.[100] The review concluded that acupuncture is practiced with varying frequency and that a systematic review assessing impacts of treatment methods on outcomes would be useful in future research. CADTH recommends that determining frequency of acupuncture sessions should be done on an individual patient basis, based on the severity of pain.

In 2012, CADTH also reviewed mindfulness training for chronic pain management.[99] Given the low-quality and sparse evidence base, no conclusions regarding the clinical benefit of mindfulness training could be drawn.

NICE[101]

The National Guideline Centre produced a systematic review and resulting set of guidelines on the clinical and economic benefits of a variety of non-invasive treatments, including acupuncture/electrotherapy, cognitive behavioral therapy, yoga, and mindfulness for low back pain with or without sciatica.

Acupuncture was not recommended as a treatment option for low back pain, primarily because its treatment effect cannot be distinguished from sham acupuncture.

CBT was recommended in combination with an active exercise therapy, with or without additional manipulative (massage, mobilization, etc.) therapies. Given the small size of the evidence base, CBT was recommended as an optional component to a treatment plan, but there was not enough evidence to determine its potential net health benefit. Cost-effectiveness evidence was also limited, so CBT was considered cost effective only when combined with physical exercise modalities. Given the very limited evidence on clinical effectiveness of mindfulness and no evidence on cost effectiveness, mindfulness was neither recommended nor not recommended by NICE.

Mind-body exercise (including yoga and tai chi) was recommended as a consideration for patients with chronic low back pain, particularly when patients preferred or requested the intervention. With mixed evidence, mind-body exercise was found to have at least small benefits compared with usual care and exercise therapy. They found that the costs of yoga and tai chi were dependent on the number of sessions provided and that individual instruction was generally more expensive than group classes. NICE summarized a previous economic evaluation that found group yoga to be cost-effective compared to usual care. They found no direct evidence on the effect of individual versus group yoga.

Appendix C. Ongoing Studies

Title, Trial Sponsor, Clinicaltrials.gov Identifier	Study Design	Treatment Arms	Patient Population	Key Outcomes	Estimated Completion Date
Predicting Analgesic Response to Acupuncture: A Practical Approach **Stanford University, National Center for Complementary and Integrative Health** **NCT02890810**	RCT Parallel Assignment Double Blind N=100	1) Verum Electroacupuncture 2) Placebo Electroacupuncture	Age 21-65 English fluency Chronic low back pain for ≥6 months Average pain over the last month ≥5/10 Exclusion Radicular low back pain Pending litigation or Worker's compensation related to low back pain Pregnant/planning to become pregnant American Society of Anesthesiologist class III or above physical status Mental health or medical conditions that would interfere with study procedures opioids ≥60mg morphine equivalent units/day, benzodiazepines, corticosteroids Bleeding disorders Acupuncture treatment in past 10 years	Primary Mean back pain intensity on 11-point NRS (7 days) Roland Morris Disability Questionnaire (1 day) Secondary Quantitative sensory testing Physical exam to determine neurological function, lumbar facet irritation, lumbar spine range of motion Blood pressure Heart rate variability	July 2018 (final data collection date for primary outcome)

Sinew Acupuncture for Neck Pain: Randomized Controlled Trial **The University of Hong Kong** **NCT02834702**	RCT Parallel Assignment Single Blind N=130	1) Sinew acupuncture 2) Sham acupuncture	Age ≥18 Able to read and write Chinese Pain between neck and shoulder; movement or palpation of the cervical region provokes symptoms Pain duration ≥3 months VAS (0-100 mm) pain score ≥30 mm at baseline No treatments for pain management received in past 2 weeks Exclusion History of neck fracture/surgery Malignant tumor Cervical congenital abnormality Severe psychiatric illness Needle phobia Acupuncture in past 3 months Other acupuncture contraindications	Primary VAS (3 weeks) Secondary VAS Northwick Park Neck Pain Questionnaire SF-36	June 2020
Strategies to Assist with Management of Pain (STAMP) **University of Wisconsin, Madison & Patient-Centered Outcomes Research Institute** **NCT03115359**	RCT Parallel Assignment Single blind N=766	1) Mindfulness meditation 2) Cognitive behavioral therapy	English-speaking Age ≥21 Chronic low back pain ≥30 mg/day of morphine-equivalent dose for ≥3 months ≥21 on Oswestry Disability Index Exclusion Prior mindfulness meditation or CBT training Current pregnancy Borderline personality, delusional, or bipolar disorder	Primary Pain intensity (baseline to 12 months) using Brief Pain Inventory Physical function (baseline to 12 months) using Oswestry Disability Index Secondary SF-12 Daily opioid dose	July 2021

Mindfulness-Oriented Recovery Enhancement for Chronic Pain and Prescription Opioid Misuse in Primary Care **University of Utah** **NCT02602535**	RCT Parallel Assignment Single blind N=260	1) Mindfulness-oriented recovery enhancement 2) Support group	Age ≥18 Current back pain diagnosis Current use of prescription opioid agonist or mixed agonist-antagonist analgesics for >90 days Exclusion Prior experience with mindfulness-based stress reduction, mindfulness-based cognitive therapy, or mindfulness-based relapse prevention Active suicidality, schizophrenia, psychotic disorder, and/or substance dependence Clinically unstable systemic illness judged to interfere with treatment	Primary Change in opioid misuse (baseline to 6 months post-treatment) Change in pain severity and interference (baseline to 6 months post-treatment) using Brief Pain Inventory Secondary Change in opioid craving Change in psychological distress (Depression Anxiety Stress Scale) Change in opioid dose	October 2021
Mechanisms of Psychosocial Chronic Pain Treatments **Rush University Medical Center, Duke University, & University of Alabama, Tuscaloosa** **NCT02133976**	RCT Parallel Assignment Single Blind N=400	1) Cognitive therapy 2) Mindfulness training 3) Behavior therapy 4) Treatment as usual	Daily chronic pain intensity (≥4 on 10-point scale) and interference in performing daily activities due to pain (≥3 on 6-point scale) for ≥6 months Musculoskeletal pain of low back and/or leg pain that may be related to history of degenerative disk disease, spinal stenosis, or disk herniation, or muscular or ligamentous strain Age 18-75 Exclusion Alcohol/substance abuse Psychotic or bipolar disorders Inadequate English Active suicidal ideation Pain due to malignant conditions, migraine/tension headache, fibromyalgia, or complex regional pain syndrome	Primary Pain interference (12 months) Secondary Activity level	September 2018 (final data collection date for primary outcome)

Stanford Center for Back Pain **Stanford University** NCT02503475	RCT Parallel Assignment Double Blind N=324	Project 1 1) Attention Regulation 2) Cognitive Regulation 3) Sham 4) Free Strategy Project 2 1) Cognitive behavioral therapy 2) Mindfulness based stress reduction Project 3 1) Acupuncture 2) Sham	Age 21-65 English fluency Chronic low back pain Exclusion MRI contraindications Pregnant/planning pregnancy Neurologic disorder, history of seizures, stroke, or brain abnormalities Mental health conditions that would interfere with study procedures	Primary Changes in Pain severity VAS (up to 12 months post treatment) Secondary Changes in pain symptom severity and well-being using PROMIS	March 2020
The Effect of Cognitive Functional Therapy on Patients with Non-Specific Chronic Low Back Pain **University of Limerick, Curtin University, Katholieke Universiteit Leuven, Mayo General Hospital (Ireland), Health Service Executive (Ireland)** NCT02145728	RCT Parallel Assignment Single Blind N=208	1) Individual Cognitive Functional Therapy 2) Group Exercise Classes	Age 18-75 Chronic low back pain >6 months >14% for disability on Oswestry Disability Index Independently mobile, able to participate in a rehabilitation program Exclusion Primary pain area not lumbar spine Leg pain as primary problem <6 months post lumbar spine or lower limb or abdominal surgery Pain relieving procedures in last 3 months Pregnancy Rheumatologic/ inflammatory disease, progressive neurological disease, unstable	Primary Change in Oswestry Disability Index (8-14 weeks; 1, 12, and 36 months) Secondary Pain intensity (NRS) Back Pain Beliefs Physical activity Coping Strategies Pain Self-Efficacy Subjective Health Complaints Inventory Nordic Musculoskeletal Screening Stress (DASS 21)	December 2017

			cardiac conditions, malignancy/cancer, acute trauma, infection, spinal cord compression/cauda equina	Patient satisfaction Orebro Musculoskeletal Screening Medication Economic evaluation	
Pain Management for Patients with Low Back Pain and Psychosocial Risk Factors in a Hospital Setting **Central Jutland Regional Hospital** **NCT03141541**	RCT Parallel Assignment Single Blind N=130	1) Usual Care 2) Group-based Pain Management (based on cognitive behavioral therapy, relaxation, and breathing exercises)	Non-specific low back pain lasting ≥3 months Psychosocial risk profile defined as a fear avoidance score >24 (Orebro Musculoskeletal Pain Questionnaire) and or bodily distress score >15 (Common Mental Disorder Questionnaire) and/or health anxiety score >9 (Common Mental Disorder Questionnaire) Speaks/understands Danish Age ≥18 Exclusion Inflammatory or malignant disease Spine surgery in past year Untreated or severe depression Psychiatric treatment in past year Abuse of drugs/alcohol Pregnancy	Primary Roland Morris Disability Questionnaire (12 months) Secondary Low Back Pain Rating Scale-Back pain, leg pain Eq-5D Pain Catastrophizing Scale Sick leave	September 2019

Source: www.ClinicalTrials.gov (NOTE: studies listed on site include both clinical trials and observational studies)

Appendix D. Comparative Clinical Effectiveness Supplemental Information

For the systematic literature review, each publication was abstracted by a single reviewer, and the abstracted data was then validated for quality assurance by a different reviewer. Five total reviewers participated in data abstraction. We used criteria published by the US Preventive Services Task Force (USPSTF) to assess the quality of RCTs, using the categories "good," "fair," or "poor" (see Appendix Tables D5 and D9).[64] Quality assessment of systematic reviews follows the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) guidelines.[65] Guidance for quality ratings using these criteria is presented below.

Good: *Meets all criteria: Comparable groups are assembled initially and maintained throughout the study; reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention is paid to confounders in analysis. In addition, intention to treat analysis is used for RCTs.*

Fair: *Studies were graded "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred with follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are addressed. Intention to treat analysis is done for RCTs.*

Poor: *Studies were graded "poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. For RCTs, intention to treat analysis is lacking.*

Inclusions from Previous Systematic Reviews

Table D1. Inclusions from the AHRQ Review[9]

Cognitive Behavioral Therapy
Lamb, S. E., et al. (2010). "Group cognitive behavioural treatment for low-back pain in primary care: a randomised controlled trial and cost-effectiveness analysis." Lancet 375(9718): 916-923.
Lamb, S. E., et al. (2012). "Group cognitive behavioural interventions for low back pain in primary care: extended follow-up of the Back Skills Training Trial (ISRCTN54717854)." Pain 153(2): 494-501.
Nicholas, M. K., et al. (1992). "Comparison of cognitive-behavioral group treatment and an alternative non-psychological treatment for chronic low back pain." Pain 48(3): 339-347.
Schweikert, B., et al. (2006). "Effectiveness and cost-effectiveness of adding a cognitive behavioral treatment to the rehabilitation of chronic low back pain." J Rheumatol 33(12): 2519-2526.
Smeets, R. J., et al. (2008). "Chronic low back pain: physical training, graded activity with problem solving training, or both? The one-year post-treatment results of a randomized controlled trial." Pain 134(3): 263-276.
Turner, J. A. (1982). "Comparison of group progressive-relaxation training and cognitive-behavioral group therapy for chronic low back pain." J Consult Clin Psychol 50(5): 757-765.
Tai Chi
Hall, A. M., et al. (2011). "Tai chi exercise for treatment of pain and disability in people with persistent low back pain: a randomized controlled trial." Arthritis Care Res (Hoboken) 63(11): 1576-1583.
Weifen, W., et al. (2013). "Effectiveness of Tai Chi Practice for Non-Specific Chronic Low Back Pain on Retired Athletes: A Randomized Controlled Study." Journal of Musculoskeletal Pain 21(1).
Yoga
Cox, H., et al. (2010). "A randomised controlled trial of yoga for the treatment of chronic low back pain: results of a pilot study." Complement Ther Clin Pract 16(4): 187-193.
Cramer, H., et al. (2013). "A systematic review and meta-analysis of yoga for low back pain." Clinical Journal of Pain 29(5): 450-460.
Acupuncture
Brinkhaus, B., et al. (2006). "Acupuncture in patients with chronic low back pain: a randomized controlled trial." Archives of Internal Medicine 166(4): 450-457.
Cherkin, D. C., et al. (2001). "Randomized trial comparing traditional Chinese medical acupuncture, therapeutic massage, and self-care education for chronic low back pain." Archives of Internal Medicine 161(8): 1081-1088.
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Haake, M., et al. (2007). "German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups." Archives of Internal Medicine 167(17): 1892-1898.
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Cho, Y. J., et al. (2013). "Acupuncture for chronic low back pain: a multicenter, randomized, patient-assessor blind, sham-controlled clinical trial." Spine (Phila Pa 1976) 38(7): 549-557.
Molsberger, A. F., et al. (2002). "Does acupuncture improve the orthopedic management of chronic low back pain--a randomized, blinded, controlled trial with 3 months follow up." Pain 99(3): 579-587.

Mindfulness-Based Stress Reduction
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Table D2. Included Studies from Neck Pain Systematic Reviews[67-70]

Acupuncture
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Sahin N, Ozcan E, Sezen K, Karatas O, Issever H (2010) Efficacy of acupunture in patients with chronic neck pain—a randomised, sham controlled trial. Acupunct Electrother Res 35: 17–27. PMID: 20578644
Fu WB, Liang ZH, Zhu XP, Yu P, Zhang JF (2009) Analysis on the effect of acupuncture in treating cervical spondylosis with different syndrome types. Chin J Integr Med 15: 426–430. doi: 10.1007/ s11655-009-0426-z PMID: 20082247
Birch S, Jamison RN (1998) Controlled trial of Japanese acupuncture for chronic myofascial neck pain: assessment of specific and nonspecific effects of treatment. Clin J Pain 14: 248–255. PMID: 9758075
Birch S, Jamison R. Controlled trial of Japanese acupuncture for chronic myofascial neck pain: assessment of specific and nonspecific effects of treatment. Clin J Pain 1998;14:248–55
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Cognitive Behavioral Therapy
Gustavsson C, von Koch L. Applied relaxation in the treatment of long-lasting neck pain: a randomized controlled pilot study. Journal ofRehabilitation Medicine 2006;38(2):100–7.
Wicksell RK, Ahlqvist J, Bring A, Melin L, Olsson GL. Can exposure and acceptance strategies improve functioning and life satisfaction in people with chronic pain and whiplashassociated disorders (WAD)? A randomized controlled trial. Cognitive Behaviour Therapy 2008;37(3):169–82.
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Soderlund A, Lindberg P. Cognitive behavioural components in physiotherapy management of chronic whiplash associated disorders (WAD)--a randomised group study. Giornale Italiano diMedicina delLavoro edErgonomia 2007;29(1 Suppl A):A5–11.
Vonk F, Verhagen AP, Geilen M, Vos CJ, Koes BW. Effectiveness of behavioural graded activity compared with physiotherapy treatment in chronic neck pain: design of a randomised clinical trial [ISRCTN88733332]. BMC Musculoskeletal Disorders 2004;5(1):34. Vonk F, Verhagen AP, Twisk JW, Köke AJ, Luiten MW, Koes BW. Effectiveness of a behaviour graded activity program versus conventional exercise for chronic neck pain patients. European Journal ofPain 2009;13(5):533–41.

Evidence Tables: Chronic Low Back Pain

Table D3. Summary Characteristics: Studies Identified Through Updated Low Back Pain Literature Search

Reference	Study Type	Intervention	Comparator	N	Follow-Up (Months)	Inclusion	Exclusion
Mindfulness-Based Stress Reduction							
Cherkin DC *JAMA* 2016[12]; Turner JA PAIN. 2016[102]	RCT	1) MBSR (n=116)	2) CBT (n=112) 3) Usual Care (n=113)	342	26 weeks – primary endpoint 52 weeks overall	Age 20-70 yrs. Back pain ≥3 mos. *Pt-rated bothersome-ness of pain ≥4 *Pt-rated pain interference with activities ≥3 *(0=not at all bothersome - 10=extremely bothersome).	Pregnancy Spine surgery in previous 2 years Disability compensation or litigation Fibromyalgia/cancer diagnosis/other major medical conditions Plans to see a medical specialist for back pain
Cherkin DC *JAMA* 2017[72]	RCT – follow up	See Cherkin *DC JAMA* 2016	See Cherkin 2016	N=276 (81% original)	24	See Cherkin *DC JAMA* 2016	See Cherkin *DC JAMA* 2016
Zgierska *Pain Med* 2016[76]	RCT Phase I/II United States	1) Meditation-CBT plus usual care Manualized training in meditation 2 hours/week for 8 weeks. Each session focused on a specific topic building on previous topics, including: defining mindfulness meditation (MM); auto-pilot triggers; using MM in daily life; MM	2) usual care (eligible to receive intervention after study completion)	1) 21 2) 14	26 weeks (6.5 months)	Age ≥21 years; fluent in English; daily CLBP (lumbosacral area pain or sciatica leg pain) treated by a clinician with daily opioid therapy (at least 30mg/day of morphine equivalent dose) ≥3 months; ability to feel thermal sensations in both hands.	Prior experience with MM training or practice; inability to consent or reliably participate; diagnosis of borderline personality, bipolar, delusional disorders; current pregnancy.

Reference	Study Type	Intervention	Comparator	N	Follow-Up (Months)	Inclusion	Exclusion
		as coping mechanism; pain catastrophizing; self-care; MM to support life balance. Skills included breath meditations; body scan meditations; mindful movement. Participants encouraged to practice formal MM at least 6 days/week for 30 mins/day. Led by 2 psychologists.					
Morone, NE. *JAMA* Intern Med. 2016	RCT Pittsburgh metropolitan area, United States	1) Mind-body program (i.e. Mindfulness Stress Reduction) Experimental group received 8-week MBSR program. Four methods of mindfulness meditation taught to participants. In addition, monthly 60-minute booster sessions were held.	2) Health Education (control) Health education program based on "10 Keys to Healthy Aging." Pain information was not included as a part of this education, although participants were taught on healthy lifestyle, hypertension management, etc. Monthly for one hour, control group also received booster sessions.	282	6	>65 years old Intact cognition A score of ≥11 on the Roland and Morris Disability Questionnaire[RMDQ] indicating a functional limitation Reported moderate chronic pain daily for > 3 months	Participation in other mindfulness programs Serious underlying medical conditions Non-ambulatory Severe mobility limitation Vision or hearing limitation that would interfere with assessments Pain in other areas of body greater intensity than low back pain Acute or terminal illness moderate to severe depressive symptoms (Geriatric Depression Scale score, ≥21

Reference	Study Type	Intervention	Comparator	N	Follow-Up (Months)	Inclusion	Exclusion
Yoga							
Bramberg EB *BMC* Musculo Disord 2017 [71]	RCT	1) Kundalini yoga 60 min/twice weekly for 6 weeks; physical activity component (typically slower pose movements than traditional forms of yoga) in addition to meditation and awareness training	2) Self-care advice 3) Strength Training Exercise For self-care, participants received "The Back Book" booklet with educational advice. For strength training, 5 supervised sessions over 6 weeks with physiotherapist. Participants instructed to perform regimen additional twice/week. Program included strengthening, endurance, and stabilization.	159	12	Non- specific low back pain, with or without neck pain; non-disabling (from perspective of work disability); 18-60 years old; ≥90 points on the OMPSQ; sufficient understanding of the Swedish language	Presence of spinal pathology (tumors or spinal fractures); Pregnancy; comorbidities affecting the ability to perform the interventions; continuous ongoing sick-listing ≥8 weeks; ongoing regular weekly yoga practice or strength training
Groessl EJ Am J Prev Med 2017[81]	RCT	1) Yoga 2 classes/week for 12 weeks; 60 minutes each. Yoga was hatha style, with physical postures, movement sequences, and breathing, directed	2) Wait list Patients in this group received usual care for six months, after which they had the opportunity to attend yoga classes.	150	6	Age ≥18 years; VA patient; diagnosis of chronic low back pain ≥ 6 months; willing to attend a yoga program or be assigned to delayed treatment with yoga; willing to complete 4 assessments;	Back surgery within the last 12 months; back pain due to specific systemic problem (e.g., lupus, scleroderma, fibromyalgia); morbid obesity (BMI > 40); significant sciatica or nerve compression < 3 months or

Reference	Study Type	Intervention	Comparator	N	Follow-Up (Months)	Inclusion	Exclusion
		attention, meditation. Participants received manual that recommended 15-20 min home practice on days without class	Both groups received usual care for the duration of the trial; participants asked to refrain from changing regular treatment during this time unless deemed medically necessary. Usual care includes prescription and nonprescription pain meds, physical therapy, spinal manipulation, exercise, self-help techniques.			English Literacy; has not begun new pain treatments or medications in the past month; willing to not change pain treatments (e.g., discontinue a treatment; increase medication dose) during the 12-week intervention period unless medically necessary	chronic lumbar radicular pain > 3 months; unstable, serious coexisting medical or psychiatric conditions; insufficient data to rule out acute, metastatic disease, (unless primary care physician approves); attended or practiced yoga > 1x in the last 12 months; positive Romberg test (with or without sensory neuropathy)
Saper RB ***Ann of Intern Med.*** **2017** [74]	12-week Single-blind 3-group Randomized noninferiority trial	Yoga (n=127)	Physical Therapy (n=129) Education (n=64)	320	12	Age 18-64 yrs *Nonspecific LBP lasting at least 12 weeks with average pain intensity ≥ 4 *(0=no pain- 10=worst pain possible)	Persons with specific causes of cLBP were excluded.
Teut, M ***Journal of Pain*** **2016**[75]	RCT	Yoga (n=61) Viniyoga method, 24 classes, 45 mins each, over 3 months. Exercises were adapted to meet	Qigong (n=58) Control (n=57) Qigong group received 12 classes over 3 months; 90 mins each.	176	6	Age ≥65 years; chronic low back pain ≥6 months; intensity of back pain according to the pain item of the Functional Rating Index	Acute disc prolapse or protrusion with acute neurological symptoms within last 3 months; severe organic or psychiatric disease; cancer/cancer-related pain in

Reference	Study Type	Intervention	Comparator	N	Follow-Up (Months)	Inclusion	Exclusion
		individual patient needs; included physical, breathing, concentration exercises in sitting, standing, laying positions. Patients in all 3 arms were allowed to continue usual care, although no physiotherapy and no opioids allowed within trial duration.	Standardized "Dantian" program and Nei Yang Gong exercises from the Training System Liu Ya Fei used. Also included was instruction on self-massage. Control group participants received no additional intervention for 6 months, although offered free participation in qigong or yoga after trial completion.			≥2 over past week; written informed consent provided.	bones; use of pain meds that works over the central nervous system pain agents (e.g. opioids); drug and/or alcohol use disorder; participation in another clinical trial within past 6 months; participation in yoga or qigong training within past year; physiotherapy planned to start within duration

Table D4. Baseline Characteristics: Studies Identified Through Updated Low Back Pain Literature Search

Reference	Group	Mean Age, yrs	%F	% W	Pain, VAS 0-10	Function	Opioid Use	Duration of Pain	Other
Mindfulness-Based Stress Reduction									
Turner JA PAIN 2016; Cherkin DC JAMA 2016[12]	(1) MBSR (2) CBT (3) Usual Care	Yr (SD) 50(11.9) 49.1(12.6) 48.9(12.5)	N (%) 71(61.2) 66(58.9) 87(77)	N (%) (1)97(84.4) (2) 93(83.0) (3) 88(80.0)	Pain bother-ness Mean (SD) 6.1(1.6) 6.0(1.5) 6.0(1.6)	Roland Disability Questionnaire Mean(SD) 11.8(4.7) 11.5(5.0) 10.9(4.8)	Opioids in last week 14(12.1) 12(10.7) 12(10.6)	Pain in last I80 days Median (IQR) 170 (115-180) 160 (100-180) 160 (100-180)	
Cherkin DC *JAMA* 2017[72]	(1) MBSR (2) CBT (3) Usual Care	See Cherkin 2016	See Cherkin 2016	See Cherkin 2016	See Cherkin 2016	See Cherkin 2016	See Cherkin 2016	See Cherkin 2016	
Zgierska Pain Med 2016[76]; Zgierska, Journal of Alternative and Complimentary Medicine 2016[103]; Zgierska J Opioid Manag 2014[104]	1) Meditation-CBT plus usual care 2) Usual care	Mean (SD) 52.7(10.5) 50.5(8.6)	N (%) 15(71.4) 13(92.9)	N (%) 16(76.2) 12(85.7)	Averaged Pain Severity Score Mean (SD) 6.3(1.2) 4.9(1.1)	ODI Mean total score (SD) 68.1(9.3) 64.5(14.1)	Morphine-eq dose (mg/d) past 28 days Mean (SD) 166.9(153.7) 120.3(76.9) Mean opioid therapy duration: 7.9 years	14.2 years (10.1)	Brief Pain Inventory; Biomarkers; Chronic pain acceptance Pain psychocal tests

Reference	Group	Mean Age, yrs	%F	% W	Pain, VAS 0-10	Function	Opioid Use	Duration of Pain	Other
							Opioid dose, MED, mg/day: 148.3 Illicit/ unprescribed drug use: 28.6%		
Morone, NE. JAMA Intern Med. 2016	1) Mind-body (n=140) 2) Education (control) (n=142)	1) 75 (7.2) 2) 74 (6.0)	1) 66.4 2) 66.2	1) 70.0 2) 71.1	Numeric Pain Rating Scale Average 1) 11.0 (4.0) 2) 10.5 (4.2) Current 1) 7.4 (4.9) 2) 7.1 (4.6) Most severe 1) 14.9 (4.2) 2) 14.0 (4.5)	Roland and Morris Disability Questionnaire 1) 15.6 (3.0) 2) 15.4 (3.0)	NR	Pain duration (months), mean (SD) 1) 137 (156.5) 2) 138 (160.3)	
Yoga									
Bramberg *EB BMC* Musculo Disord 2017 [71]	1) Kundalini yoga (n=52) 2) Self-care advice (n=55) 3) Strength Training Exercise (n=52)	1) 46.9 (9.6) 2) 43.9 (11.7) 3) 46.3 (9.3)	1) 71.7 2) 80 3) 61.5	NR	CPGS range from 0-100 Back Pain Intensity, mean (SD) 1) 57.1 (18.5) 2) 55.6 (18.7) 3) 57.7 (15.4)	NR	NR	NR	% w/ chronic Low Back Pain 1) 94 2) 93 3) 96 Back Disability, mean (SD) 1) 37.2 (23.4) 2) 38.6 (21.4) 3) 37.6 (20.9)

Reference	Group	Mean Age, yrs	%F	% W	Pain, VAS 0-10	Function	Opioid Use	Duration of Pain	Other
	**All groups include both chronic LBP & LNP unstratified.*				Neck Pain Intensity, mean (SD) 1) 44.4 (24.5) 2) 37.6 (26.1) 3) 46.5 (24.4)				Neck Disability, mean (SD) 1) 25.0 (23.3) 2) 23.7 (22.7) 3) 28.5 (24.1)
Groessl EJ Am J Prev Med 2017[81]	1) Yoga (n=75) 2) Delayed Yoga (usual care) (n=75)	Mean (SD) 1) 53.3 (12.7) 2) 53.6 (13.9)	1) 27 2) 25	1) 47 2) 52	Brief Pain Inventory (BPI) 0-10 scale, score (SD) 1) 4.64 (1.76) 2) 4.68 (2.16)	RMDQ 0-24 scale, score (SD) 1) 9.40 (5.15) 2) 10.3 (5.87)	Currently using narcotic medication, n (%) 1) 14 (19) 2) 16 (21)	Mean years since first sought medical care for LBP (SD): 1) 15.4 (10.4) 2) 14.6 (13.5)	
Saper RB Ann of Intern Med. 2017 [74]	(1) Yoga (n=127) (2) Physical Therapy (n=129) (3) Education (n=64)	Mean(SD) (1) 46.4(10.4) (2) 46.4(11.0) (3) 44.2(10.8)	N (%) (1) 72(56.7)((2) 90(69.8) (3) 42(65.6)	N (%) (1) 26(20.5) (2) 20(15.5) (3) 11(17.2)	*Mean(SD)back pain intensity score (1) 7.1(1.5) (2) 7.2(1.5) (3) 7.0(1.4) *(0=no pain-10=worst pain possible)	*Baseline RMDQ mean(SD) score (1) 13.9(5.6) (2) 15.6(5.1) (3) 15.0(5.0) *Higher scores=worse function	N (%) (1) 28(22) (2) 23(17.8) (3) 12(18.8)	NR	**QoL* Mean SF-36 physical health score (1) 36.2 (2) 35.2 (3) 36.6 Mean SF-36 mental health score (1) 43.4 (2) 41.4 (3) 42.3

Reference	Group	Mean Age, yrs	%F	% W	Pain, VAS 0-10	Function	Opioid Use	Duration of Pain	Other
									*Score range 0-100, higher scores=better HRQol *Comorbidity* Depression, % (1) 16.5 (2) 25.6 (3) 18.8
Teut, M *Journal of Pain* 2016[75]	1) Yoga (n=61) 2) Qigong (n=58) 3) Control (n=57)	Mean (SD) 1) 73.0 (5.6) 2) 72.4 (5.7) 3) 72.6 (6.0)	1) 88.5 2) 86.2 3) 91.2	NR	Average Pain Intensity past week (VAS 0-100), mean (SD) 1) 51.5 (18.7) 2) 50.6 (19.5) 3) 50.6 (21.3) Functional Rating Index, mean (SD) 1) 2.6 (0.7) 2) 2.4 (0.6) 3) 2.5 (0.6)	FFbHR back function questionnaire (mean [SD], range of 0-100%) 1) 68.7 (15.4) 2) 70.4 (18.7) 3) 69.2 (19.1)	Medication intake because of low back pain, n (%) 1) 37 (60.7) 2) 37 (63.8) 3) 36 (63.2)	Duration of low back pain, mean years (SD) 1) 18.7 (12.2) 2) 18.1 (13.2) 3) 19.6 (16.3)	SF-36 Physical Health (SD): 1) 36.3 (8.7) 2) 37.5 (7.8) 3) 36.5 (9.3) Mental Health: 1) 49.0 (11.8) 2) 50.6 (11.1) 3) 49.9 (10.3) Geriatric depression Scale (SD): 1) 2.9 (2.6) 2) 2.1 (2.5) 3) 2.8 (2.8)

Table D5. Quality Assessment: Studies Identified Through Updated Low Back Pain Literature Search

Reference	Comparable Groups	Maintain Comparability	Double Blind	Measurements Equal and Valid	Clear Definition of Intervention	Key Outcomes Assessed	Analysis Appropriate	Quality
Mindfulness-Based Stress Reduction								
Turner JA PAIN. 2016; Cherkin DC JAMA. 2016[12]	Yes	Yes	No	Yes	Yes	Yes	Yes	Fair
Cherkin DC *JAMA* 2017[72]	Yes	Yes	No	Yes	Yes	Yes	Yes	Fair
Morone, NE *JAMA Intern Med* 2016[73]	Yes	Yes	No – outcome assessments conducted by staff members blinded to intervention	Yes	Yes	Yes	Yes	Good
Zgierska Pain Med 2016[76]	No	No	No	Yes	Yes	Yes, but not in a useful format	Yes	Poor
Yoga								
Bramberg *EB BMC* Musculo Disord 2017 [71]	Yes	No	No, single-blind	Yes	Yes	No	Yes	Fair
Groessl EJ Am J Prev Med 2017[81]	Yes	Yes	No	Yes	Yes	Yes	Yes	Good
Saper RB Ann of Intern Med. 2017 [74]	No	No	No, single-blind	Yes	Yes	Yes	Yes	Poor
Teut M J of Pain. 2016 [75]	No	Yes	No	Yes	Yes	No	Yes	Good

Table D6. Key Outcomes: Studies Identified Through Updated Low Back Pain Literature Search

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
Mindfulness-Based Stress Reduction							
Cherkin DC JAMA. 2016[12]	(1) MBSR (2) CBT (3) Usual Care	% of patients with Clinically Meaningful Improvement Pain Bothersomeness Results: (1) (2) (3) Wk 26: 43.6, 44.9, 26.6 Wk 52: 48.5, 39.6, 31 Mean Change from Baseline Pain Bothersomeness Results: (1) (2) (3) Wk 26: -1.48, -1.56, -0.84 Wk 52: -1.95, -1.76, -1.10	% of patients with Clinically Meaningful Improvement RMDQ results: (1) (2) (3) Wk 26: 60.5, 57.7, 44.1 Wk 52: 68.6, 58.8, 48.6 Mean Change from Baseline RMDQ results: (1) (2) (3) Wk 26: -4.33, -4.38, -2.96 Wk 52: -5.3, -4.78, -3.43	* Mean change estimates SF-12 Physical score Week 8 (1) 3.69 (2) 3.24 (3) 2.21 Week 26 (1) 3.58 (2) 3.78 (3) 3.27 Week 52 (1) 3.87 (2) 3.79 (3) 2.93 SF-12 Mental score Week 8 (1) 1.68 (2) 1.77 (3) -0.65 Week 26	NR	*Mean change estimates PHQ-8 Week 8 (1) -1.60 (2) -2.29 (3) -0.12 Week 26 (1) -1.32 (2) -1.80 (3) -0.64 Week 52 (1) -1.51 (2) -1.72 (3) -0.88	NR

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
				(1) 0.45 (2) 2.13 (3) -1.11 Week 52 (1) 2.01 (2) 1.81 (3) 0.75			
Cherkin DC *JAMA* 2017[72]	(1) MBSR (2) CBT (3) Usual Care	Patients with clinically meaningful improvement in Pain bothersomeness (≥ 30%), %(95%CI) 41.2(33.2 to 51.0) 39.6 (31.4 to 49.8) 31.1 (23.9 to 40.5) Relative risk (95%CI) 0.96 (0.71 to 1.30) CBT to MBSR 1.27 (0.90 to 1.79) CBT to usual care 1.32 (0.95 to 1.85) MBSR to usual care Change from baseline Pain Bothersomeness, 104 weeks, 95% CI: 1) -1.57 (-1.97 to -1.17) 2) -1.79 (-2.21 to -1.37)	Patients with clinically meaningful improvement in RDI (≥ 30%), %(95%CI) 55.4(46.9 to 65.5) 62.0(53.5 to 71.7) 42.0(33.8 to 52.2) Relative risk (95%CI) 1.12 (0.90 to 1.39) CBT to MBSR 1.48 (1.13 to 1.92) CBT to usual care 1.32 (1.00 to 1.74) MBSR to usual care Change from baseline RDQ, 104 weeks, 95% CI: 1) -4.09 (-5.08 to -3.10) 2) -4.59 (-5.60 to -3.57) 3) -2.74 (-3.81 to -1.68)	NR	NR	NR	

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
		3) -1.25 (-1.69 to -0.81)					
Morone, NE ***JAMA Intern Med* 2016**[73]	1) Mind-body (n=140) 2) Education (n=142)	6-month outcomes: Average Numeric Pain Rating [NRS] Score (SD) [on 0-20 range] / change from baseline 1) 9.5 (5.1) / -1.5 2) 10.6 (4.7) / +0.1 Current NRS/change from baseline 1) 6.8 (5.2) / -0.6 2) 8.6 (5.6) / +1.5 Most severe NRS/change from baseline 1) 12.3 (5.5) / -2.6 2) 13.4 (4.9) / -0.6 % achieving meaningful improvement NRS, Average/Current/Most Severe 1) 36.7/44.4/35.9 2) 26.7/25.2/22.2 P=0.09/0.001/0.02	6-month outcomes: Mean RMDQ score (SD) / change from baseline 1) 12.2 (5.1) / -3.4 2) 12.6 (5.0) / -2.8 % achieving meaningful improvement 1) 49.2 2) 48.9 P=0.97	At 6 months: SF-36 mean score (SD) / change from baseline Global Health Composite: 1) 42.4 (9.2) / +1.9 2) 42.1 (9.8) / +1.5 Physical Health Composite: 1) 41.2 (8.2) / +2.4 2) 41.2 (8.5) / +2.3			
Zgierska Pain Med 2016[76]	1) Meditation-CBT 2) Usual care	Brief pain inventory (difference in average pain); mean (95%CI) Baseline-8wks: control v experimental 0.9 (0.01 to 1.7) Cohen's d=0.69	ODI, % achieved score change from baseline to 26 weeks (estimated from graph) + worsens disability; - improves disability (decreased) + 0-4 points: 1) 34%	NR	NR	NR	26 weeks: Brief Pain Inventory Pain Intensity, % change from baseline 1) -8%

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
		Baseline-26 weeks: control vs experimental 1.03(0.2 to 1.9); Cohen's d=0.86 P for repeat measures=0.045	2) 25% + 4-8 points: 1) 20% 2) 11% + >8 points: 1) 0% 2) 23% 0 points: 1) 0% 2) 5% - 0-4 points: 1) 0% 2) 16% - 4-8 points: 1) 18% 2) 24% - 8-12 points: 1) 7% 2) 0% - >12 points: 1) 19% 2) 0% ODI total score difference, mean (95% CI) Baseline-8 weeks control vs experimental 1.9(-5.5 to 9.3); Cohen's d=0.15				2) + 10%

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
			Baseline-26 weeks control vs experimental 6.5 (-1.0 to 14.0); Cohen's d=0.68				
Yoga							
Bramberg *EB BMC* Musculo Disord 2017 [71]	1) Kundalini yoga 2) Self-care advice 3) Strength Training Exercise	CPGS range from 0-100 6 Months Back Pain Intensity, mean (SD) / change from baseline 1) 47.0 (24.3) / -10.1 2) 50.2 (23.9) / -5.4 3) 41.7 (20.6) / -16.0 Neck Pain Intensity, mean (SD) / change from baseline 1) 35.0 (21.1) / -9.4 2) 34.3 (27.2) / -3.3 3) 29.8 (20.7) / -16.7	NR	NR	NR	NR	Back Disability, mean (SD) / change from baseline 1) 29.4 (24.2) / -7.8 2) 32.8 (27.8) / -5.8 3) 24.8 (24.2) / -12.8 Neck Disability, mean (SD) / change from baseline 1) 16.3 (20.1) / -8.7 2) 21.5 (26.4) / -2.2 3) 13.3 (18.3) / -15.2

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
Groessl EJ Am J Prev Med 2017[81]	1) Yoga (n=75) 2) Delayed Yoga (usual care) (n=75)	*BPI change from baseline at 6 months (95% CI) 1) -0.44 (-0.78, -0.11) 2) 0.15 (-0.18, 0.47) *Between-group difference (95% CI) -0.59 (-1.05, -0.13), p = 0.013 **results of linear mixed-effects model* % achieved clinically meaningful difference at 6 months (BPI score change ≥1.0 points) 1) 39 2) 18 P=0.020	*RMDQ change from baseline at 6 months (95% CI) 1) -3.37 (-4.51, -2.23) 2) -0.89 (-2.02, 0.23) *Between-group difference (95% CI) -2.48 (-4.08, -0.87), p = 0.003 **results of linear mixed-effects model* % achieved clinically meaningful difference at 6 months (RDMQ ≥30% decrease) 1) 57 2) 24 P<0.001	NR	NR	NR	% of patients using narcotic pain medications at 6 months / change from baseline 1) 9 / -10 2) 7 / -14 P=0.395
Saper RB Ann of Intern Med. 2017 [74]	(1) Yoga (2) Physical Therapy (3) Education	*Mean back pain intensity score at 12 weeks (measured right at end of intervention) (1) 5.3(2.1) (2) 5.0(2.1) (3) 5.6(2.2) *(0=no pain-10=worst pain possible) Data on 52 weeks is in graph format. See limitations of study.	* Mean RMDQ score at 12 weeks (measured right at end of intervention) (1) 11.0(4.9) (2) 11.3(5.1) (3) 12.3(5.0) *Higher scores=worse function Data on 52 weeks is in graph format. See limitations of study.	Mean SF-36 physical health score (1) 41.4 (2) 40.1 (3) 41.2 Mean SF-36 mental health score (1) 47.1 (2) 45.2	NR	NR	Opioids, n (%) (1) 28 (22.6) (2) 15 (13.6) (3) 11 (18.0)

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
				(3) 44.2 *Score range 0-100, higher scores=better HRQol			
Teut M J of Pain. 2016 [75]	(1) Yoga (n=61) (2) Qigong (n=58) (3) Control (n=57)	6 months: Adjusted mean Pain Functional Rating Index (0-4) [95% CI] (1) 1.71 (1.50 – 1.91) (2) 1.51 (1.28 – 1.75) (3) 1.83 (1.65 – 2.02) Between group difference yoga vs. control (95% CI) -0.13 (-0.38 – 0.12), p=0.318 Adjusted mean average pain intensity last 7 days (VAS 0-100 mm) [95% CI] 1) 42.05 (36.65 – 47.45) 2) 34.14 (28.51 – 39.78) 3) 41.25 (36.07 – 46.42) Between group difference yoga vs. control (95% CI) 0.8 (-6.31 – 7.91), p=0.825	6 months: Adjusted mean back function; FFbHR (0-100) [95% CI] (1) 66.55 (62.89 – 70.21) (2) 69.23 (65.97 – 72.49) (3) 65.25 (62.59 – 72.49) Between group difference yoga vs. control (95% CI) 1.3 (-3.15 – 5.75), p=0.568	6 months: Adjusted mean SF-36 physical component score (95% CI) (1) 36.41 (34.36 – 38.47) (2) 40.01 (37.71 – 42.32) (3) 37.60 (35.45 – 39.75) Between group difference yoga vs. control -1.19 (-3.85 – 1.48), p=0.382 Adjusted mean SF-36 mental component score (1) 48.70 (45.82 – 51.58)	NR	6 months: Geriatric depression scale (GDS) adjusted mean (0-15) 1) 2.76 (2.16 – 3.35) 2) 3.06 (2.54 – 3.58) 3) 3.40 (2.59 – 4.21) Between group difference yoga vs. control -0.64 (-1.55 – 0.26), p=0.162	6 months: Change in % patients taking pain medication from baseline 1) -24 2) -27 3) -21 P=0.861

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
				(2) 48.72 (46.23 – 51.20) (3) 48.41 (45.74 – 51.08) Between group difference yoga vs. control 0.29 (-3.27 – 3.85), p=0.873			

Evidence Tables: Chronic Neck Pain

Table D7. Summary Characteristics: Studies Identified Through Updated Neck Pain Literature Search

Reference	Study	Intervention	Comparator	N	Follow-up (Months)	Inclusion	Exclusion
Acupuncture							
Zhang SP Hong Kong Med 2013[80]	Double-blind RCT	1) Electroacupuncture (n=103) Acupuncture 3 times a week for 3 weeks; sterile acupuncture needles 25-40 mm long with a diameter of 0.25-0.30 mm inserted into Hegu (LI4, x2), Houxi (SI3, x2), Feng Chi (GB20,x2), Jiangjing (GB21, x2), and Bailao and stimulated with an electroacupuncture machine for 45 minutes. Two additional points could be chosen from tender points or acupuncture points immediately near the tender points	2) Sham laser acupuncture (n=103) Sham acupuncture 3 times a week for 3 weeks; acupuncture delivered via a mock laser pen that only emitted a red light. Patients nor practitioners were informed that laser pen was inactivated. Each point was treated for 2 minutes, with the pen at a distance of 0.5 to 1 cm from the skin	206	6	Adults; chronic mechanical neck pain for ≥3 months	Surgery to the neck, neurological deficits, history of malignancy, congenital abnormality of the spine, systemic diseases; acupuncture in previous 6 months

Reference	Study	Intervention	Comparator	N	Follow-up (Months)	Inclusion	Exclusion
Cho J-H, *Acupunc Med* 2014[82]	RCT Pilot study, assessor-blind	1) Acupuncture plus NSAID Participants took NSAID (zaltoprofen 80mg/day) for 3 weeks while receiving 9 acupuncture sessions (3x/week). Acupuncture methods for Groups 1 and 3: Points selected in cervical region were SI9-12, SI14, BL11-12, TE14-17, GB21. Standard points on extremities were S13, S14, BL65. 0.25mm x 40mm stainless steel needles inserted 20 mm until participant felt acupuncture sensation, then needle left inserted for 15 mins.	2) NSAID 3) Acupuncture NSAID group took NSAIDs daily. NSAIDs were taken 3x/day, and patients were instructed to record missed doses in a patient diary. Acupuncture group received 9 acupuncture sessions total, 3x/week for 3 weeks.	45	7 weeks (3-week intervention)	Age 25–55 years; neck pain or neck and shoulder stiffness ≥3 months; score of ≥5 on the visual analogue scale (VAS) at baseline.	Received acupuncture or NSAID treatment for neck pain within the past 3 months; had serious medical disease or cancer; had history of spinal trauma, had undergone surgery on the neck or had systematic neurological or other skeletal disorders; pregnant or breast feeding.

Reference	Study	Intervention	Comparator	N	Follow-up (Months)	Inclusion	Exclusion
MacPherson, Ann Intern Med 2015[79]	RCT Open, pragmatic, parallel-group	1) Acupuncture 12 sessions, 50-minutes each plus usual care. Sessions once/week initially and moved to once every 2 weeks. Sessions based upon traditional Chinese medical theory.	2) Alexander Technique 3) Usual care 2) Participants offered 20 one-to-one lessons of 30 mins duration plus usual care. Lessons once/week, with option of being delivered twice/week initially and every two weeks later. Verbal and hands-on guidance used in line with usual practice. 3) General and neck-pain specific treatments routinely provided to primary care patients, such as prescribed medications and visits to physical therapists.	1) 173 2) 172 3) 172	12	Age ≥18 years; consulted GP in past 2 years for chronic neck pain; neck pain ≥3 months; score ≥ 28% on NPQ for neck pain and associated disability (10 of 36 points for car drivers and 9 of 32 for nondrivers).	Serious underlying pathology; prior cervical spine surgery; history of psychosis; rheumatoid arthritis; ankylosing spondylitis; osteoporosis; hemophilia; cancer; HIV or hepatitis; history of alcohol or drug dependency; actively pursuing compensation or with litigation pending; unable to communicate in English; participation in other trial that may interfere; attendance to 1-1 Alexander Technique lessons within past 2 yrs

Reference	Study	Intervention	Comparator	N	Follow-up (Months)	Inclusion	Exclusion
Tai Chi							
Lauche R J Pain 2016[78]	Open label RCT	1) Tai chi weekly 75-90-min (Yang style) session for 12 weeks; sessions included warm up, relaxation period, Tai Chi form practice, educational units, breathing exercises, and relaxation music. Participants received illustrated written info that covered movement sequences learned in the previous session. They were asked to practice Tai Chi outside of classes ≥15 mins/day	2) Neck exercises weekly 60- 75 min session for 12 weeks; basic training of ergonomic principles, proprioceptive exercises, and isometric and dynamic mobilization, stretching, strengthening neck and core exercises, and relaxation exercises. Participants received illustrated and written info and were asked to execute the exercises for ≥15mins/day 3) Wait list Continued usual activities/therapies and offered tai chi or neck exercises at trial's end	114	6	Age ≥18 years; chronic nonspecific neck pain ≥3 consecutive months ≥5 days/week; moderate pain (≥45 mm or higher on VAS 0-100 mm)	Additional low back or arm pain; neck pain caused by trauma, disc protrusion, whiplash, congenital deformity of the spine, spinal stenosis, neoplasm, inflammatory rheumatic disease, neurological disorder, active oncologic disease, severe affective disorder, addiction, and psychosis; pregnant; invasive tx of the spine in previous 4 weeks or spinal surgery within previous year; initiated /modified drug regimen recently; taking opiates; regular practice of tai chi, Qi gong, or yoga in past 6 months

Table D8. Baseline Characteristics: Studies Identified Through Updated Neck Pain Literature Search

Reference	Group	Mean Age, yrs	%F	% W	Pain, VAS 0-10	Function	Opioid Use	Duration of Pain	Other
Acupuncture									
Zhang SP Hong Kong Med 2013[80]	1) Electroacupuncture (n=103) 2) Sham laser acupuncture (n=103)	45.8	~70	0	Northwick Park Neck Pain Questionnaire score (95% CI) 1) 40.7 (38.5-42.9) 2) 41.1 (38.7-43.5) Numeric pain intensity scale score (95% CI) 1) 54.7 (50.9-58.4) 2) 51.6 (47.6-55.7)	NR	NR	75.4 months	NR
MacPherson, Ann Intern Med 2015[79]	1) Acupuncture (n=173) 2) Alexander Technique (n=172) 3) Usual care (n=172)	1) 52 2) 53.6 3) 53.9	1) 68.8 2) 69.8 3) 68.6	1) 92.9 2) 89.4 3) 88.9	NR	Mean NPQ Score: 1) 39.64 2) 39.38 3) 40.46	NR	Median, months: 1) 60 2) 60 3) 96	Reduced hours or stopped working due to neck pain, % 1) 15 2) 17 3) 19
Cho J-H, *Acupunct Med* 2014[82]	1) Acupuncture (n=15) 2) NSAID (n=15) 3) Acupuncture + NSAID (n=15)	Mean (SD) 1) 39.1 (9.0) 2) 38.2 (10.2) 3) 39.2 (9.1)	1) 53.3 2) 60.0 3) 80.0	NR	VAS Neck Pain within last week (0-10 cm), mean [SD] 1) 6.7 (0.7)	NDI, mean (SD) 1) 23.2 (5.9) 2) 22.3 (4.0) 3) 26.3 (5.0)	NR	NR	Beck's Depression Inventory, mean (SD) 1) 28.7 (4.8)

					2) 6.07 (0.5) 3) 7.1 (1.3)				2) 30.7 (5.6) 3) 33.1 (7.8) EQ-5D 1) 7.4 (1.7) 2) 7.4 (1.5) 3) 7.5 (1.3) SF-36 1) 85.2 (1.2) 2) 86.2 (2.0) 3) 84.2 (1.7)
Tai Chi									
Lauche R J Pain 2016[78]	1) Tai chi (n=38) 2) Neck exercises (n=37) 3) Wait list (n=39)	1) 52.0 (10.9) 2) 47.0 (12.3) 3) 49.2 (11.7)	1) 73.7 2) 83.8 3) 82.1	NR	Recent pain intensity (0-100 VAS) 1) 54.2 (20.5) 2) 46.2 (19.2) 3) 51.5 (21.1) Pain considered tolerable (0-100 VAS) 1) 21.7 (14.5) 2) 20.5 (11.7) 3) 20.7 (12.1) POM (Pain on Movement) 1) 43.1 (19.2) 2) 43.6 (14.6) 3) 41.3 (19.7)	Disability NDI total score (0-100) 1) 30.8 (8.0) 2) 30.1 (9.8) 3) 29.3 (8.2) Disability in days (VAS) 1) 3.0 (4.5) 2) 4.2 (5.1) 3) 2.9 (3.8) Everyday function (VAS) 1) 31.1 (24.7) 2) 29.3 (19.7) 3) 30.0 (21.8)	Patients taking opiates were excluded from trial Previous medication 1) 34.2 2) 56.8 3) 61.5	NR	SF-36 PCS 1) 44.13 (7.0) 2) 41.8 (7.4) 3) 43.6 (7.3) SF-36 MCS 1) 46.3 (10.3) 2) 46.9 (8.3) 3) 46.9 (10.5) HADS Depression 1) 3.8 (2.9) 2) 3.8 (2.4) 3) 4.5 (3.0)

Table D9. Quality Assessment: Studies Identified Through Updated Neck Pain Literature Search

Reference	Comparable Groups	Maintain Comparability	Double Blind	Measurements Equal and Valid	Clear Definition of Intervention	Key Outcomes Assessed	Analysis Appropriate	Quality
Acupuncture								
Zhang SP Hong Kong Med 2013[80]	Yes	No	Yes	Yes	Yes	Yes	Yes	Fair
MacPherson, Ann Intern Med 2015[79]	Yes	[37]Yes	No	Yes	Yes	Yes	Yes	Fair
Cho J-H, *Acupunct Med* 2014	No	No	No- single blind	Yes	Yes	Yes	Yes	Poor
Tai Chi								
Lauche R J Pain 2016[78]	Yes	No	No	Yes	Yes	Yes	Yes	Fair

Table D10. Key Outcomes: Studies Identified Through Updated Neck Pain Literature Search

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
Acupuncture							
Zhang SP Hong Kong Med 2013[80]	1) Electroacupuncture (n=103) 2) Sham laser acupuncture (n=103)	Northwick Park Pain Questionnaire score (95% CI) 1) 33.5 (30.7-36.4) 2) 34.3 (31.1-37.6) p=0.808 Numeric pain intensity scale score (95% CI) 1) 46.8 (42.0-51.5) 2) 43.6 (38.8-48.4) p=0.813	NR	SF-36 PCS (95% CI) 1) 53.0 (52.0-53.9) 2) 53.2 (52.3-54.0) p=0.559 MCS (95% CI) 1) 45.4 (44.5-46.3) 2) 44.4 (43.4-45.4) p=0.246	NR	NR	NR
Cho J-H, *Acupunct Med* 2014	1) Acupuncture (n=15) 2) NSAID (n=15) 3) Acupuncture + NSAID (n=15)	7 weeks: VAS 1-10 cm average pain in last week, mean (SD) 1) 4.3 (2.0)** 2) 4.5 (2.2)* 3) 3.8 (1.6)** *p<0.05 **p<0.01	7 weeks: Neck Disability Index, mean (SD) 1) 17.5 (4.9)** 2) 17.3 (5.7)** 3) 17.7 (5.4)** *p<0.05 **p<0.01	7 weeks: EQ-5D, mean (SD) 1) 7.0 (1.3) 2) 7.3 (1.9)* 3) 6.7 (1.7) *p<0.01	*NR*	7 weeks: Beck's Depression Inventory, mean (SD) 1) 25.7 (4.4) 2) 28.5 (7.3) 3) 27.2 (6.3) P<0.05 for all	7 weeks: SF-36, mean (SD) 1) 83.9 (1.9) 2) 88.6 (1.5) 3) 84.3 (1.1)

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
Macpherson, Ann Intern Med 2015[79]	1) Acupuncture (n=173) 2) Alexander Technique (n=172) 3) Usual care (n=172)		Mean NPQ score (descriptive, unadjusted raw) 3 months: 1) 29.56 2) 32.50 3) 36.30 6 months: 1) 27.00 2) 27.11 3) 33.07 12 months: 1) 26.76 2) 27.14 3) 31.25 Adjusted Mean NPQ Scores (3/6/12 months) Acupuncture vs. Usual Care 1) 37.23/35.35/37.07 3) 43.46/40.90/40.99 Alexander Technique vs. Usual Care	NR	NR	NR	Harms Serious AEs, n (%) 1) 9 (5.2) 2) 13 (7.6) 3) 8 (4.7) Withdrawals due to serious AEs, n (%) 1) 3 (1.7) 2) 3 (1.7) 3) 0

Reference	Group	Pain, VAS	Function	Quality of Life	Return to Work	Depression	Other
			2) 38.62/32.65/33.39 3) 42.22/37.64/37.18				
Tai Chi							
Lauche R J Pain 2016[78]	1) Tai chi (n=38) 2) Neck exercises (n=37) 3) Wait list (n=39)	Pain (VAS) 1) 35.0 (27.7) 2) 33.1 (20.9) 3) 44.6 (20.0) POM (mean score) 1) 29.1 (19.0) 2) 34.9 (14.4) 3) 45.5 (19.7) POM=pain on movement	Disability Total NDI (0-100) 1) 24.3 (14.1) 2) 25.1 (12.9) 3) 29.4 (12.7) Disability in days (VAS) 1) 1.9 (3.4) 2) 2.7 (3.7) 3) 2.7 (3.0) Everyday function (VAS) 1) 22.0 (24.3) 2) 24.4 (19.6) 3) 29.6 (20.5)	SF-36 PCS 1) 46.5 (8.9) 2) 44.0 (7.5) 3) 42.0 (8.0) MCS 1) 47.0 (12.2) 2) 46.9 (9.1) 3) 46.4 (10.13)	NR	HADS, depression 1) 4.1 (3.8) 2) 4.1 (2.8) 3) 5.4 (4.0)	HADS, anxiety 1) 6.1 (4.5) 2) 5.5 (3.1) 3) 6.7 (3.4)

Appendix E. Comparative Value Supplemental Information

Table E1. Impact Inventory (adapted from Sanders et al., JAMA. 2016;316(10):1093-1103)[105]

Sector	Type of Impact	Included in This Analysis from… Perspective?		Notes on Sources
		Health Care Sector	Societal	
Formal Health Care Sector				
Health Outcomes	Longevity effects	✓	✓	
	Health-related quality of life effects	✓	✓	
	Adverse events	NA	NA	
Medical Costs	Paid by third-party payers	✓	✓	
	Paid by patients out-of-pocket	✓	✓	
	Future related medical costs	✓	✓	
	Future unrelated medical costs	✓	✓	
Informal Health Care Sector				
Health-Related Costs	Patient time costs	NA	☐	
	Unpaid caregiver-time costs	NA	☐	
	Transportation costs	NA	☐	
Non-Health Care Sectors				
Productivity	Labor market earnings lost	NA	☐	
	Cost of unpaid lost productivity due to illness	NA	✓	
	Cost of uncompensated household production	NA	☐	
Consumption	Future consumption unrelated to health	NA	☐	
Social Services	Cost of social services as part of intervention	NA	☐	
Legal/Criminal Justice	Number of crimes related to intervention	NA	NA	
	Cost of crimes related to intervention	NA	NA	
Education	Impact of intervention on educational achievement of population	NA	☐	
Housing	Cost of home improvements, remediation	NA	☐	
Environment	Production of toxic waste pollution by intervention	NA	☐	

NA: not applicable

Table E2. Probability of Chronic Low Back Pain Recurrence at Six Months

	Value	Source
Annual Probability	0.6	Norton et al., 2015[88]
Six-Month Probability	0.259	Calculation using equation $Probability = 1 - \exp(-rate\ x\ time)$ Rate = 0.6 Time = 0.5 (six months)

Table E3. Probabilistic Sensitivity Analysis Inputs

Parameter	Distribution	Range	Source
Transition Probabilities to Pain Improvement from Chronic Pain State			
Acupuncture	Beta	α = 91.64; β = 66.36	Cherkin et al., 2009[11]
CBT	Beta	α = 53.08; β = 38.92	Cherkin et al., 2016[12]
MBSR	Beta	α = 57.48; β = 37.53	Cherkin et al., 2016[12]
Yoga	Beta	α = 54.78; β = 28.22	Sherman et al., 2011[13]
Tai Chi	Beta	α =40; β = 40	Hall et al., 2011[14]
Usual Care	Beta	α =47.18; β = 59.81	Cherkin et al., 2016[12]
Transition Probabilities of Recurrence to Chronic Pain State (All Interventions and Comparator)			
Recurrence	Beta	α =25.9; β = 74.1	Norton et al., 2015[88]
Health State Utility			
Improved Pain	Triangular	Min Value = 0.675* Max Value = 0.825* Mode = 0.75[†]	Johnson et al., 2007[15]; Calculation (Wright)[106]
Intervention cost per session			
Acupuncture	Uniform	Min Value = $72.51 Max Value = $134.65	Calculation[‡]
CBT	Uniform	Min Value = $74.12 Max Value = $37.65	Calculation[‡]
MBSR	Uniform	Min Value = $53.81 Max Value = $99.94	Calculation[‡]
Yoga	Uniform	Min Value = $42 Max Value = $78	Calculation[‡]
Tai Chi	Uniform	Min Value = $12.25 Max Value = $22.75	Calculation[‡]
Office visit intervention (CPT Code: 99213)	Uniform	Min Value = $48.49 Max Value = $69.97	Centers for Medicare & Medicaid Services[23]
Usual Care (CPT Code: 99214)	Uniform	Min Value = $100.07 Max Value = $140.37	Centers for Medicare & Medicaid Services[23]
Background Health Care Costs			
Chronic Pain	Uniform	Min Value = $490.81 Max Value = $911.51	Calculation[‡]
Improved Pain	Uniform	Min Value = $210.91 Max Value = $391.70	Calculation[‡]

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction

*Assumed to be ±10% of the base-case estimate

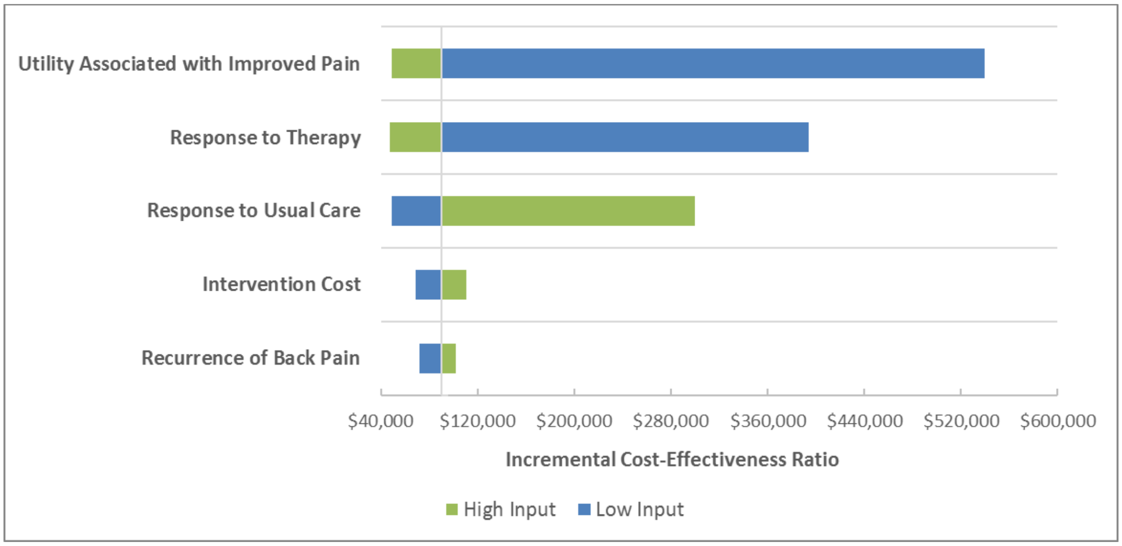
[†]Mode is equal to the mean since we assumed a symmetric distribution

[‡] Assumed to be ±30% of the base-case estimate

One-Way Sensitivity Analyses: Results

Acupuncture

Figure E1. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Acupuncture Versus Usual Care



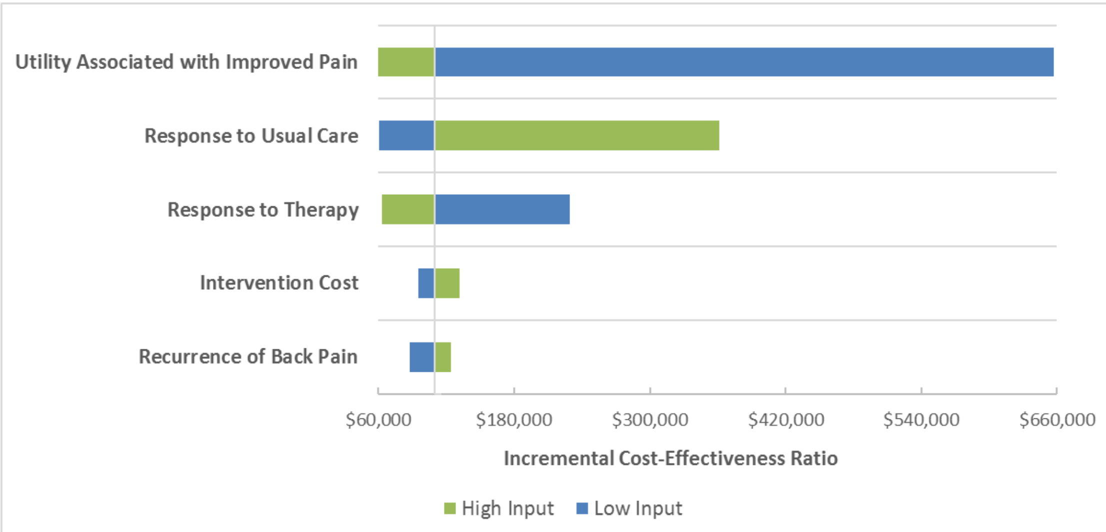
Base-case ICER: $89,888 per QALY gained

Table E4. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Acupuncture Versus Usual Care

	Low Input	High Input	Low Value	High Value	Range
Intervention Cost	$84.71	$124.30	$68,981	$110,794	$41,813
Response to Therapy	0.48	0.72	$393,806	$47,405	$346,402
Response to Usual Care	0.359	0.542	$48,840	$300,028	$251,188
Recurrence of Back Pain	0.126	0.356	$71,636	$101,878	$30,241
Utility Associated with Improved Pain	0.675	0.825	$539,327	$49,030	$490,297

Mindfulness-Based Stress Reduction

Figure E2. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Mindfulness-Based Stress Reduction Versus Usual Care



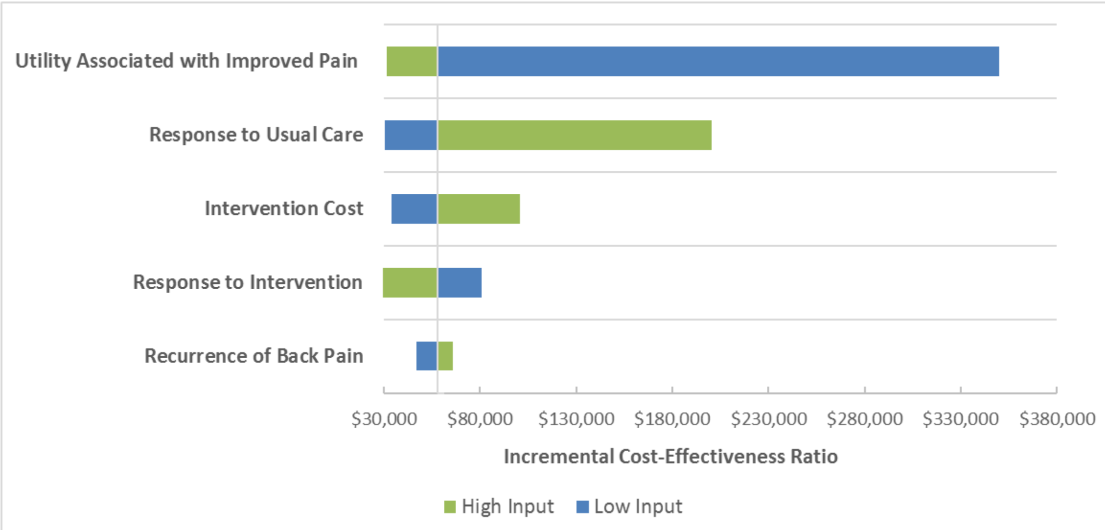
Base-case ICER: $109,486 per QALY gained

Table E5. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Mindfulness-Based Stress Reduction Versus Usual Care

	Low Input	High Input	Low Value	High Value	Range
Intervention Cost	$68.13	$90.63	$95,357	$131,688	$36,331
Response to Therapy	0.52	0.703	$229,355	$62,950	$166,405
Response to Usual Care	0.359	0.542	$60,294	$361,320	$301,026
Recurrence of Back Pain	0.126	0.356	$87,613	$123,854	$36,241
Utility Associated with Improved Pain	0.675	0.825	$656,914	$59,719	$597,194

Yoga

Figure E3. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Yoga Versus Usual Care



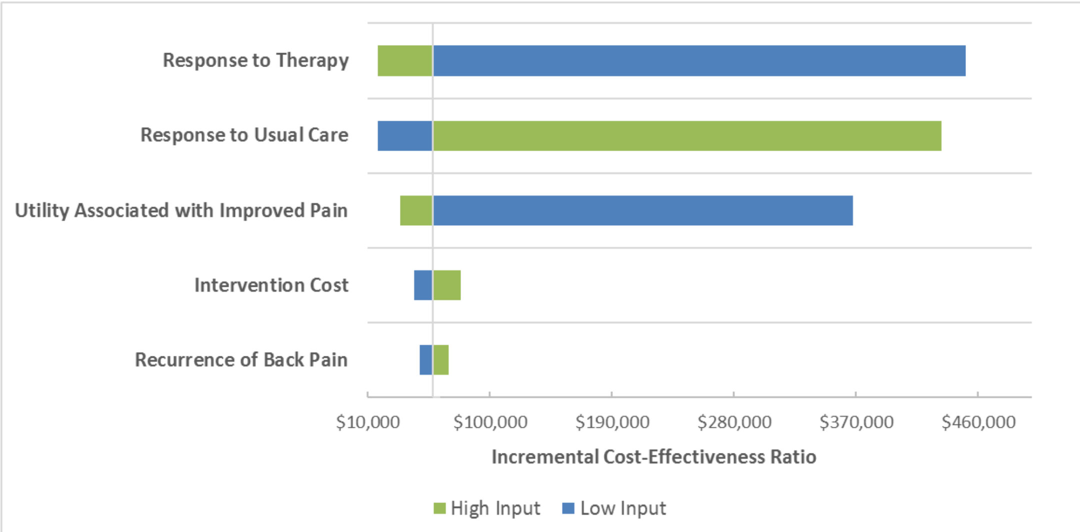
Base-case ICER: $58,017 per QALY gained

Table E6. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Yoga Versus Usual Care

	Low Input	High Input	Low Value	High Value	Range
Recurrence of Back Pain	0.126	0.356	$46,914	$66,225	$19,311
Response to Therapy	0.56	0.78	$80,940	$22,646	$58,294
Intervention Cost	$40	$95	$34,004	$100,934	$66,930
Response to Usual Care	0.359	0.542	$30,744	$200,534	$169,791
Improved Pain Utility	0.675	0.825	$350,054	$31,823	$318,231

Tai Chi

Figure E4. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Tai Chi Versus Usual Care



Base-case ICER: $61,265 per QALY gained

Table E7. One-Way Sensitivity Analysis: Incremental Cost-Effectiveness Ratio for Tai Chi Versus Usual Care

	Low Input	High Input	Low Value	High Value	Range
Intervention Cost	$14.00	$21.00	$44,131	$78,399	$34,268
Response to Therapy	0.44	0.6	$450,994	$17,145	$126,980
Response to Usual Care	0.359	0.49	$17,117	$433,2831	$138,428
Recurrence of Back Pain	0.126	0.356	$48,303	$69,781	$21,478
Utility Associated with Improved Pain	0.675	0.825	$367,592	33,417	$334,175

Probabilistic Sensitivity Analysis Results

Table E8. Probability of Cost-Effectiveness at Three Willingness-To-Pay Thresholds

Intervention	Percentage Cost-Effective at Willingness-To-Pay Thresholds		
	$50,000 per QALY	$100,000 per QALY	$150,000 per QALY
Acupuncture	10.74%	44.34%	65.62%
CBT	1.38%	16.46%	36.28%
MBSR	10.36%	43.78%	65.80%
Yoga	61.16%	87.94%	95.24%
Tai Chi	43.30%	59.80%	66.38%

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction, QALY: Quality-Adjusted Life Year

Figure E5. Acupuncture Cost-Effectiveness Acceptability Curve

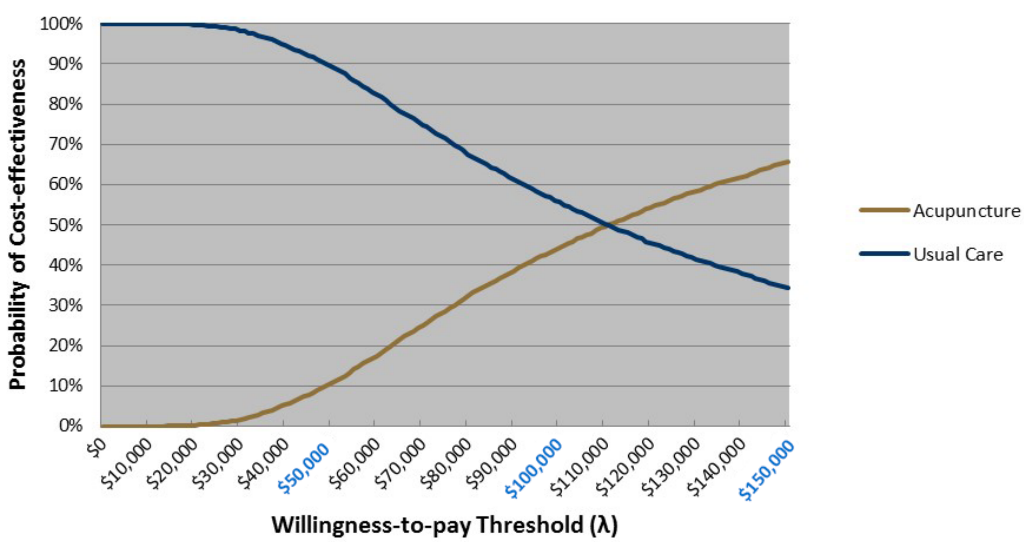
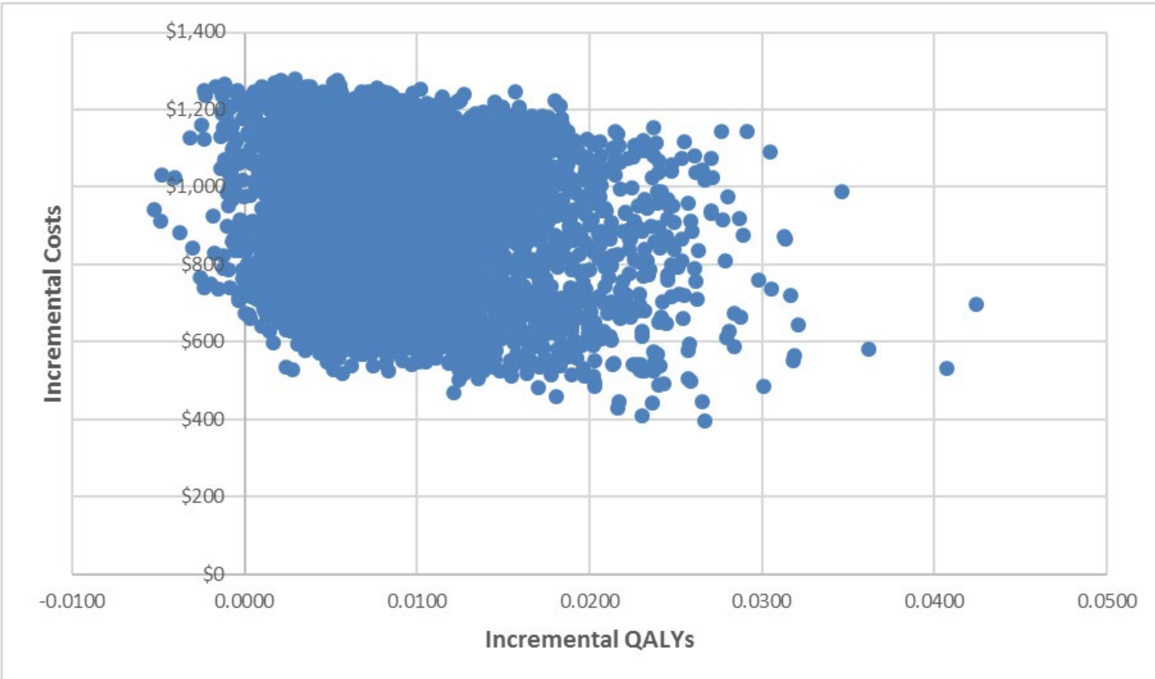


Figure E6. Incremental Cost-Effectiveness Scatter Plot for 5,000 Simulations of Acupuncture Versus Usual Care



QALY: Quality-Adjusted Life Year

Figure E7. Cognitive Behavioral Therapy Cost-Effectiveness Acceptability Curve

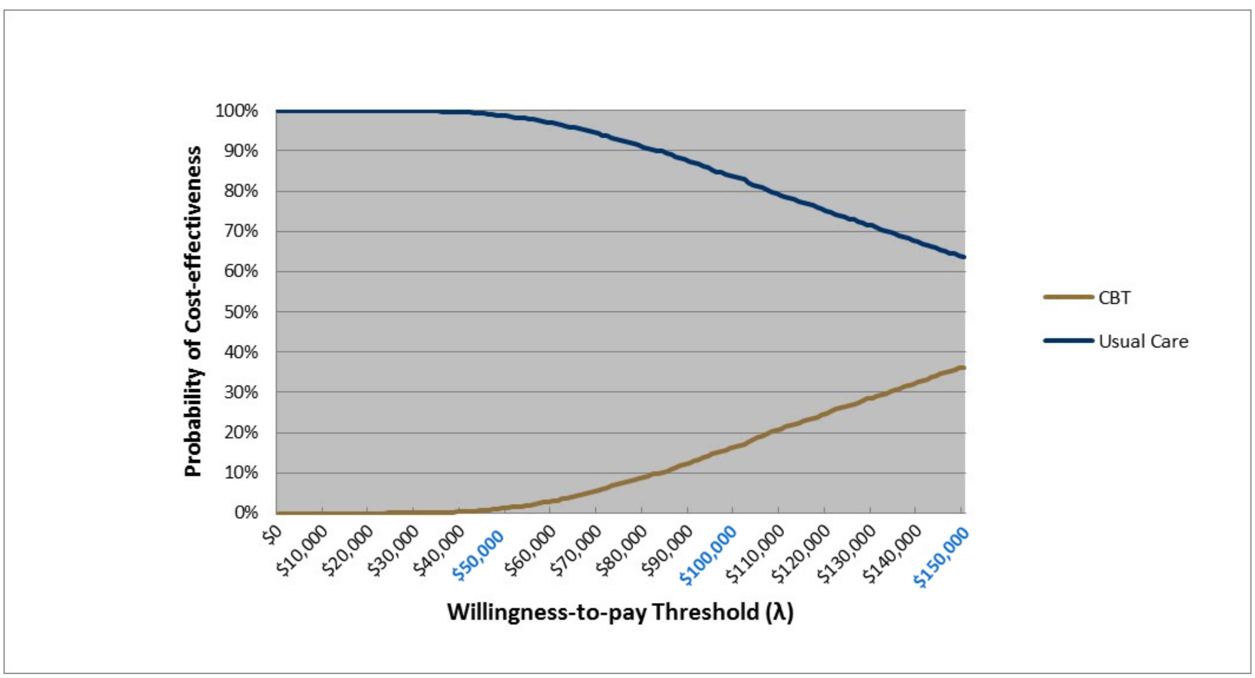
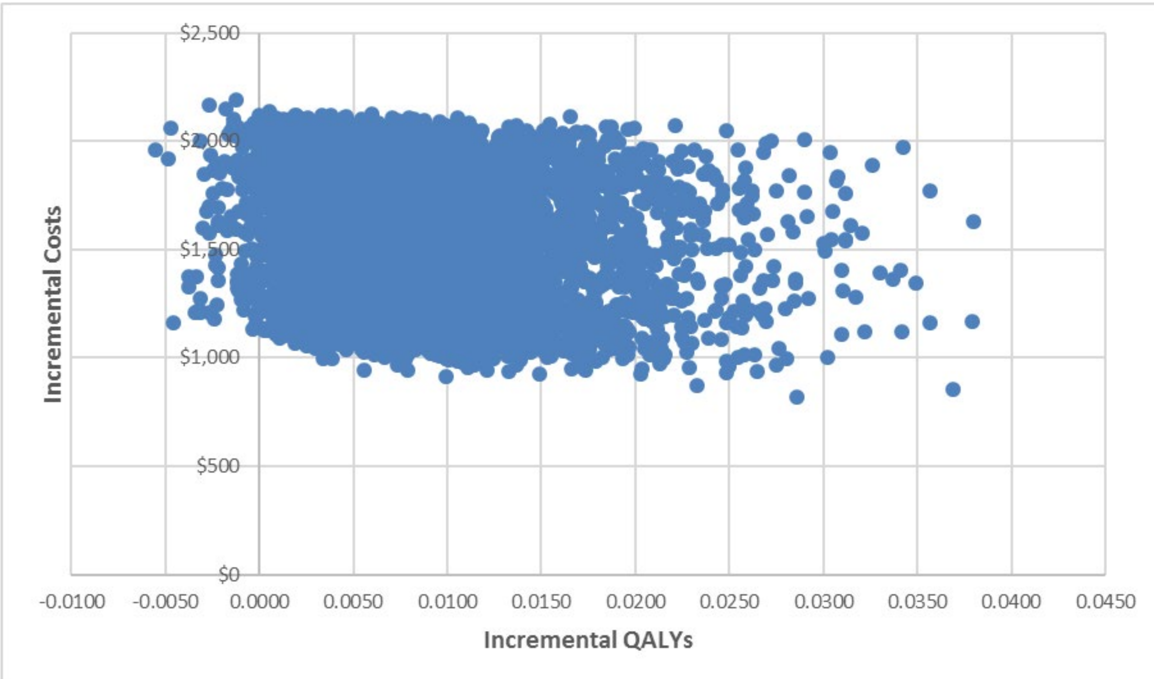


Figure E8. Incremental Cost-Effectiveness Scatter Plot for 5,000 Simulations of Cognitive Behavioral Therapy Versus Usual Care



QALY: Quality-Adjusted Life Year

Figure E9. Mindfulness-Based Stress Reduction Cost-Effectiveness Acceptability Curve

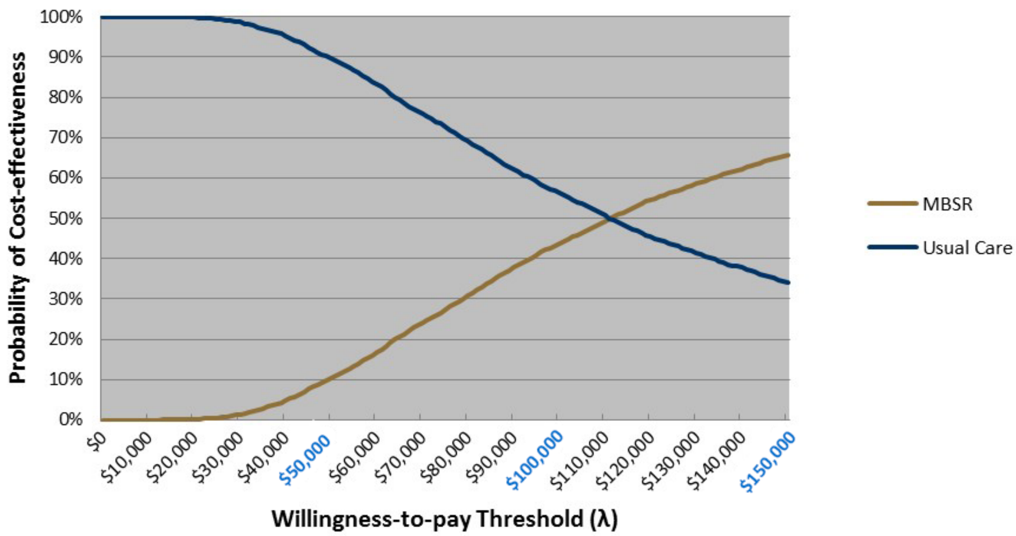
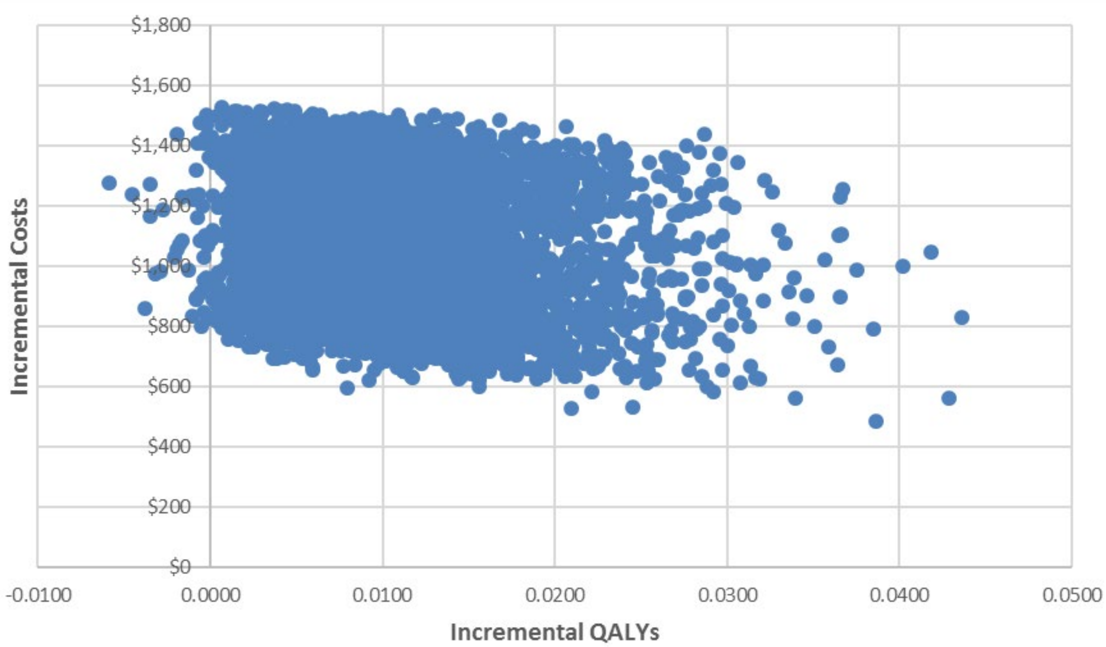


Figure E10. Incremental Cost-Effectiveness Scatter Plot for 5,000 Simulations of Mindfulness-Based Stress Reduction Versus Usual Care



QALY: Quality-Adjusted Life Year

Figure E11. Yoga Cost-Effectiveness Acceptability Curve

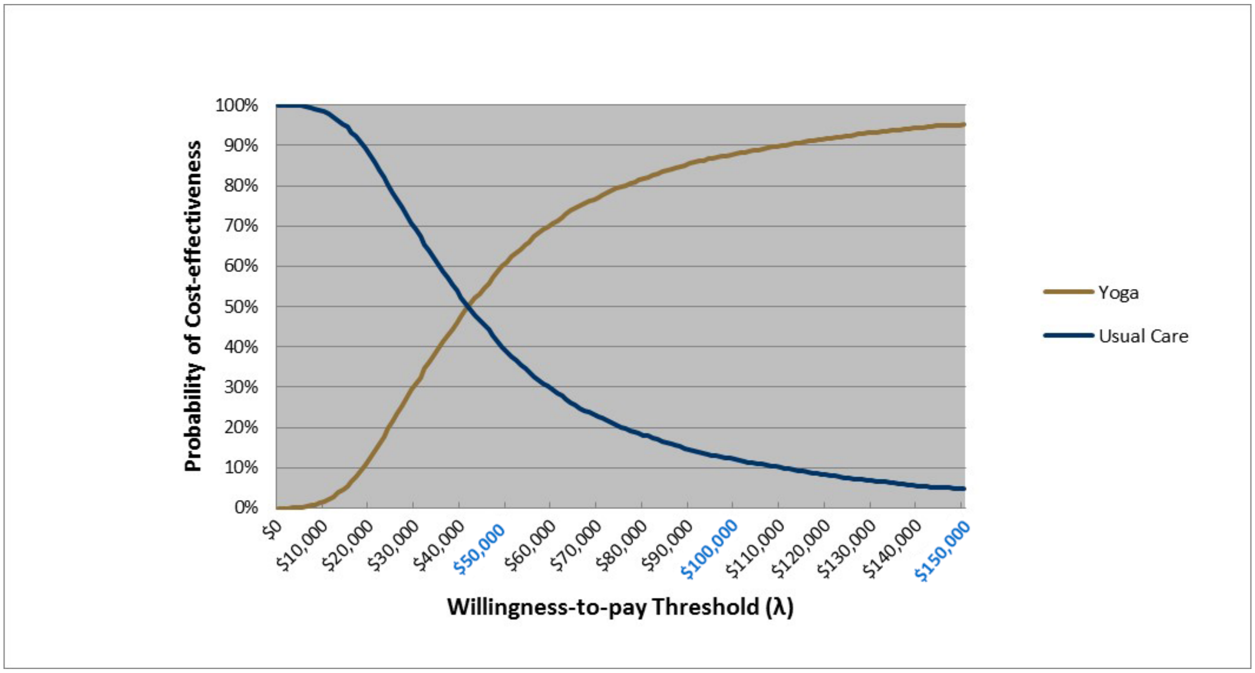
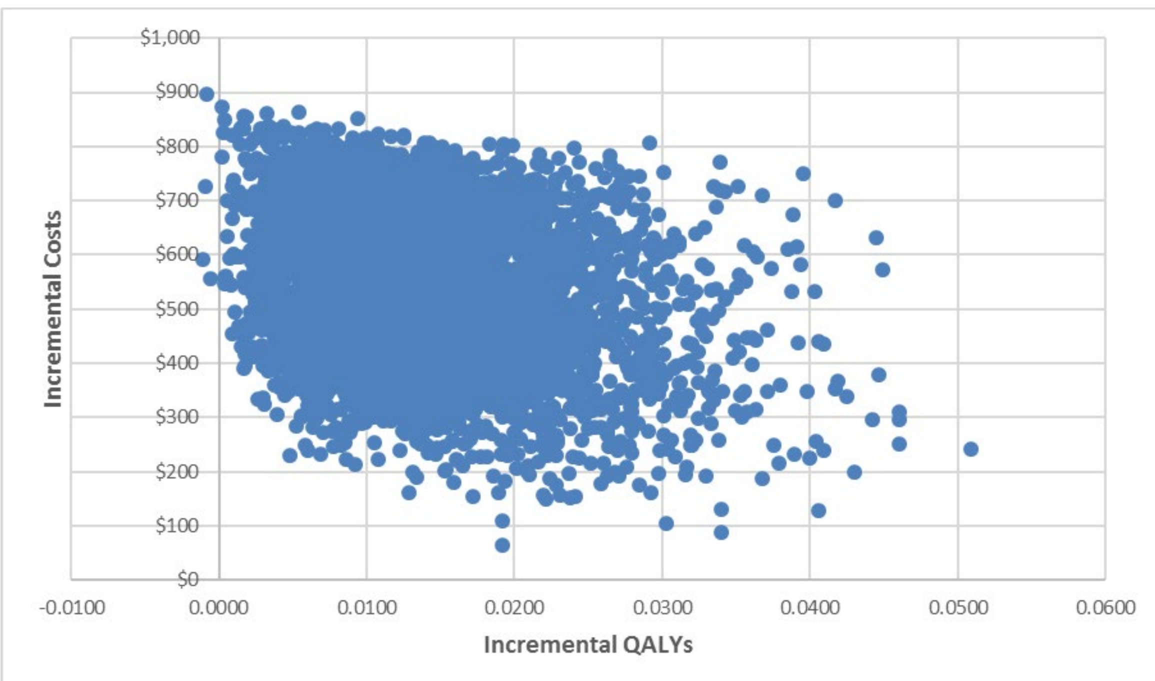


Figure E12. Incremental Cost-Effectiveness Scatter Plot for 5,000 Simulations of Yoga Versus Usual Care



QALY: Quality-Adjusted Life Year

Figure E13. Tai Chi Cost-Effectiveness Acceptability Curve

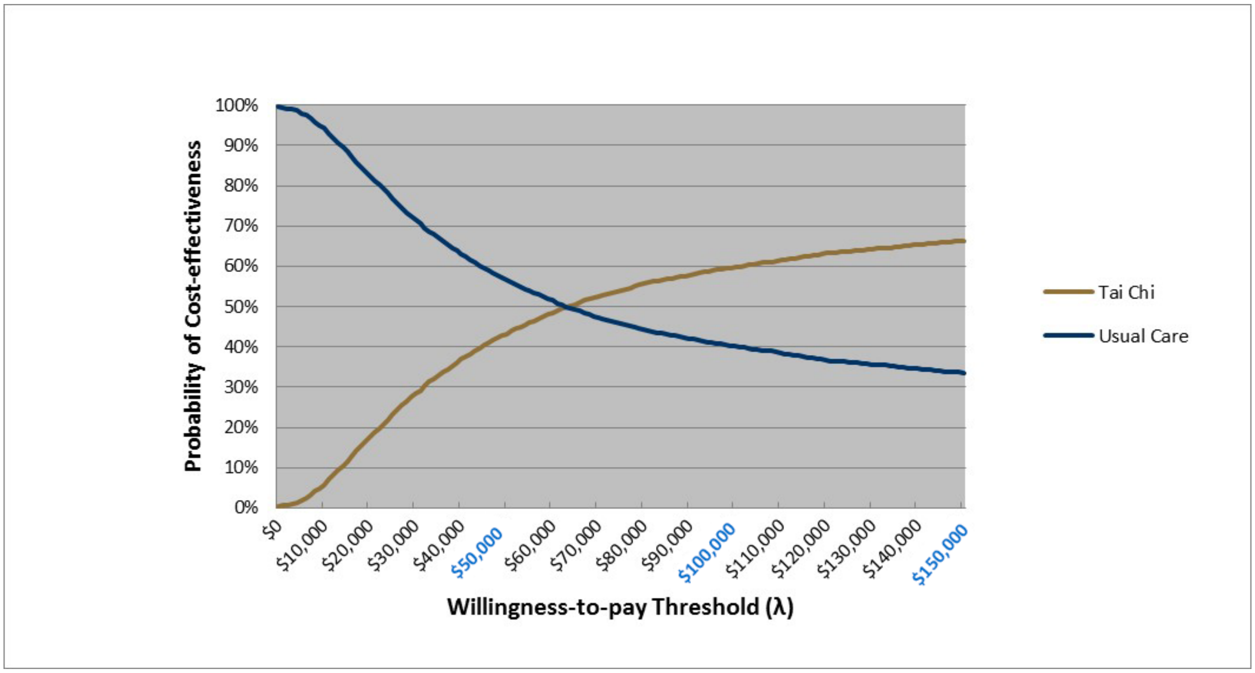
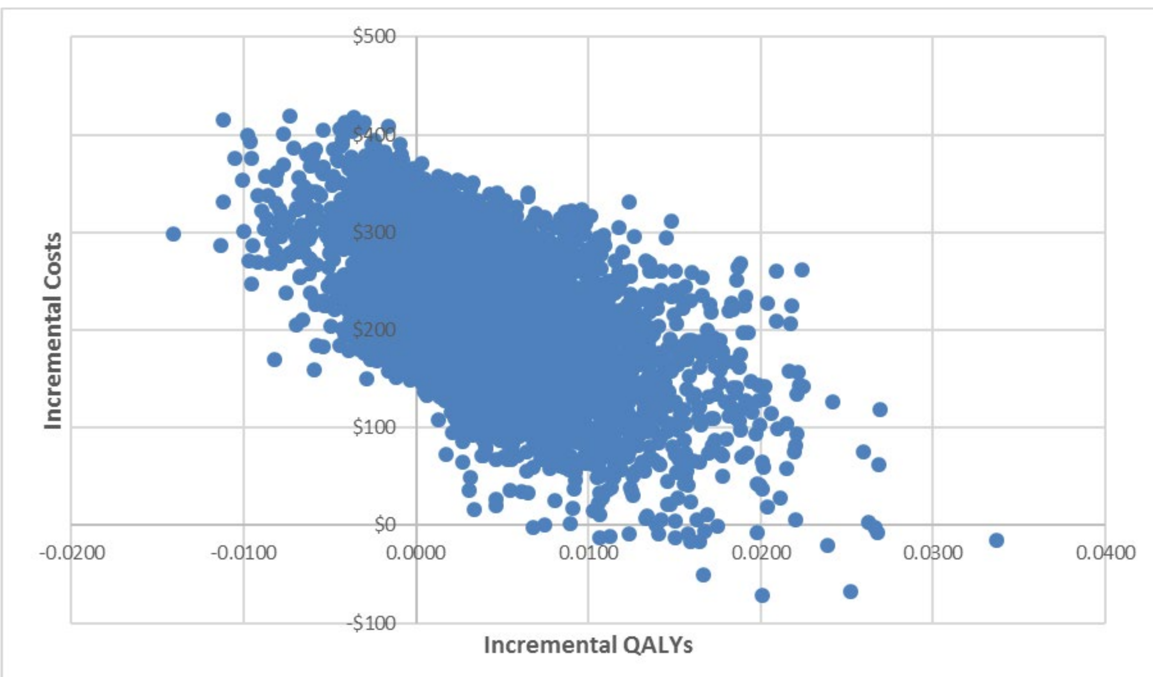


Figure E14. Incremental Cost-Effectiveness Scatter Plot for 5,000 Simulations of Tai Chi Versus Usual Care



QALY: Quality-Adjusted Life Year

Scenario Analyses: Results

Varying Time Horizon

Table E9. Incremental Cost Per QALY Gained for Interventions Versus Usual Care Over a One- and Three-Year Time Horizon

	Acupuncture	CBT	MBSR	Yoga	Tai Chi
One year	$269,216	$456,290	$324,395	$179,483	$188,628
Three years	$90,368	$157,134	$110,061	$58,342	$61,606
Five years (base case)	$89,888	$156,331	$109,486	$58,071	$61,265

CBT: cognitive behavioral therapy, MBSR: mindfulness-based stress reduction

Modified Societal Perspective

Table E10. Incremental Cost-Effectiveness Results Versus Usual Care from a Modified Societal Perspective Over a Five-Year Time-Horizon

Intervention	Incremental Cost Effectiveness Ratio (Cost per QALY Gained)
Acupuncture	$86,648
CBT	$153,091
MBSR	$106,245
Yoga	$54,777
Tai Chi	$58,025

CBT: Cognitive Behavioral Therapy, MBSR: Mindfulness-Based Stress Reduction, QALY: Quality-Adjusted Life Year