# Evidence Map of Acupuncture as Treatment for Adult Health Conditions Update from 2013–2021

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The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

# PREFACE

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

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

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

The present report was developed in response to a request from the Integrative Health Coordinating Center under the Office of Patient Centered Care & Cultural Transformation. The scope was further developed with input from Operational Partners (below), the ESP Coordinating Center, and the review team. The ESP consulted several technical and content experts in designing the research questions and review methodology. In seeking broad expertise and perspectives, divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Ultimately, however, research questions, design, methodologic approaches, and/or conclusions of the review may not necessarily represent the views of individual technical and content experts.

## ACKNOWLEDGMENTS

The authors are grateful to the following individuals for their contributions to this project:

## **Operational Partners**

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

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#### **Peer Reviewers**

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

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# EVIDENCE MAP

# **INTRODUCTION**

# PURPOSE

The Evidence Synthesis Program (ESP) is responding to a request from the VHA Office of Patient Centered Care & Cultural Transformation, Integrative Health Coordinating Center to provide current evidence regarding use of acupuncture for adult health conditions of interest to VA. Findings from this review will be used by VA referring providers, site leadership, and policy makers to improve Veteran access to non-pharmacologic treatment approaches and improve outcomes for Veterans by utilizing evidence-based care pathways.

## BACKGROUND

Acupuncture is a technique that is part of a larger system of care often referred to as Traditional Chinese Medicine. The *Huangdi Neijing*, also known as the *Yellow Emperor's Inner Classic*, dates to approximately the second century BCE and is one of the oldest known medical texts with references to acupuncture.<sup>1</sup> Trained practitioners stimulate specific points on the body, commonly by inserting thin needles into the skin with the intention of restoring and balancing the *qi* or energy of the mind and body and promoting health.<sup>2</sup> Acupuncture has continued to grow in popularity since a *New York Times* journalist wrote in 1971 about receiving acupuncture for pain after an emergency appendectomy, and the following year, the use of acupuncture in the surgical setting was observed during a Presidential visit to China.<sup>3</sup>

Multiple national surveys in the early 1990s showed that many individuals, including Veterans, were using complementary and integrative health (CIH) approaches. In 1998, the NIH formed the National Center for Complementary and Alternative Medicine (NCCAM). Since its inception it has funded research for and supported the use of acupuncture in certain pain conditions <sup>4</sup> In 2011, the Office of Patient Centered Care and Cultural Transformation (OPCC&CT) was established by the Veteran's Health Administration, and in 2014 leadership launched the Integrative Health Coordinating Center (IHCC) to work to bring CIH approaches to the VA. In 2017, the VHA Whole Health System of care included acupuncture as one of the complementary and integrative health modalities, VHA Directive 1137-Provision of Complementary and Integrative Health, included in the VA's medical benefits package.<sup>5</sup>

The VA strives to promote evidence-based practice and utilizes evidence maps such as this to provide guidance to VA leadership and to inform policy and clinical decision-making. The original Evidence Synthesis Program (ESP) report published in 2014 by VA Health Services Research & Development (HSR&D) has for years been among the most highly downloaded report from the ESP database.<sup>6</sup> With the increasing popularity of acupuncture among both Veterans and civilians and a growing body of available research on acupuncture, an update of this report was essential.

# **METHODS**

## **TOPIC DEVELOPMENT**

This topic was developed in response to a nomination from Juli Olson, DC, DACM, National Lead for Acupuncture, Integrative Health Coordinating Center. The scope was further developed with input from the topic nominator, the ESP Coordinating Center, and the review team. The scope of this report includes the following:

- 1. Evidence maps that provide a visual overview of the distribution of evidence for acupuncture.
- 2. An accompanying narrative that helps stakeholders interpret the state of the evidence to inform policy and clinical decision-making.

## DATA SOURCES AND SEARCHES

The literature searches used for these maps are based on the searches used for the original Evidence Map of acupuncture completed in 2012 and early 2013. Four databases were included in the search, which covered March 2013 to April 2021: PubMed, Allied and Complementary Medicine Database (AMED), Cochrane Database of Systematic Reviews (CDSR), and DARE (Database of Abstracts of Reviews of Effects, ending search in 2014 when DARE ceased production). See Appendix A for full search strategies.

## **STUDY SELECTION**

Each title was screened independently by 2 authors for relevance; any article chosen by either reviewer was included in the abstract screen. Abstracts were then reviewed in duplicate with any discrepancies resolved by group discussion. In order to be included, abstracts or titles needed to be about efficacy or effectiveness of acupuncture for an adult health condition and be a systematic review. A systematic review was defined as a review that had a documented systematic method for identifying and critically appraising evidence. At this stage, we also selected titles and abstracts of systematic reviews about treatments and conditions for which acupuncture might be included; for example, we included titles such as "Interventions for the reduction of prescribed opioid use in chronic non-cancer pain" or "Non-pharmacologic treatments for symptoms of diabetic peripheral neuropathy: A systematic review." Systematic reviews were still eligible if they covered other interventions and results for acupuncture were reported separately. We did so because reviews with mixed acupuncture, moxibustion alone, needling, and traditional Chinese medicine (TCM) without mention of acupuncture and fire acupuncture were excluded.

We abstracted condition type when reviewing abstracts and presented a list of conditions for which we found reviews to the Operational Partner to determine which conditions were of interest to the VA. Any conditions not selected by the Operational Partner were then excluded from further review.

From this large collection of systematic reviews that included acupuncture as a treatment, we next restricted eligibility to reviews that used formal methods to assess the certainty (or strength



or quality) of the evidence for conclusions. In general, this meant using Grading of Recommendations, Assessment, Development and Evaluations (GRADE).<sup>7</sup> However, other formal methods were also included, such as the approach utilized by the US Agency for Healthcare Research & Quality Evidence-based Practice Center program.<sup>8</sup> To remain eligible, an included review had to both 1) state or cite the method used and 2) report the certainty (or strength or quality) of evidence for each conclusion (see footnote 1).

After applying this restriction, many health conditions had only 1 systematic review meeting eligibility criteria, and we used this review for the map.

For some conditions, we identified more than 1 review meeting the eligibility criteria. For these conditions, we first assessed whether the reviews differed in some other feature used to classify reviews on our map – for example, a systematic review on condition X included only studies comparing acupuncture to sham, while another systematic review on condition X only included studies comparing acupuncture to other active therapies. In such cases, we included both reviews on the map, with the appropriate designations (such as "versus sham" and "versus active therapy"). If there were multiple reviews on the same condition, and they did not differ in some other feature, then we selected the 1 systematic review that we judged as being most informative for readers. In general, this was the most recent review or the review with the greatest number of included studies. Systematic reviews otherwise meeting eligibility criteria that were not included in the map for this reason are listed in Appendix B.

## **Eligibility Criteria**

The ESP included studies that met the following criteria:

<b>P</b> opulation:	Adult conditions that may be addressed by acupuncture	
Intervention:	Acupuncture, Electro-acupuncture, Battlefield Acupuncture, National Acupuncture Detoxification Association (NADA) protocol	
Comparator:	Sham/placebo, usual care, other therapies, no treatment	
Outcomes:	Health outcomes	
Timing:	Any	
Setting:	Any	
<b>S</b> tudy Design:	Systematic reviews	

*Footnote 1*. We made one exception to this rule for the individual patient data (IPD) meta-analysis by Vickers and colleagues.<sup>9</sup> An IPD meta-analysis can be more informative than a conventional meta-analysis of aggregate data, but they are often not given certainty of evidence assessments because some GRADE criteria, such as consistency, are not as applicable in an IPD meta-analysis. Rather than exclude the Vickers review, which would essentially be penalizing it for being a stronger study design than a conventional review, we applied the GRADE criteria to that portion of the Vickers review that was a conventional meta-analysis, which yielded a Certainty of Evidence rating of "Moderate" (reduced 1 level from "High" due to inconsistency).



## DATA ABSTRACTION AND ASSESSMENT

Each included systematic review had data abstracted by 1 reviewer and verified by a second reviewer. Abstracted data included: number of studies included in the review that had acupuncture as the intervention, condition, type of acupuncture, comparators, certainty of evidence statement(s), and main findings relevant to acupuncture as treatment for condition.

### **SYNTHESIS**

Our evidence mapping process resulted in a visual depiction of the evidence for acupuncture, as well as an accompanying narrative with ancillary figures and tables. The visual depiction or evidence map uses a bubble plot format to display information on 4 dimensions: bubble size, bubble label, x-axis, and y-axis. This allowed us to provide the following types of information about each included systematic review, as follows:

**Number of articles in systematic review (bubble size)**: Each systematic review bubble's size is proportional to the number of primary research studies included in that systematic review related to the effect of acupuncture.

**Condition (bubble label)**: Each bubble is labeled with the condition discussed by that systematic review.

**Shapes and colors**: Intervention characteristics for each condition are presented in the form of shapes (type of acupuncture) and colors (comparators). For type of acupuncture, rectangle denotes electro-acupuncture only and circle denotes all other types (manual/standard, electro-acupuncture). For comparators, the color red represents sham/placebo, blue for active/usual care, purple for mixed comparators with subgroups, and gray for mixed comparators with no subgroups. A condition can show up more than once if multiple systematic reviews had included either different acupuncture interventions and/or different comparators.

**Strength of findings (rows)**: Each condition is plotted on the map based on the certainty of evidence statement as reported in the systematic review. Many reviews report more than 1 conclusion. Thus, to keep reviews mutually exclusive, we have 3 categories: "All conclusions are rated as low or very low certainty," "at least 1 conclusion rated as moderate certainty," and "at least one conclusion rated as high or strong certainty." For reviews with multiple certainty of evidence statements, we selected the highest certainty of evidence statement.

**Effect of acupuncture (columns)**: Each condition is plotted in either "benefit" or "no benefit" as effect of acupuncture based on conclusion of systematic review.

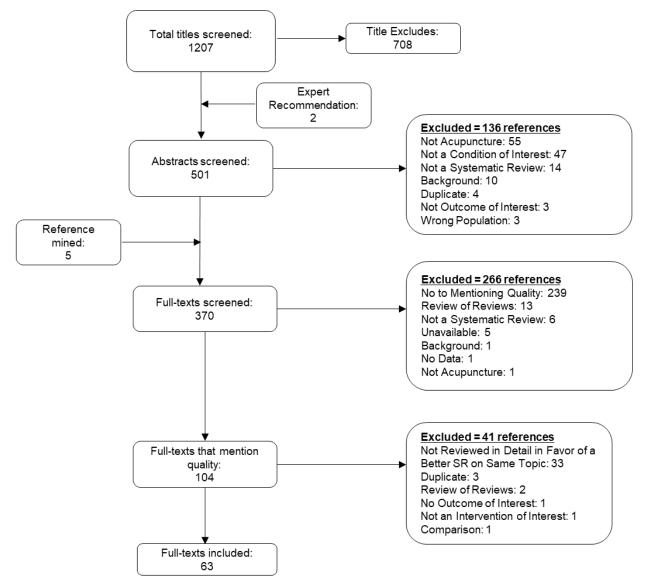
**Narrative synthesis**: The narrative synthesis expands upon the visual evidence map to provide overarching conclusions from the maps. Details about the conclusions in individual reviews are included in an appendix.

# RESULTS

## LITERATURE FLOW

The literature flow diagram (Figure 1) summarizes the results of the study selection process (full list of excluded studies available in Appendix C).

### Figure 1. Literature Flowchart



## LITERATURE OVERVIEW

We identified 1,207 potentially relevant citations (Figure 1). Including 2 publications recommended by experts, we applied the inclusion and exclusion criteria to these 1,209 titles. A total of 501 abstracts were reviewed at abstract stage. From these, a total of 136 abstracts were excluded for the following reasons: not acupuncture (N = 55), not a condition of interest (N = 47), not a systematic review (N = 14), background (N = 10), duplicate (N = 4), not outcome of

interest (N = 3), and wrong population (N = 3). After reference mining the cited literature in our screened full-text articles, we identified an additional 5 titles to be reviewed at the full-text stage, resulting in a total of 370 publications. From these, 266 publications were excluded for the following reasons: did not use formal method for grading evidence (N = 239), review of reviews (N = 13), not a systematic review (N = 6), unavailable (N = 5), background (N = 1), no data (N = 1), and not acupuncture (N = 1). A full list of excluded reviews from the full-text review is included in Appendix C.

A total of 104 publications were retained for further review to potentially be included on the map. Of these, 41 reviews were excluded from the map for the following reasons: the review overlapped a more recent/larger review which was already included on the map (N = 33), duplicate (N = 3), review of reviews (N = 2), no outcome of interest (N = 1), not an intervention of interest (N = 1), and comparison (N = 1). See Appendix B for a full list of publications not included on the map because they overlapped with an included review. We included 63 publications in this map.

### **Characteristics of Included Reviews**

The number of studies included for acupuncture in the included reviews ranged from 1 study to 73 studies. Twenty-eight reviews included fewer than 10 studies about acupuncture, 25reviews included 10 to 25 studies, and 10 reviews included 25 or more studies. Eighteen of the included reviews were completed by the Cochrane Collaboration, with 1 review published as a journal article in a peer-reviewed journal.<sup>9</sup> The US Agency for Health Research and Quality conducted 3 of the included reviews, with 1 review published as a journal article in a peer-reviewed journal.<sup>10</sup>

The country of origin for reviews varied, with the highest number of reviews originating from China (N = 22). Other countries included Australia (N = 4), Brazil (N = 1), Italy (N = 1), Korea (N = 6), Taiwan (N = 1), United Kingdom (N = 2), and the United States (N = 7). Nineteen reviews involved teams from multiple countries; teams included reviewers from China and Norway,<sup>11</sup> China and Australia,<sup>12</sup> China (Hong Kong) and the United Kingdom,<sup>13</sup> Spain and the United Kingdom,<sup>14</sup> Canada and the United Kingdom,<sup>15</sup> Germany, the United Kingdom, and the United States,<sup>16</sup> and Korea and the United States.<sup>17</sup>

Forty-seven reviews included more than 1 type of acupuncture, while 16 reviews included only 1 type of acupuncture as the intervention. Almost all of the mapped reviews included manual or standard acupuncture as the intervention, with the exception of 1 review including only electro-acupuncture as the intervention for the reduction of prescribed opioid use in chronic non-cancer pain.<sup>18</sup> A variety of comparators were included in the reviews, often involving more than 1 comparator. Thirty-six reviews included more than 1 comparator and conducted separate analyses of the effect of acupuncture by comparator, while 7 reviews that had included more than 1 comparator did not conduct separate analyses. Fourteen reviews employed active or usual care only, and 8 reviews included sham or placebo as comparator only.

The included 63 reviews were categorized into 41 conditions, of which 14 conditions were further categorized into sub-conditions: back pain (N = 4), cancer-related pain (N = 4), chronic fatigue syndrome (N = 2), depression (N = 4), fertility (N = 4), fibromyalgia (N = 4), headache (N = 5), insomnia (N = 2), mixed pain-not specific (N = 3), osteoarthritis (N = 2), other acute pain (N = 3), post-operative pain (N = 3), shoulder pain (N = 2), and substance use disorder (N = 2). These conditions and sub-conditions were then grouped by type of condition, resulting in 5



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maps (Figure 2). Three reviews discussed multiple conditions and thus appeared in the maps more than once.<sup>19-21</sup> Most conditions were related to pain, which were separated into 2 maps: general pain (N = 23) and musculoskeletal pain (N = 11). The remaining conditions were categorized into maps for mental health (N = 12), women's health (N = 9), and other conditions (N = 9). Appendix D shows the breakdown of conditions and related sub-conditions by map.

This map includes 9 conditions that were not part of the 2014 map (Table 1).

#### Table 1. Conditions in 2022 Evidence Map Not in 2014 Evidence Map

Angina	Irritable Bowel Disorder	
Diabetic Peripheral Neuropathy	Lateral Elbow Pain	
Dyspepsia	Peripheral Neuropathy	
Herpes Zoster	Post-herpetic Neuralgia	
Primary Trigeminal Neuralgia		

Because we applied an additional criterion that reviews had to report a method used for grading certainty of evidence in order to be included in this map, a few conditions that had appeared in the 2014 map were not included in this map (Table 2). Four such conditions are plantar heel pain, nausea, restless leg syndrome, and blood pressure. For plantar heel pain, we identified 1 publication for inclusion but it did not use a formal method for grading certainty of evidence and was not included in the map. For nausea, we did not identify citations to be reviewed at full text. For restless leg syndrome, we identified 2 publications for inclusion but neither used a formal method for grading certainty of evidence and were not included in the map. For blood pressure, we identified 2 publications for full-text review. One review was excluded because it was not about acupuncture, and the other did not use a formal method for grading certainty of evidence and was not included in map.

Condition	New Systematic Review Identified in Update Search?	Used Formal Method for Grading Evidence?
Plantar heel pain	Yes	No
Nausea	No	N/A
Restless Leg Syndrome	Yes	No
Blood Pressure	Yes	No

For ease of comparison, we divided the included conditions into 5 evidence maps:

- All pain (other than musculoskeletal pain)<sup>9, 13, 15, 17-19, 22-38</sup> (Figure 2A)
- Musculoskeletal pain<sup>10, 12, 14, 16, 20, 21, 39-43</sup> (Figure 2B)
- Mental health conditions<sup>44-54</sup> (Figure 2C)
- Women's health<sup>55-63</sup> (Figure 2D)
- Other conditions<sup>11, 64-71</sup> (Figure 2E)

## **EVIDENCE MAPS**

In each evidence map, columns correspond to whether a conclusion of the review was that 1) there was a benefit of acupuncture relative to a comparison treatment, or 2) there was no benefit of acupuncture relative to the comparison treatment. Columns *are not* mutually exclusive. A review could have more than 1 conclusion, and those conclusions could differ in the benefit of acupuncture.

Rows correspond to GRADE Working Group grades of evidence:<sup>7</sup>

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

All rows *are* mutually exclusive. The top row indicates that at least 1 conclusion in the review was rated by its authors as having high (or strong) certainty of evidence (also sometimes called strength of evidence or quality of evidence). The middle row indicates that at least 1 conclusion was rated as moderate certainty of evidence (and none rated as high or strong, in which case it would be in the right-hand column). The bottom row indicates that all conclusions in the review were rated as low or very low certainty of evidence. Since GRADE assesses certainty of evidence, it is possible for a body of evidence to demonstrate low or moderate estimates of effect but with high certainty of evidence; conversely, it is possible to have evidence demonstrating high effectiveness but with low certainty.

Each conclusion (or general conclusion, see below) is then mapped onto this framework and identified by the name of the condition or sub-condition, *eg*, "pain management in cancer," "fibromyalgia," "migraine," *etc.* Colors are used to distinguish between the types of comparison treatments: conclusions only about comparisons to sham/placebo, conclusions only about comparisons to active therapies or usual care, conclusions where the comparison treatments were a mix of these and no subgroup analysis was presented, and conclusions where comparison treatments were a mix of these with subgroup analyses. Symbols are used to identify the few reviews specific to certain types of acupuncture, namely reviews of electro-acupuncture only. We were only able to report to the degree of specificity the original authors report. When they called it electro-acupuncture, we called it electro-acupuncture. When they referred to it simply as acupuncture, we classified it as manual acupuncture, since the systematic reviews that included multiple types of acupuncture and specified the type for each included study had shown the great majority of included studies were about manual acupuncture.

The size of the bubble is used to indicate how many original research studies were included in the review. For example, in Figure 2A, the large yellow circle in the left-hand column indicates

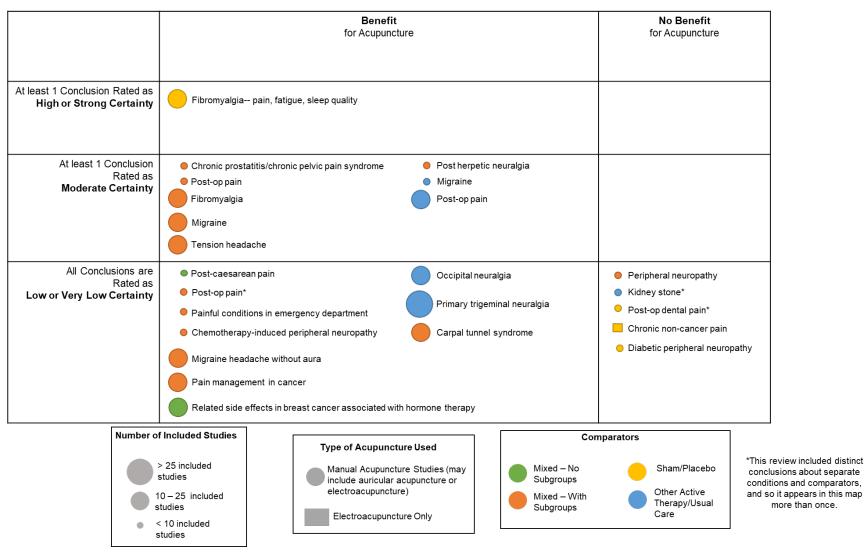


there is a review about fibromyalgia that included between 10-25 original studies and had at least 1 conclusion that was rated as high certainty of evidence that acupuncture was better than the comparison treatment of sham/placebo. In the same figure, the small light blue dot in the lower right-hand corner indicates there is a review about kidney stone pain that included fewer than 10 original studies where all conclusions were rated as low or very low certainty of evidence that acupuncture was not of greater benefit than the comparison treatment of active/usual care.

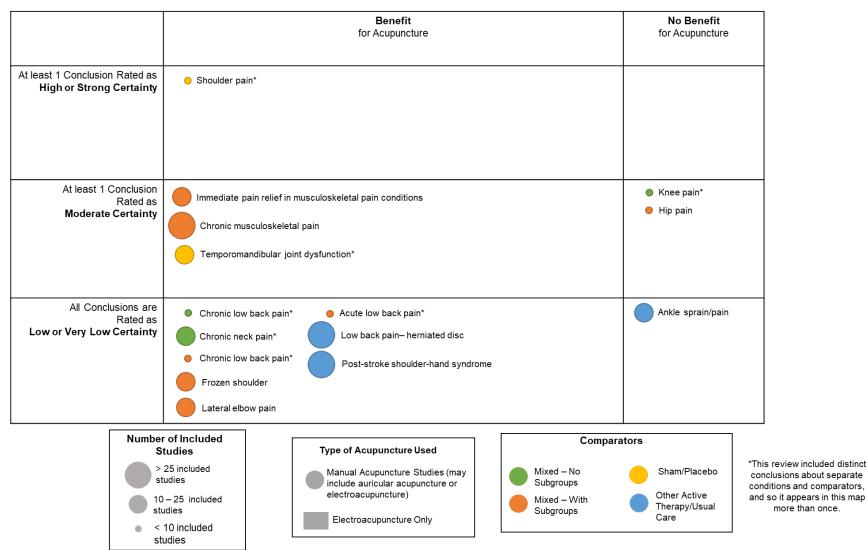
As noted above, reviews could contain more than 1 conclusion and enter the map at different spots. Also note that for ease of presentation we made the following decisions. If a review had 3 or fewer conclusions, we extracted and mapped them all. If a review had more than 3 conclusions (some reviews had >10 conclusions with, for example, separate statements for each kind of acupuncture assessed, each different comparison treatment, and each different assessed outcome), rather than attempt to map all of these, we instead mapped the overall conclusion the review authors gave to the overall body of evidence (usually found in the abstract or summary).

#### Figure 2. Condition Maps

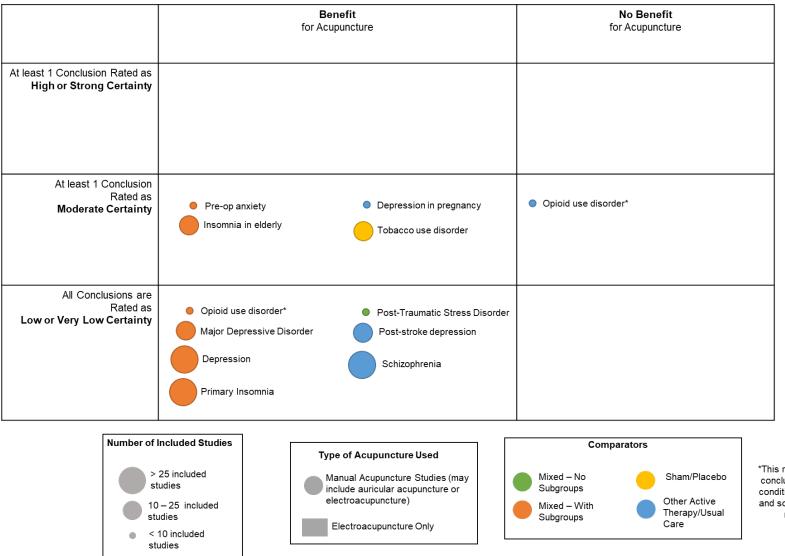
#### 2A. All Pain Other than Musculoskeletal Pain



#### 2B. Musculoskeletal Pain



#### 2C. Mental Health



\*This review included distinct conclusions about separate conditions and comparators, and so it appears in this map more than once.

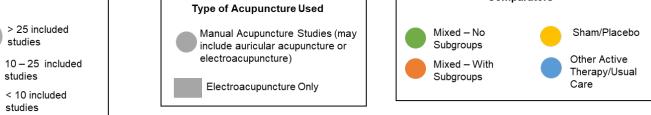


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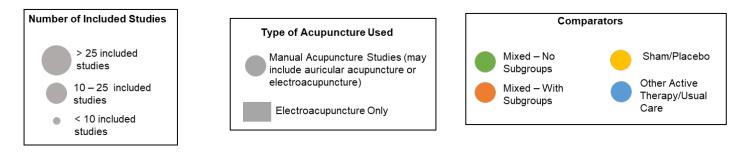
#### 2D. Women's Health

	Benefit for Acupuncture	No Benefit for Acupuncture
At least 1 Conclusion Rated as High or Strong Certainty		Assistive reproductive therapy
At least 1 Conclusion Rated as <b>Moderate Certainty</b>	Pregnancy - low back and pelvic pain	
All Conclusions are Rated as Low or Very Low Certainty	<ul> <li>Polycystic ovary syndrome/ovarian hyperstimulation</li> <li>Resumption of menses</li> <li>Oocyte retrieval</li> <li>Premenstrual syndrome</li> <li>Menopause</li> </ul>	Anovulatory fertility     Dysmenorrhea
	f Included Studies     Type of Acupuncture Used       > 25 included studies     Manual Acupuncture Studies (main include auricular acupuncture or include auricular acupunctur	



#### 2E. Other Conditions

	Benefit for Acupuncture	No Benefit for Acupuncture
At least 1 Conclusion Rated as High or Strong Certainty		
At least 1 Conclusion Rated as Moderate Certainty	<ul> <li>Chronic fatigue syndrome</li> <li>Angina</li> <li>Herpes zoster</li> <li>Improvement of cognitive impairment after stroke</li> </ul>	
All Conclusions are Rated as Low or Very Low Certainty	Chronic fatigue syndrome Functional dyspepsia	<ul> <li>Health-related quality of life in cancer patients</li> <li>Tinnitus</li> </ul>





Three high-level observations are worth making. First, most published reviews were about painful conditions, and there are more mapped conclusions for painful conditions than for all other conditions combined. Second, the number of reviews with at least 1 conclusion rated as high certainty of evidence is very small (N = 3). Third, although a greater number of reviews have at least 1 conclusion rated as moderate certainty of evidence, the majority of reviews reported conclusions rated as low or very low certainty of evidence.

In addition to these maps, we collected all conclusions rated as high certainty of evidence in Table 3 and all conclusions rated as moderate certainty of evidence in Table 4. Lastly, all conclusions from mapped reviews are collected in a large appendix table (Appendix E).

The conclusions from the 3 systematic reviews graded as high certainty of evidence by the original review authors (Table 3) are:

- No difference between acupuncture and sham acupuncture in birth outcomes in patients undergoing embryo transfer (as part of in vitro fertilization).<sup>57</sup>
- Better pain, sleep, and general status outcomes in patients with fibromyalgia syndrome treated with acupuncture compared to sham.<sup>72</sup>
- Better pain relief in patients with shoulder pain treated with acupuncture compared to sham.<sup>21</sup>

There are many more conclusions authors of included systematic reviews graded as moderate certainty of evidence (see Table 4). More than 75% of these conclusions were comparing acupuncture to sham or control acupuncture, or no treatment. Only a small number of these conclusions were about comparisons of acupuncture to usual care or other active therapies. About 25% of the conclusions rated as moderate certainty were findings that acupuncture was no better than the comparator. A little more than half of the conclusions rated as moderate certainty were about painful conditions or pain outcomes.

All of the remaining conclusions from the remaining reviews were judged by the original authors as being low or very low certainty of evidence, meaning "Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect" or "We have very little confidence in the effect estimate." See Appendix E.

# Table 3. Conclusions Rated as High Certainty of Evidence from Systematic Reviews Included in the EvidenceMap

Author, Year	Condition	Sub-Condition	High Certainty of Evidence Conclusion
Coyle, 2021 <sup>57</sup>	Fertility	Assistive Reproductive Therapy	When compared with sham acupuncture, acupuncture performed at the time of embryo transfer does not result in better outcomes for live birth rate or for miscarriage rate.
Kim, 2019 <sup>72</sup>	Fibromyalgia	Pain, Fatigue, Sleep Quality	Verum acupuncture is more effective than sham acupuncture for pain relief, improving sleep quality, and improving general status in fibromyalgia syndrome post-treatment.
Yuan, 2016 <sup>21</sup>	Shoulder Pain	None	Acupuncture is superior to sham acupuncture in the relief of pain.

# Table 4. Conclusions Rated as Moderate Certainty of Evidence from Systematic Reviews Included in the Evidence Map

Author, Year	Condition	Sub-Condition	Moderate Certainty of Evidence Conclusion
Yang, 2019 <sup>64</sup>	Angina	None	Compared to sham acupuncture, acupuncture may be effective for improving average pain intensity, 6-minute walk test, anxiety level and depression level.
Tong, 2021 <sup>44</sup>	Anxiety	Pre-operative Anxiety	Acupuncture therapy, compared with sham therapy, significantly reduced the STAI-S score for patients with preoperative anxiety.
Wang, 2014 <sup>11</sup>	Chronic Fatigue Syndrome	None	No statistically significant difference in physical symptoms as measured by the Chalder Fatigue Scale-1 between acupuncture and sham.
Vickers, 2018 <sup>16</sup>	Chronic Musculoskeletal Pain	None	Acupuncture is effective for the treatment of chronic pain, with treatment effects persisting over time.
Smith, 2019 <sup>46</sup>	Depression	Depression in Pregnancy	Acupuncture compared to control may reduce antenatal depression.
Zhang, 2019 <sup>27</sup>	Fibromyalgia	None	Compared to sham, real acupuncture was more effective in reducing pain and improving quality of life after treatment in the short term.
Giovanardi, 2020 <sup>28</sup>	Headache	Migraine	Acupuncture is mildly more effective and much safer than medication for the prophylaxis of migraine.
Linde, 2016 <sup>32</sup>	Headache	Tension-type Headache	Acupuncture reduces headache frequency over usual care and sham.

Author, Year	Condition	Sub-Condition	Moderate Certainty of Evidence Conclusion
Linde, 2016 <sup>31</sup>	Headache	Migraine	Compared with no acupuncture, acupuncture was associated with a moderate reduction of headache frequency over no acupuncture after treatment.
			Comparison with sham, both after treatment and at follow-up, acupuncture was associated with a small but statistically significant frequency reduction over sham.
			Compared with prophylactic drug treatment, acupuncture reduced migraine frequency significantly more than drug prophylaxis after treatment.
Cui, 2021 <sup>68</sup>	Herpes Zoster	None	Compared with active treatment, acupuncture was associated with reduction on the overall incidence of post-herpetic neuralgia
Wang, 2020 <sup>69</sup>	Inflammatory Bowel Disease	None	Acupuncture may be more effective in treating ulcerative colitis compared to conventional medicine (metronidazole combined with sulfasalazine).
Kwon, 2020 <sup>49</sup>	Insomnia	Insomnia in Elderly	Using Pittsburgh Sleep Quality Index score, acupuncture and acupuncture combined with relaxation were both more effective in improving sleep quality compared to relaxation alone, but acupuncture was less effective compared to acupuncture combined with relaxation.
Guo, 2020 <sup>70</sup>	Irritable Bowel Syndrome	None	Compared with loperamide, acupuncture showed more effectiveness in weekly defecation. Compared to dicetel, acupuncture produced more significant effect related to the total symptom score and IBS Symptom Severity Scale.
Xiang, 2017 <sup>41</sup>	Mixed Not Specified Pain	Immediate Pain Relief in Musculoskeletal Pain Conditions	Acupuncture was associated with a greater immediate pain relief effect compared to sham acupuncture.
Manheimer, 2018 <sup>42</sup>	Osteoarthritis	Hip pain	Acupuncture probably has little or no effect in reducing pain or improving function relative to sham acupuncture in people with hip osteoarthritis.
Skelly, 2020 <sup>20</sup>	Osteoarthritis	Knee pain	There were no differences between acupuncture versus control interventions (sham acupuncture, waitlist, or usual care) on function in the intermediate term.
			There were no clinically meaningful differences between acupuncture versus control interventions (sham acupuncture, waitlist, or usual care) on pain in the intermediate term.

Author, Year	Condition	Sub-Condition	Moderate Certainty of Evidence Conclusion
Zhou, 2020 <sup>71</sup>	Other Specific	Improvement of Cognitive Impairment After Stroke	Acupuncture was effective in improving PSCI (post-stroke cognitive impairment).
Franco, 2019 <sup>9</sup>	Pelvic Pain	Chronic Prostatitis/ Chronic Pelvic pain syndrome	Acupuncture probably reduced prostatitis symptoms (compared to sham). Acupuncture may have reduced prostatitis symptoms compared with medical treatment
Pei, 2019 <sup>34</sup>	Post-herpetic Neuralgia	None	Acupuncture was more effective in reducing post-herpetic neuralgia pain intensity compared to control.
Tedesco, 2017 <sup>37</sup>	Post-operative Pain	None	Acupuncture significantly increases time to first request for analgesia compared to sham or no treatment.
Yin, 2020 <sup>36</sup>	Post-operative Pain	None	Acupuncture did not show significant differences in the reduction in pain or incidence of postoperative nausea and vomiting, but was more effective in reducing time to first defecation or first flatus compared to conventional medicine.
			Acupuncture in combination with conventional medicine did not show significant differences in the incidence of postoperative nausea and vomiting, but was more effective in reducing time to first defecation.
Liddle, 2015 <sup>63</sup>	Pregnancy	Low Back and Pelvic Pain	There was evidence from single studies that acupuncture significantly improves evening pelvic pain better than stabilizing exercise or usual prenatal care.
Chen, 2018 <sup>53</sup>	Substance Use Disorder	Opioid Use Disorder	There was no significant difference in number of positive urine samples for opioids, sleep quality, or sleep time between acupuncture and sham acupuncture. There was no difference between acupuncture and medication related to craving for opioid, anxiety, and retention of treatment.
White, 2014 <sup>54</sup>	Substance Use Disorder	Tobacco Use Disorder	Compared to sham, acupuncture resulted in greater short-term smoking cessation.
Yuan, 2016 <sup>21</sup>	Temporomandibular Pain	None	Real acupuncture showed a favorable effect on pain relief compared to sham.

### **Adverse Events**

In addition to maps of effectiveness outcomes, we also created a map for adverse events. Most of the 63 included reviews assessed adverse events, with 16 reviews explicitly grading evidence for adverse events. Figure 3 presents these 16 reviews mapped by certainty of evidence conclusions about adverse events,<sup>8, 17, 19, 20, 31, 32, 35, 37, 45, 48, 50, 52, 56, 58, 62</sup> of which 3 reviews appeared twice showing different certainty of evidence conclusions for different comparators.<sup>17, 20, 47</sup>

Much like our approach for maps described above, only reviews with certainty of evidence conclusions specifically for adverse events were included in this map. The certainty of evidence conclusions were reviewed separately from conclusions for effectiveness outcomes such that it is possible to find a low or very low certainty of evidence conclusion for benefit of acupuncture and a high certainty of evidence conclusion for more adverse outcomes in the acupuncture group.<sup>58</sup>

This map shows 3 categories depicted in rows: whether the certainty of evidence conclusion of the review for adverse events was low or very low, moderate, or high. As for columns, we listed whether there were fewer adverse events in the acupuncture group, no difference between groups, insufficient evidence to determine difference between groups, or more adverse events in the acupuncture group. A review could be mapped more than once for adverse events if different comparators had different certainty of evidence conclusions for adverse events. As we did for the effectiveness maps, we mapped each conclusion by name of condition or sub-condition. The legend for this map is the same, with colors denoting comparators, shapes denoting types of acupuncture, and size of bubble used to indicate the number of original research studies about acupuncture included in the review.

In the 16 mapped reviews that had included certainty of evidence conclusions about adverse events, a majority of the reviews reported either fewer adverse events in the acupuncture group (low or very low certainty of evidence) or no difference between groups (very low to high certainty of evidence). Only 2 reviews reported more adverse events in the acupuncture group. The first review about anovulatory infertility concluded that "true acupuncture probably worsens adverse events compared to sham acupuncture" (moderate certainty of evidence).<sup>58</sup> The second review about electro-acupuncture for carpal tunnel syndrome concluded there were more adverse events in the electro-acupuncture group (very low certainty of evidence).<sup>17</sup> See Table 5 for additional details about included reviews with certainty of evidence conclusions for adverse events.

As part of our search, we also identified 3 reviews that were solely about adverse events, and not necessarily restricted to adult health conditions.<sup>73-75</sup> One review was an overview of existing systematic review (*ie*, a review of reviews) and included 17 existing reviews.<sup>73</sup> About half of these were based on case reports. The authors were unable to calculate incidence rates, though they did conclude that serious complications were "rare." A second review was restricted to adverse events of auricular therapy, which included more kinds of therapy than just acupuncture (such as auricular bloodletting therapy).<sup>74</sup> The third systematic review collected 33 years' worth of case reports of adverse events in China.<sup>75</sup> 182 cases were found, including 30 cases of pneumothorax, 37 cases of central nervous system injury, 22 cases of organ injury, 17 cases of infection, 10 cases of hemorrhage, 7 cases of broken needles, *etc*.

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Although an incidence rate cannot be calculated from these estimates because there is no denominator, we can hazard an upper bound estimate if we assume that in any year no more than 1% of the Chinese population received acupuncture. Over 33 years, then, even if the number of case reports in this review is an underestimate of the true number by a factor of 10, or even a factor of 100, the incidence rate of serious adverse events is likely exceedingly small (potentially less than 1 in 100,000 patients).

studies

studies

studies

•

10-25 included

< 10 included

### Figure 3. Adverse Events

	Fewer Adverse Events in Acupuncture Group	No Difference Between Groups	Insufficient Evidence to Determine Difference	More Adverse Events in Acupuncture Group
High or Strong Certainty of Evidence		Migraine		
Moderate Certainty of Evidence		Knee pain	Depression*	<ul> <li>Anovulatory fertility*</li> </ul>
Low or Very Low Certainty of Evidence	<ul> <li>Kidney stone</li> <li>Schizophrenia</li> <li>Primary insomnia</li> <li>Dysmenorrhea</li> <li>Post-stroke depression</li> </ul>	<ul> <li>Premenstrual syndrome</li> <li>Peripheral neuropathy</li> </ul>	<ul> <li>Post-caesarean pain</li> <li>Anovulatory infertility*</li> <li>Major depressive disorde</li> <li>Tension headache</li> <li>Depression*</li> </ul>	Carpel tunnel syndrome*
	Included Studies 25 included tudies Type of Acupuncture Use Manual Acupuncture Stud	d Mixed – No		*This review included distinct conclusions about separate

Subgroups

Mixed – With Subgroups

(may include auricular acupuncture

or electroacupuncture)

Electroacupuncture Only

conclusions about separate conditions and/or comparators, and so it appears in this map more than once.

Other Active

Care

Therapy/Usual

#### Table 5. Certainty of Evidence Conclusions for Adverse Events in Reviews Included in Evidence Map

Author, Year	Condition	Sub-condition	Certainty of Evidence Conclusion
Linde, 2016 <sup>31</sup>	Headache	Migraine	There is no difference in the number of participants experiencing serious adverse events between acupuncture and sham acupuncture.

#### High Certainty of Evidence for Adverse Events

#### Moderate Certainty of Evidence for Adverse Events

Author, Year	Condition	Sub-condition	Certainty of Evidence Conclusion
Smith, 2018 <sup>47</sup>	Depression	None	It is unclear whether there are differences in the risk of adverse events between persons receiving acupuncture or sham acupuncture.
Lim, 2019 <sup>58</sup>	Fertility	Anovulatory infertility	True acupuncture probably worsens adverse events compared with sham acupuncture.
Skelly, 2020 <sup>20</sup>	Osteoarthritis	Knee pain	There was no difference in the risk of serious adverse events between any form of acupuncture and the control group.

#### Low or Very Low Certainty of Evidence for Adverse Events

Author, Year	Condition	Sub-condition	Certainty of Evidence Conclusion
Skelly, 2020 <sup>20</sup>	Back pain	Chronic low back pain	Serious adverse events were rare with acupuncture and control.
Choi, 2018 <sup>17</sup>	Carpal tunnel syndrome	None	Acupuncture was associated with fewer or no serious adverse events compared to active or sham groups.
Choi, 2018 <sup>17</sup>	Carpal tunnel syndrome	None	Electro-acupuncture was associated with more adverse events when compared with night splints.
Liu, 2021 <sup>45</sup>	Depression	Post-stroke depression	Acupuncture was associated with fewer adverse events than antidepressants, but there was no significant difference in the occurrence of adverse events between the combination of acupuncture and conventional treatments versus conventional treatments.
Smith, 2018 <sup>47</sup>	Depression	None	The risk of adverse events with acupuncture is unclear, as most trials did not report adverse events adequately.
Sorbero, 2016 <sup>48</sup>	Depression	Major Depressive Disorder	Insufficient data to determine if there are differences between groups for adverse events.
Smith, 2016 <sup>56</sup>	Dysmenorrhea	None	Adverse events were less common in the acupuncture group compared to NSAID.
Lim, 2019 <sup>58</sup>	Fertility	Anovulatory infertility	Insufficient data to determine if there are differences between acupuncture and usual care or active treatment for adverse events.

Evidence Map of Acupuncture: Update from 2013-2021

Author, Year	Condition	Sub-condition	Certainty of Evidence Conclusion
Linde, 2016 <sup>32</sup>	Headache	Tension-type Headache	There is no evidence to conclude that adverse events differ between patients receiving acupuncture or sham acupuncture.
Cao, 2019 <sup>50</sup>	Insomnia	Primary Insomnia	Fewer adverse events from acupuncture than Western medications.
Chou, 2020 <sup>19</sup>	Other acute pain	Kidney Stone	For kidney stone pain, acupuncture vs NSAID or acetaminophen, there were few adverse events in 1 trial.
Ju, 2017 <sup>33</sup>	Peripheral neuropathy	None	No clear differences were observed between acupuncture and sham or active groups.
Zimpel, 2020 <sup>35</sup>	Post-operative pain	Post-Caesarean pain	It is uncertain whether acupuncture (vs no treatment) or acupuncture plus analgesia (vs analgesia) has any effect on the risk of adverse effects.
Armour, 2018 <sup>62</sup>	Premenstrual syndrome	None	There was insufficient evidence to determine whether there was a difference between acupuncture and sham or no treatment in the rates of adverse events.
Shen, 2014 <sup>52</sup>	Schizophrenia	None	Acupuncture compared with standard antipsychotic treatment alone; adverse effects were less for the acupuncture group.

# DISCUSSION

There is a vast literature of original randomized trials and systematic reviews of randomized trials of acupuncture as a treatment for dozens of health conditions. Despite this, the number of conditions for which authors of systematic reviews have concluded that there is at least moderate certainty of evidence regarding health outcome effects of acupuncture is modest, and most of these involve comparisons of acupuncture to sham or control acupuncture, and then mostly for painful conditions. Evidence that acupuncture causes adverse health effects is rare, and reviews that compared acupuncture to usual care and included conclusions about adverse effects all concluded that acupuncture was at least as safe or safer than usual care.

## LIMITATIONS

There are 3 main limitations to this evidence map. The first, common to all systematic reviews, is that we may have not identified all the potentially eligible evidence. If a systematic review was published in a journal not indexed in any of the 4 databases we searched, and we did not identify it as part of our search of references of included publications, then we would have missed it. Nevertheless, our search strategy did identify 370 systematic reviews, so we did not suffer from any lack of potential reviews to evaluate. An extension to this limitation is the included systematic reviews may themselves have missed some original research studies eligible for their review. The total number of studies included, across all the reviews that entered into our map, is more than 900 original research studies. As with reviews, therefore, the map does not suffer from a lack of original research studies.

The second limitation of evidence maps is that we did not independently evaluate the source evidence; in other words, we took the conclusions of the authors of the systematic review "at face value." That is the nature of an evidence map. Particular to this application of the mapping process, we did not map all the eligible reviews; for health conditions that had more than one eligible review, we only mapped the one we deemed most informative. This necessarily requires judgment, and others could disagree with that judgment. We list in the appendix all the reviews that were excluded from the map for this "overlap" reason, and interested readers can review them and select for themselves the one they judge most informative. As in all evidence-based products, and particularly in one such as this covering a large and complex evidence base, it is possible there are errors of data extraction and compilation. We used dual review to minimize the chance of such errors, but if we are notified of errors we will correct them.

Lastly, a limitation to assessing the effect of acupuncture is the variation (and controversy) with which sham acupuncture is designed. Some studies defined sham as standard needling technique at non-active points, some included shallow needling in both active and non-active points, and more contemporarily, non-penetrating needles used at both active and non-active points. One of the major controversies around the use of sham as an inert comparator is that the unintended physiologic effects beyond placebo have not been considered;<sup>76</sup> thus, the exact mechanism by which acupuncture is effective is unclear when compared to "sham" acupuncture. The uncertainty around what is considered "sham" acupuncture and the lack of clear understanding of the exact mechanism by which acupuncture is effective compared to sham acupuncture calls into question how we should assess conclusions from studies employing "sham" as a comparator. This uncertainty also renders conclusions about the effect of acupuncture compared to sham

more challenging to interpret than, for example, the comparison of a pharmaceutical intervention to placebo, in which case the placebo is confidently assumed to be inert.

## **FUTURE RESEARCH**

The vast majority of the conclusions of the eligible systematic reviews were classified as low or very low certainty of evidence, indicating that the most critical research need is for better evidence to increase certainty of evidence for acupuncture. Studies comparing acupuncture to placebo or sham are probably not the priority; rather the priority should be studies comparing acupuncture to other recommended/accepted/active therapies for the condition. In such studies, the type and schedule of acupuncture treatment needs careful documentation so findings can be applied in other settings. Studies comparing acupuncture to other recommended therapies should also have a sufficiently long follow-up time period to allow any nonspecific effects (*eg*, of getting something "new") to dissipate. For example, for studies of chronic painful conditions, this time period has been proposed to be at least 6 months.

For health conditions of priority to the VA that currently do not have at least moderate-certainty evidence supporting use of acupuncture, new studies that address limitations of existing research are needed. More rigorous evidence on acupuncture is likely the best way to expand access to acupuncture among Veterans most likely to benefit from it. The need for more rigorous research also applies to the acupuncture community at large. We note that in the 9 years covered by this update, we identified 370 new systematic reviews of acupuncture. This compares to about 370 new RCTs of acupuncture published in the same time period and included in the systematic reviews in our map. Thus, researchers interested in acupuncture are producing about as many systematic reviews (that generally conclude the certainty of evidence is low or very low) as new RCTs needed to raise the certainty of evidence. This seems to be a mismatch between resources and need. The field of acupuncture would be best advanced with resources devoted to producing more high-quality RCTs and producing fewer new systematic reviews.

## **CONCLUSIONS**

There are many systematic reviews of acupuncture for more than 4 dozen adult health conditions. The number of conclusions about the effectiveness of acupuncture that were judged to have at least moderate certainty of evidence is small relative to the large number of existing RCTs and reviews. Most of these studies compare acupuncture to sham or control acupuncture for painful conditions or pain outcomes. There is no evidence that acupuncture is less safe than usual care for these conditions.

# REFERENCES

- 1. Unschuld P, Andrews B. *Traditional Chinese Medicine*. Columbia University Press; 2018.
- 2. National Center for Complementary and Integrative Health. *Acupuncture: In Depth.* 2015. <u>https://www.nccih.nih.gov/health/acupuncture-in-depth</u>
- 3. Li Y. *Acupuncture journey to America: A turning point in 1971*. Vol. Journal of Traditional Chinese Medical Sciences. 2015.
- 4. Institute of Medicine (US) Committee on the Use of Complementary and Alternative Medicine by the American Public. *Complementary and Alternative Medicine in the United States*. 2005. <u>https://www.ncbi.nlm.nih.gov/books/NBK83804/</u>
- 5. Department of Veterans Affairs. *Provision of Complementary and Integrative Health*. 2017.
- Hempel S, Taylor, S. L., Solloway, M., Miake-Lye, I. M., Beroes, J. M., Shanman, R., Booth, M. J., Siroka, A. M., Shekelle, P. G. *Evidence Map of Acupuncture*. Vol. VA-ESP Project #05-226. 2013. <u>https://www.ncbi.nlm.nih.gov/books/NBK185072/</u>
- 7. GRADE Working Group. gradeworkinggroup.org. Accessed 2022.
- 8. Berkman ND, Lohr KN, Ansari MT, et al. Grading the strength of a body of evidence when assessing health care interventions: an EPC update. *J Clin Epidemiol*. Nov 2015;68(11):1312-24. doi:10.1016/j.jclinepi.2014.11.023
- 9. Franco JVA, Turk T, Jung JH, et al. Non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome: a Cochrane systematic review. *BJU Int*. Aug 2019;124(2):197-208. doi:10.1111/bju.14492
- 10. Chou R, Deyo R, Friedly J, et al. Nonpharmacologic Therapies for Low Back Pain: A Systematic Review for an American College of Physicians Clinical Practice Guideline. *Ann Intern Med.* Apr 4 2017;166(7):493-505. doi:10.7326/m16-2459
- 11. Wang YY, Li XX, Liu JP, Luo H, Ma LX, Alraek T. Traditional Chinese medicine for chronic fatigue syndrome: a systematic review of randomized clinical trials. *Complement Ther Med.* Aug 2014;22(4):826-33. doi:10.1016/j.ctim.2014.06.004
- 12. Liu S, Zhang CS, Cai Y, et al. Acupuncture for Post-stroke Shoulder-Hand Syndrome: A Systematic Review and Meta-Analysis. *Front Neurol.* 2019;10:433. doi:10.3389/fneur.2019.00433
- Chia KL, Lam RPK, Lam CK, Tsui SH. Acupuncture in the emergency department: a systematic review of randomised controlled trials. *Acupunct Med.* Jun 2018;36(3):183-192. doi:10.1136/acupmed-2017-011547
- Navarro-Santana MJ, Sanchez-Infante J, Gómez-Chiguano GF, Cummings M, Fernández-de-Las-Peñas C, Plaza-Manzano G. Effects of manual acupuncture and electroacupuncture for lateral epicondylalgia of musculoskeletal origin: a systematic review and meta-analysis. *Acupunct Med.* Dec 17 2020:964528420967364. doi:10.1177/0964528420967364
- 15. Savage J, Waddell A. Tinnitus. BMJ Clin Evid. Oct 20 2014;2014
- 16. Vickers AJ, Vertosick EA, Lewith G, et al. Acupuncture for Chronic Pain: Update of an Individual Patient Data Meta-Analysis. *J Pain*. May 2018;19(5):455-474. doi:10.1016/j.jpain.2017.11.005
- 17. Choi GH, Wieland LS, Lee H, Sim H, Lee MS, Shin BC. Acupuncture and related interventions for the treatment of symptoms associated with carpal tunnel syndrome.



*Cochrane Database Syst Rev.* Dec 2 2018;12(12):Cd011215. doi:10.1002/14651858.CD011215.pub2

- Eccleston C, Fisher E, Thomas KH, et al. Interventions for the reduction of prescribed opioid use in chronic non-cancer pain. *Cochrane Database Syst Rev.* Nov 13 2017;11(11):Cd010323. doi:10.1002/14651858.CD010323.pub3
- 19. Chou R, Wagner J, Ahmed AY, et al. AHRQ Comparative Effectiveness Reviews. *Treatments for Acute Pain: A Systematic Review*. Agency for Healthcare Research and Quality (US); 2020.
- 20. Skelly AC, Chou R, Dettori JR, et al. AHRQ Comparative Effectiveness Reviews. Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review Update. Agency for Healthcare Research and Quality (US); 2020.
- 21. Yuan QL, Wang P, Liu L, et al. Acupuncture for musculoskeletal pain: A meta-analysis and meta-regression of sham-controlled randomized clinical trials. *Sci Rep.* Jul 29 2016;6:30675. doi:10.1038/srep30675
- 22. Yuanqing P, Yong T, Haiqian L, et al. Acupuncture for Hormone Therapy-Related Side Effects in Breast Cancer Patients: A GRADE-Assessed Systematic Review and Updated Meta-Analysis. *Integr Cancer Ther.* Jan-Dec 2020;19:1534735420940394. doi:10.1177/1534735420940394
- 23. Hwang MS, Lee HY, Choi TY, et al. A systematic review and meta-analysis of the efficacy of acupuncture and electroacupuncture against chemotherapy-induced peripheral neuropathy. *Medicine (Baltimore)*. Apr 2020;99(17):e19837. doi:10.1097/md.000000000019837
- 24. Hu C, Zhang H, Wu W, et al. Acupuncture for Pain Management in Cancer: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med.* 2016;2016:1720239. doi:10.1155/2016/1720239
- 25. Amato Nesbit S, Sharma R, Waldfogel JM, et al. Non-pharmacologic treatments for symptoms of diabetic peripheral neuropathy: a systematic review. *Curr Med Res Opin*. Jan 2019;35(1):15-25. doi:10.1080/03007995.2018.1497958
- 26. Kim J, Kim SR, Lee H, Nam DH. Comparing Verum and Sham Acupuncture in Fibromyalgia Syndrome: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med.* 2019;2019:8757685. doi:10.1155/2019/8757685
- 27. Zhang XC, Chen H, Xu WT, Song YY, Gu YH, Ni GX. Acupuncture therapy for fibromyalgia: a systematic review and meta-analysis of randomized controlled trials. *J Pain Res.* 2019;12:527-542. doi:10.2147/jpr.S186227
- 28. Giovanardi CM, Cinquini M, Aguggia M, et al. Acupuncture vs. Pharmacological Prophylaxis of Migraine: A Systematic Review of Randomized Controlled Trials. *Front Neurol.* 2020;11:576272. doi:10.3389/fneur.2020.576272
- 29. Yun JM, Lee SH, Cho JH, Kim KW, Ha IH. The effects of acupuncture on occipital neuralgia: a systematic review and meta-analysis. *BMC Complement Med Ther*. Jun 3 2020;20(1):171. doi:10.1186/s12906-020-02955-y
- 30. Xu J, Zhang FQ, Pei J, Ji J. Acupuncture for migraine without aura: a systematic review and meta-analysis. *J Integr Med.* Sep 2018;16(5):312-321. doi:10.1016/j.joim.2018.06.002
- Linde K, Allais G, Brinkhaus B, et al. Acupuncture for the prevention of episodic migraine. *Cochrane Database Syst Rev.* Jun 28 2016;2016(6):Cd001218. doi:10.1002/14651858.CD001218.pub3

- 32. Linde K, Allais G, Brinkhaus B, et al. Acupuncture for the prevention of tension-type headache. *Cochrane Database Syst Rev.* Apr 19 2016;4:Cd007587. doi:10.1002/14651858.CD007587.pub2
- Ju ZY, Wang K, Cui HS, et al. Acupuncture for neuropathic pain in adults. *Cochrane Database Syst Rev.* Dec 2 2017;12(12):Cd012057. doi:10.1002/14651858.CD012057.pub2
- 34. Pei W, Zeng J, Lu L, Lin G, Ruan J. Is acupuncture an effective postherpetic neuralgia treatment? A systematic review and meta-analysis. *J Pain Res.* 2019;12:2155-2165. doi:10.2147/jpr.S199950
- 35. Zimpel SA, Torloni MR, Porfírio GJ, Flumignan RL, da Silva EM. Complementary and alternative therapies for post-caesarean pain. *Cochrane Database Syst Rev.* Sep 1 2020;9:Cd011216. doi:10.1002/14651858.CD011216.pub2
- Yin Z, Xiao Q, Xu G, et al. Acupuncture for the Postcholecystectomy Syndrome: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med*. 2020;2020:7509481. doi:10.1155/2020/7509481
- Tedesco D, Gori D, Desai KR, et al. Drug-Free Interventions to Reduce Pain or Opioid Consumption After Total Knee Arthroplasty: A Systematic Review and Meta-analysis. *JAMA Surg.* Oct 18 2017;152(10):e172872. doi:10.1001/jamasurg.2017.2872
- 38. Hu H, Chen L, Ma R, Gao H, Fang J. Acupuncture for primary trigeminal neuralgia: A systematic review and PRISMA-compliant meta-analysis. *Complement Ther Clin Pract.* Feb 2019;34:254-267. doi:10.1016/j.ctcp.2018.12.013
- 39. Kim TH, Lee MS, Kim KH, Kang JW, Choi TY, Ernst E. Acupuncture for treating acute ankle sprains in adults. *Cochrane Database Syst Rev.* Jun 23 2014;(6):Cd009065. doi:10.1002/14651858.CD009065.pub2
- 40. Tang S, Mo Z, Zhang R. Acupuncture for lumbar disc herniation: a systematic review and meta-analysis. *Acupunct Med.* Apr 2018;36(2):62-70. doi:10.1136/acupmed-2016-011332
- 41. Xiang A, Cheng K, Shen X, Xu P, Liu S. The Immediate Analgesic Effect of Acupuncture for Pain: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med.* 2017;2017:3837194. doi:10.1155/2017/3837194
- 42. Manheimer E, Cheng K, Wieland LS, et al. Acupuncture for hip osteoarthritis. *Cochrane Database Syst Rev.* May 5 2018;5(5):Cd013010. doi:10.1002/14651858.Cd013010
- 43. Ben-Arie E, Kao PY, Lee YC, Ho WC, Chou LW, Liu HP. The Effectiveness of Acupuncture in the Treatment of Frozen Shoulder: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med.* 2020;2020:9790470. doi:10.1155/2020/9790470
- 44. Tong QY, Liu R, Zhang K, Gao Y, Cui GW, Shen WD. Can acupuncture therapy reduce preoperative anxiety? A systematic review and meta-analysis. *J Integr Med.* Jan 2021;19(1):20-28. doi:10.1016/j.joim.2020.10.007
- 45. Liu R, Zhang K, Tong QY, Cui GW, Ma W, Shen WD. Acupuncture for post-stroke depression: a systematic review and meta-analysis. *BMC Complement Med Ther*. Apr 1 2021;21(1):109. doi:10.1186/s12906-021-03277-3
- 46. Smith CA, Shewamene Z, Galbally M, Schmied V, Dahlen H. The effect of complementary medicines and therapies on maternal anxiety and depression in pregnancy: A systematic review and meta-analysis. *J Affect Disord*. Feb 15 2019;245:428-439. doi:10.1016/j.jad.2018.11.054

- 47. Smith CA, Armour M, Lee MS, Wang LQ, Hay PJ. Acupuncture for depression. *Cochrane Database Syst Rev.* Mar 4 2018;3(3):Cd004046. doi:10.1002/14651858.CD004046.pub4
- 48. Sorbero ME, Reynolds K, Colaiaco B, et al. Acupuncture for Major Depressive Disorder: A Systematic Review. *Rand Health Q.* May 9 2016;5(4):7.
- 49. Kwon CY, Lee B, Cheong MJ, et al. Non-pharmacological Treatment for Elderly Individuals With Insomnia: A Systematic Review and Network Meta-Analysis. *Front Psychiatry*. 2020;11:608896. doi:10.3389/fpsyt.2020.608896
- 50. Cao HJ, Yu ML, Wang LQ, Fei YT, Xu H, Liu JP. Acupuncture for Primary Insomnia: An Updated Systematic Review of Randomized Controlled Trials. J Altern Complement Med. May 2019;25(5):451-474. doi:10.1089/acm.2018.0046
- 51. Grant S, Colaiaco B, Motala A, Shanman R, Sorbero M, Hempel S. Acupuncture for the Treatment of Adults with Posttraumatic Stress Disorder: A Systematic Review and Meta-Analysis. *J Trauma Dissociation*. Jan-Feb 2018;19(1):39-58. doi:10.1080/15299732.2017.1289493
- 52. Shen X, Xia J, Adams CE. Acupuncture for schizophrenia. *Cochrane Database Syst Rev.* Oct 20 2014;(10):Cd005475. doi:10.1002/14651858.CD005475.pub2
- 53. Chen Z, Wang Y, Wang R, Xie J, Ren Y. Efficacy of Acupuncture for Treating Opioid Use Disorder in Adults: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med.* 2018;2018:3724708. doi:10.1155/2018/3724708
- 54. White AR, Rampes H, Liu JP, Stead LF, Campbell J. Acupuncture and related interventions for smoking cessation. *Cochrane Database Syst Rev.* Jan 23 2014;2014(1):Cd000009. doi:10.1002/14651858.CD000009.pub4
- 55. Jo J, Lee YJ, Lee H. Effectiveness of Acupuncture for Primary Ovarian Insufficiency: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med.* 2015;2015:842180. doi:10.1155/2015/842180
- 56. Smith CA, Armour M, Zhu X, Li X, Lu ZY, Song J. Acupuncture for dysmenorrhoea. Cochrane Database Syst Rev. Apr 18 2016;4:Cd007854. doi:10.1002/14651858.CD007854.pub3
- 57. Coyle ME, Stupans I, Abdel-Nour K, et al. Acupuncture versus placebo acupuncture for in vitro fertilisation: a systematic review and meta-analysis. *Acupunct Med*. Feb 2021;39(1):20-29. doi:10.1177/0964528420958711
- 58. Lim CED, Ng RWC, Cheng NCL, Zhang GS, Chen H. Acupuncture for polycystic ovarian syndrome. *Cochrane Database Syst Rev.* Jul 2 2019;7(7):Cd007689. doi:10.1002/14651858.CD007689.pub4
- 59. Kwan I, Wang R, Pearce E, Bhattacharya S. Pain relief for women undergoing oocyte retrieval for assisted reproduction. *Cochrane Database Syst Rev.* May 15 2018;5(5):Cd004829. doi:10.1002/14651858.CD004829.pub4
- 60. Jo J, Lee YJ. Effectiveness of acupuncture in women with polycystic ovarian syndrome undergoing in vitro fertilisation or intracytoplasmic sperm injection: a systematic review and meta-analysis. *Acupunct Med.* Jun 2017;35(3):162-170. doi:10.1136/acupmed-2016-011163
- 61. Dodin S, Blanchet C, Marc I, et al. Acupuncture for menopausal hot flushes. *Cochrane Database Syst Rev.* Jul 30 2013;2013(7):Cd007410. doi:10.1002/14651858.CD007410.pub2
- 62. Armour M, Ee CC, Hao J, Wilson TM, Yao SS, Smith CA. Acupuncture and acupressure for premenstrual syndrome. *Cochrane Database Syst Rev.* Aug 14 2018;8(8):Cd005290. doi:10.1002/14651858.CD005290.pub2



- 63. Liddle SD, Pennick V. Interventions for preventing and treating low-back and pelvic pain during pregnancy. *Cochrane Database Syst Rev.* Sep 30 2015;2015(9):Cd001139. doi:10.1002/14651858.CD001139.pub4
- 64. Yang M, Sun M, Du T, et al. The efficacy of acupuncture for stable angina pectoris: A systematic review and meta-analysis. *Eur J Prev Cardiol*. Sep 17 2019:2047487319876761. doi:10.1177/2047487319876761
- 65. Lin WF, Zhong MF, Zhou QH, et al. Efficacy of complementary and integrative medicine on health-related quality of life in cancer patients: a systematic review and meta-analysis. *Cancer Manag Res.* 2019;11:6663-6680. doi:10.2147/cmar.S195935
- 66. Zhang Q, Gong J, Dong H, Xu S, Wang W, Huang G. Acupuncture for chronic fatigue syndrome: a systematic review and meta-analysis. *Acupunct Med.* Aug 2019;37(4):211-222. doi:10.1136/acupmed-2017-011582
- 67. Pang B, Jiang T, Du YH, et al. Acupuncture for Functional Dyspepsia: What Strength Does It Have? A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Evid Based Complement Alternat Med.* 2016;2016:3862916. doi:10.1155/2016/3862916
- Cui Y, Wang F, Li H, Zhang X, Zhao X, Wang D. Efficacy of Acupuncture for Herpes Zoster: A Systematic Review and Meta-Analysis. *Complement Med Res.* Apr 6 2021:1-10. Wirksamkeit von Akupunktur bei Herpes Zoster: Eine systematische Übersicht und Metaanalyse. doi:10.1159/000515138
- 69. Wang X, Zhao NQ, Sun YX, et al. Acupuncture for ulcerative colitis: a systematic review and meta-analysis of randomized clinical trials. *BMC Complement Med Ther*. Oct 14 2020;20(1):309. doi:10.1186/s12906-020-03101-4
- 70. Guo J, Xing X, Wu J, et al. Acupuncture for Adults with Diarrhea-Predominant Irritable Bowel Syndrome or Functional Diarrhea: A Systematic Review and Meta-Analysis. *Neural Plast.* 2020;2020:8892184. doi:10.1155/2020/8892184
- 71. Zhou L, Wang Y, Qiao J, Wang QM, Luo X. Acupuncture for Improving Cognitive Impairment After Stroke: A Meta-Analysis of Randomized Controlled Trials. *Front Psychol.* 2020;11:549265. doi:10.3389/fpsyg.2020.549265
- 72. Tang HY, Tang W, Yang F, Wu WW, Shen GM. Efficacy of acupuncture in the management of post-apoplectic aphasia: a systematic review and meta-analysis of randomized controlled trials. *BMC Complement Altern Med.* Oct 25 2019;19(1):282. doi:10.1186/s12906-019-2687-1
- 73. Chan MWC, Wu XY, Wu JCY, Wong SYS, Chung VCH. Safety of Acupuncture: Overview of Systematic Reviews. *Sci Rep.* Jun 13 2017;7(1):3369. doi:10.1038/s41598-017-03272-0
- 74. Tan JY, Molassiotis A, Wang T, Suen LK. Adverse events of auricular therapy: a systematic review. *Evid Based Complement Alternat Med.* 2014;2014:506758. doi:10.1155/2014/506758
- 75. Wu J, Hu Y, Zhu Y, Yin P, Litscher G, Xu S. Systematic Review of Adverse Effects: A Further Step towards Modernization of Acupuncture in China. *Evid Based Complement Alternat Med.* 2015;2015:432467. doi:10.1155/2015/432467
- 76. Kim TH, Lee MS, Birch S, Alraek T. Plausible Mechanism of Sham Acupuncture Based on Biomarkers: A Systematic Review of Randomized Controlled Trials. *Front Neurosci*. 2022;16:834112. doi:10.3389/fnins.2022.834112