Acupuncture for Chronic Migraine or Chronic Tension Headache: Assessing Signals for Update

Aggregate Analytics, Inc.

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1. Previous Coverage Decision

A health technology assessment titled: *Treatment of chronic migraine and chronic tension-type headache*, was published on April 14, 2017 by the Health Care Authority. Acupuncture was one of a group of interventions investigated for the treatment for chronic headache. Findings and Coverage Decision was adopted on July 14, 2017 and revised on July 13, 2018. The Committee's Coverage Decision is summarized below.

HTCC Coverage Determination

Acupuncture is **not a covered benefit**.

HTCC Reimbursement Determination

Not applicable.

Committee Decision

Based on the deliberations of key health outcomes the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and state agency utilization information. The committee also determined that current evidence was sufficient to make a determination on this topic. The committee discussed and voted separately on the evidence for use of Onabotulinumtoxin-A injections, massage, trigger point injections, manipulation, and transcranial magnetic stimulation, and acupuncture treatment for chronic migraine and chronic tension headaches. Only the decision regarding acupuncture is reflected here. The committee considered the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. The committee found that acupuncture was not supported by sufficient evidence regarding whether it is safe and efficacious for the treatment of chronic migraine and for chronic tension headaches. Based on these findings, the committee voted 7 to 2 to not cover acupuncture.

Medicare Decision
CMS' national coverage determination (NCD) states that acupuncture is not a covered benefit. Acupuncture is not considered reasonable and necessary, as an anesthetic, analgesic or for other therapeutic purposes.

2. Purpose of Report

The purpose of this literature update is to determine whether there is sufficient evidence published after the original report to conduct a re-review of the acupuncture portion of the prior report based on the presence of preset signal criteria (see Figure 1). The key questions in the included original report pertaining to acupuncture are listed below.

In adults with chronic migraine or chronic tension-type headache:

1. What is the evidence of the short- and long-term efficacy and effectiveness of acupuncture compared with standard alternative treatment options, placebo, sham, waitlist or no treatment?
2. What is the evidence regarding short- and long-term harms and complications of acupuncture compared with standard alternative treatment options, placebo, sham, waitlist or no treatment?
3. Is there evidence of differential efficacy, effectiveness, or safety of acupuncture compared with standard alternative treatment options, placebo, sham, waitlist or no treatment?

4. What is the evidence of cost-effectiveness of acupuncture compared with standard alternative treatment options, placebo, sham, waitlist or no treatment?

3. Methods

3.1 Literature Searches

We conducted an electronic literature search for the period July 1, 2016 to February 10, 2021 using identical search terms used for the original report for key questions 1 through 4. This search included 2 main databases: PubMed and Cochrane Library. Clinical trials.gov was also searched; see Appendix A for search methodology and additional details. The searches were focused on the use of acupuncture in chronic migraine and chronic tension-type headache. In addition, more detailed evaluation of citations listed in a stakeholder petition to the HTAP was done.

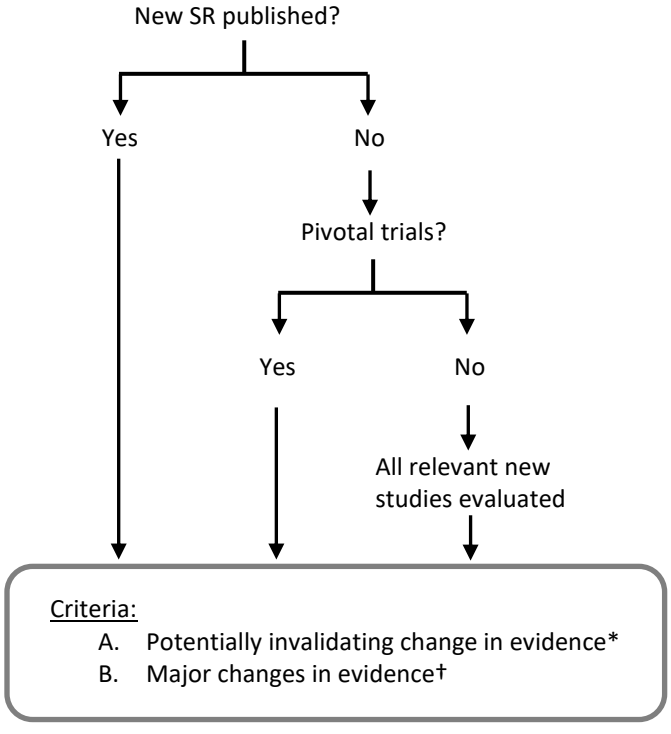
3.2 Study selection

We sought systematic reviews (SR) of randomized controlled trials (RCTs) of efficacy and safety with meta-analysis that included articles that met inclusion and exclusion criteria similar to the original report and that specifically related to the use of acupuncture. Consistent with the 2017 HTA, study selection focused on patients with chronic migraine or chronic tension-type headache as defined in the original report. High quality SRs and RCTs that directly assessed the efficacy and safety of acupuncture as a treatment in these populations were sought. A preliminary assessment of systematic review quality using AMSTAR-II was done if relevant SRs were identified. We attempted to focus on SRs that were the most comprehensive and of higher quality based on the following: report of search strategies (two or more databases and description of dates searched), number of included relevant studies (preferably RCTs), pre-stated inclusion and exclusion criteria, information on methodologies used for synthesis of data, inclusion of patient reported or safety outcomes and evaluation of the strength of the body of literature using GRADE or another analogous system. Individual RCTs not included in or published after included SRs or the 2017 HTA were also considered. While formal risk of bias assessment with dual review is not routinely done, the most important components are captured in the data abstraction (see Appendix B). A summary of the included studies is found in Appendix B. A list of citations excluded at full text is found in Appendix C.

3.3 Compilation of Findings and Conclusions

For this assessment we constructed a summary table that included the key questions, the original conclusions regarding acupuncture, new sources of evidence, new findings, and conclusions based on available signals. To assess whether the conclusions might need updating, we used an algorithm based on a modification of the Ottawa method, Figure 1.

Figure 1. Algorithm of the modified Ottawa Method of Identifying Signals for SR Updates



*A-1. Opposing findings: Pivotal trial or SR including at least one new trial that characterized the treatment in terms opposite to those used earlier

A-2. Substantial harm: Pivotal trial or SR whose results called into question the use of the treatment based on evidence of harm or that did not proscribe use entirely but did potentially affect clinical decision making (e.g., the risk of harm outweighs the benefits, identification of new serious adverse events)

A-3. Superior new treatment: Pivotal trial or SR whose results identified another treatment as significantly superior to the one evaluated in the original review, based on efficacy or harm

†B-1. Important changes in effectiveness short of "opposing findings"

B-2. Clinically important expansion of treatment (e.g., to new conditions or subgroups of subjects or additional FDA indications)

B-3. Clinically important caveat

B-4. Opposing findings from discordant meta-analysis or nonpivotal trial

Additional general criterion to consider:

- Quantitative signals include a change in statistical significance in which a statistically significant result in the original report is now NOT statistically significant or vice versa which is substantial and/or a change in effect size of at least 50%.

4. Results

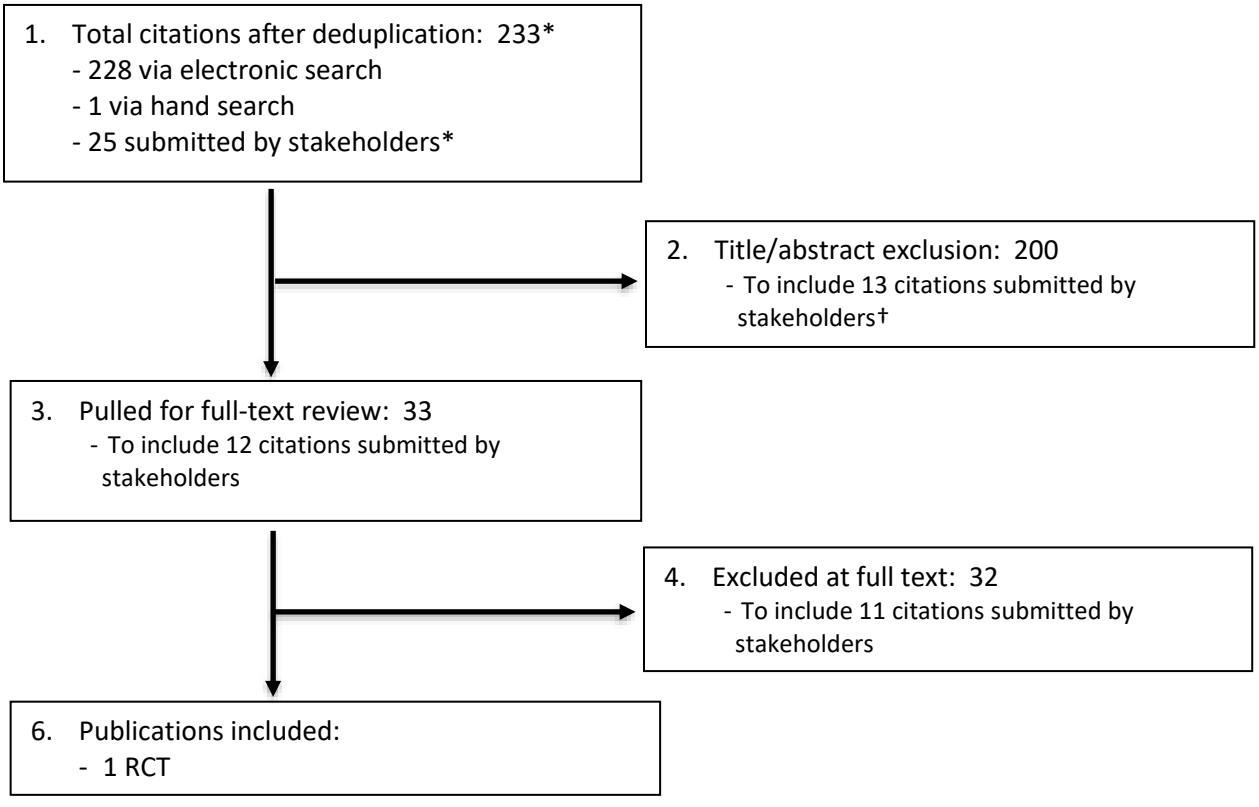
4.1 Search and citations suggested by stakeholders

After deduplication, the signal update search, handsearching, and the list of citations provided to the HTAP by stakeholders, together, identified a total of 233 citations (Figure 2). After excluding citations at the title abstract level, publications were pulled for full-text review. Of note, seven of the articles excluded at title abstract were irretrievable; they were not in English and were not indexed in the National Library of Medicine. After full-text review, 32 publications were excluded, 13 of which did not meet the definition for chronic headache as specified in the 2017 HTA or it was unclear from the information provided whether the population was chronic or episodic (see Appendix C for reasons for exclusion after full text review and Appendix G for inclusion/exclusion criteria from the prior HTA). Only one RCT met inclusion criteria and is included in this signal update.[1] This RCT was both captured by our search and one of the citations listed by the stakeholders. Given that only one RCT was identified, we performed a risk of bias assessment using our standard criteria; this RCT was considered to be moderately high risk of bias (see Table B2).

As mentioned above, a list of citations from stakeholders was provided to the HTAP in March of 2020 at which time we performed a limited evaluation of their applicability. Upon closer review, only one of the studies met our inclusion criteria (Naderinabi 2017, included in this signal update).[1] Musil 2018,[2] which was previously considered potentially includable, was excluded as patients with either chronic or episodic migraine appear to have been included; no data specific to those with chronic migraine were reported. Reasons for exclusion for all citations provided by the stakeholders can be found in Appendix C and Appendix D.

Although no relevant SRs were identified for inclusion, an update of an individual patient data meta-analysis by Vickers 2018 was identified which evaluated acupuncture for chronic headache (migraine, tension-type, or a combination) in a subset of nine trials.[3] All nine trials were reviewed per our usual process for the 2017 HTA and none met inclusion criteria for this signal update (see Appendix F, Table F1 for details). Additionally, we found a recently published Agency for Healthcare Research and Quality (AHRQ) review on the acute treatment of episodic migraines which found low strength of evidence that acupuncture may improve pain; however, this report was not in our patient population of interest (i.e., chronic migraine).[4]

Figure 2. Flow chart showing results of literature search



*21 of the 25 citations were also identified by the literature search.
†See Appendix D, Table D1 for details.

4.2 Identifying signals for re-review

Table 1 shows the original key questions, the conclusions of the original report, the conclusions from this signal search, the new sources of evidence, the new findings, and the recommendations of Aggregate Analytics, Inc. (AAI) regarding the need for update (Figure 1) as they relate to acupuncture.

The new evidence (1 RCT) identified pertains only to chronic migraine and compares acupuncture with pharmacological treatment and with botulinum toxin (new comparator). Because no new evidence was found for the following conditions and comparators from the prior HTA, they are not included in the table below:

Chronic Migraine

- Acupuncture vs. Usual Care

Chronic Tension-Type Headache

- Acupuncture vs. Sham
- Acupuncture vs. Physical Training/Exercise
- Acupuncture vs. Physiotherapy
- Acupuncture vs. Relaxation

Chronic Daily Headache/Co-existent Chronic Migraine and Tension Headache

- No evidence identified previously

Table 1. Summary Table of findings from the previous report and new evidence identified by the signal search

Conclusions from CER Executive Summary	New Sources of Evidence	New Findings	Conclusion from AAI
Key Question 1. What is the evidence of the short- and long-term <u>efficacy and effectiveness</u> of acupuncture compared with standard alternative treatment options, placebo, sham, waitlist or no treatment?			
Chronic Migraine: Acupuncture vs. Pharmacological treatment			

• 1 RCT (N=66) [Yang 2011]
  • In the short-term (4 weeks), acupuncture resulted in a statistically greater improvement in all outcomes measured compared with topiramate (low quality evidence for all): proportion of patients achieving ≥50% reduction headache days (any and moderate/severe); and mean reduction from baseline in headache days (any and moderate/severe) per month and in the Migraine Disability Assessment (MIDAS); for the latter outcome, it is unclear if the difference is clinically meaningful.
  • No data on intermediate- or long-term outcomes were available.
	• **1 new RCT** Naderinabi 2017[1] (N=100) (vs. sodium valproate)
	
	Moderately high RoB
		• In the short, intermediate and longer term (4, 8, 12 weeks): acupuncture resulted in statistically greater improvement (reduction) in mean VAS pain scores (clinical importance not described), mean number of headache days per month, mean number of times needing medication per month and in the proportion of patients who needed headache medication and who were absent from work (less in the acupuncture group for the latter two).	Although an additional trial was identified (for N=166 across both trials) and reports outcomes over the longer term, the conclusions reached are similar and do not provide major changes in the evidence (Criteria B1).
			The new evidence is insufficient to justify a rereview.

Chronic Migraine: Acupuncture vs. Botulinum toxin			
None identified	• **1 new RCT** Naderinabi 20171 (N=100) (vs. Botulinum toxin-A) *Moderately high RoB*	• In the short term (4 weeks), acupuncture resulted in statistically greater improvement (reduction) in mean number of headache days per month and mean number of times needing medication per month compared with Botulinum toxin-A, but less improvement in mean VAS pain scores and in the proportion of patients needing to take medication and absent from work or social activities. • In the intermediate and longer-term (8 and 12 weeks), acupuncture resulted in statistically greater improvement (reduction) in all the above-mentioned outcomes except for the proportion of patients absent from work or social activities for which there were no significant differences.	Although a new comparator was identified, data from one RCT (N=100) shows results similar to those seen for acupuncture versus other active comparators and does provide major changes in the evidence and is unlikely to change the conclusions of the previous report (Criteria B1). The new evidence is insufficient to justify a rereview.

Conclusions from CER Executive Summary	New Sources of Evidence	New Findings	Conclusion from AAI
Key Question 2. What is the evidence of the short- and long- term harms and complications of acupuncture compared with standard alternative treatment options, placebo, sham, waitlist or no treatment?			
Chronic Migraine: Acupuncture vs. Pharmacological treatment			
• 1 RCT (N=66) [Yang 2011] • Significantly fewer side effects were seen following acupuncture compared with topiramate. In the acupuncture group, all adverse effects were related to the local insertion of the needles (i.e., local pain, local paresthesia, ecchymosis); in the topiramate group, most events were mild and self-limiting. No patient in the acupuncture group withdrew early due to needle-related side effects.	• 1 new RCT Naderinabi 20171 (N=100) (vs. sodium valproate) *Moderately high RoB*	• Similar incidence of nausea and vomiting between groups (data NR) • Other side effects occurred less frequently following acupuncture (6%, primarily bleeding or subcutaneous hematoma) compared with sodium valproate (range, 4%-18%; anorexia, weight gain, insomnia, asthenia, alopecia, tremor and somnolence).	Although an additional trial was identified (for N=166 across both trials) the conclusions reached regarding safety are similar and do not provide major changes in the evidence (Criteria B1). The new evidence is insufficient to justify a rereview.
Chronic Migraine: Acupuncture vs. Botulinum toxin			
None identified	• 1 new RCT Naderinabi 20171 (N=100) (vs. Botulinum toxin-A) *Moderately high RoB*	• Similar incidence of nausea and vomiting between groups (data NR) • Other side effects occurred less frequently following acupuncture (6%, primarily bleeding or subcutaneous hematoma) compared with botulinum toxin (22%; ptosis, facial masking or asymmetry), p=0.021	Although a new comparator was identified, the safety data from one RCT (N=100) does not provide major changes in the evidence and is unlikely to change the conclusions of the previous report (Criteria B1). The new evidence is insufficient to justify a rereview

AAI = Aggregate Analytics, Inc.; NR = not reported; RCT = randomized controlled trial; RoB = risk of bias; VAS = visual analog scale

5. Summary of Results and Conclusions

Key Question 1:

- Only one new RCT (at moderately high risk of bias) was identified that met inclusion criteria which compared acupuncture versus Botulinum toxin-A and versus pharmacological treatment for chronic migraine.
- The data from the new trial is consistent with findings in the original HTA suggesting that acupuncture may improve outcomes compared with other active treatments (i.e., pharmacological care). The addition of one RCT with similar conclusions does not provide major changes in the evidence. This section does not need updating.

Key Question 2:

- Only one new RCT (at moderately high risk of bias) was identified that met inclusion criteria which compared acupuncture versus Botulinum toxin-A and versus pharmacological treatment for chronic migraine.
- Although an additional trial was identified the conclusions reached regarding safety are similar and do not provide major changes in the evidence. This section does not need updating.

Key Question 3:

- No new studies were identified that met inclusion criteria

Key Question 4:

- No new studies were identified that met inclusion criteria

REFERENCES

1. Naderinabi B, Saberi A, Hashemi M, et al. Acupuncture and botulinum toxin A injection in the treatment of chronic migraine: a randomized controlled study. Caspian journal of internal medicine. 2017;8(3):196-204. doi: 10.22088/cjim.8.3.196. PMID: CN-01395676.

2. Musil F, Pokladnikova J, Pavelek Z, et al. Acupuncture in migraine prophylaxis in Czech patients: an open-label randomized controlled trial. Neuropsychiatric disease and treatment. 2018;14:1221-8. doi: 10.2147/NDT.S155119. PMID: CN-01611066.

3. Vickers AJ, Vertosick EA, Lewith G, et al. Acupuncture for Chronic Pain: Update of an Individual Patient Data Meta-Analysis. J Pain. 2018 May;19(5):455-74. doi: 10.1016/j.jpain.2017.11.005. PMID: 29198932.

4. Singh RBH, VanderPluym JH, Morrow AS, et al. Acute Treatments for Episodic Migraine. Comparative Effectiveness Review No. 239. (Prepared by the Mayo Clinic Evidence-based Practice Center under Contract No. 290-2015-00013-I.) AHRQ Publication No. 21-EHC009. Rockville, MD: Agency for Healthcare Research and Quality; December 2020. AHRQ Comparative Effectiveness Reviews. https://www.ncbi.nlm.nih.gov/pubmed/33411427.

APPENDIX A. SEARCH STRATEGIES

Cochrane CENTRAL Search Strategy

Search number	Search terms	Number of hits
#1	MeSH descriptor: [Headache] this term only	2409
#2	MeSH descriptor: [Headache Disorders] this term only	135
#3	MeSH descriptor: [Migraine Disorders] this term only	2560
#4	MeSH descriptor: [Tension-Type Headache] this term only	305
#5	"tension headache":ti,kw,ab	608
#6	migrain*:ti,kw,ab	7668
#7	tension*:ti,kw,ab	10849
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	19934
#9	*acupuncture:ti,kw,ab	15861
#10	#8 AND #9	606
#11	#8 AND #9 (Custom year range: 2016 to 2021)	158

PubMed Search Strategy

Search number	Search terms	Number of hits
#1	Headache Disorders[MeSH] OR Headache Disorders, Primary[MeSH] OR Tension-Type Headache[MeSH] OR Migraine Disorders[MeSH] OR Headache/therapy [MeSH] OR "tension headache"[TIAB] OR "migraine"[TIAB] OR migrain*[TIAB] OR tension*[TIAB]	163595
#2	Acupuncture[MeSH] OR Acupuncture Therapy[MeSH] OR "acupuncture"[TIAB] OR "acupuncture therapy"[TIAB] OR "manual acupuncture"[TIAB] OR "electroacupuncture"[TIAB] OR "auricular acupuncture"[TIAB] OR "eye acupuncture"[TIAB] or "scalp acupuncture"[TIAB] OR acupunct*[TIAB] OR acupuncture*[TIAB] OR electroacupunct*[TIAB] OR electro-acupunct*[TIAB]	32430
#3	#1 AND #2 Filters: Abstract, Humans, English, from 2016/7/1 - 3000/12/12	102

Total hits from combined search results: 260

Total found via hand searching: 1

Total hits from combined search after deduplication: 229

APPENDIX B. SUMMARY OF INCLUDED STUDIES

Appendix Table B1. Study characteristics and results of new RCT

Author (Year)	Demographics	Results	Author's Conclusions	Comments
	Acupuncture vs. botulinum toxin-A vs. pharmacological treatment			
Naderinabi 2017	N=150 Headache type: Chronic migraine *Acupuncture vs. Botulinum toxin vs. Pharmacological treatment* Age, mean: 37.2 vs. 36.8 vs. 37.6 years Female: 58% vs. 54% vs. 66% Duration of chronicity, mean: 10.3 vs. 9.2 vs. 9.2 years Frequency of migraine, mean: 21.3 vs. 23.6 vs. 21.0 days/month Duration of drug use, mean: 4.2 vs. 3.2 vs. 4.1 years Number of drug use/month, mean: 14.6 vs. 17.8 vs. 14.1 Concomitant medication overuse headache: 0% (excluded) History of receiving acupuncture or botulinum toxin: 0% (excluded) Acupuncture (n=50): Traditional Chinese medicine acupoints; 10-12 needles (32 length, 25 and 40 mm); insertion depth 10-15 mm; manual manipulation, lifting, thrusting and rotating until deqi sensation; 30 sessions in 60 days Botulinum toxin (n=50): Botulinum toxin A (total dose 155 U) 31 fixed-site, fixed-dose, intramuscular injections across 7 specific head/neck muscle areas every 12 weeks for 24 weeks (two cycles).	*Acupuncture vs. Botulinum toxin vs. Pharmacological treatment* VAS pain severity (0-10), mean (SD): • Baseline: 8.6 (1.3) vs. 8.9 (1.2) vs. 8.4 (1.4), p=ns • 1 month: 5.1 (NR) vs. 4.2 (NR) vs. 5.9 (NR); p=0.001 • 2 months: 3.7 (NR) vs. 4.2 (NR) vs. 4.5 (NR); p=0.001 • 3 months: 3.8 (NR) vs. 5.0 (NR) vs. 5.0 (NR); p=0.0001 Frequency headache days/month, mean (SD) • Baseline: 21.3 (6.8) vs. 23.6 (6.5) vs. 21.0 (4.4); p=ns • 1 month: 10.8 (NR) vs. 11.8 (NR) vs. 15.8 (NR); p=0.0001 • 2 months: 7.6 (NR) vs. 9.7 (NR) vs. 13.4 (NR); p=0.001 • 3 months: 8.0 (NR) vs. 13.1 (NR) vs. 13.1 (NR); p=0.0001 Frequency of migraine medication use/month, mean (SD): • Baseline: 14.6 (5.6) vs. 17.8 (6.2) vs. 14.1 (5.1); p=0.006 • 1 month: 8.3 (4.5) vs. 9.2 (4.0) vs. 11.3 (5.4); p=0.0001 • 2 months: 3.1 (3.7) vs. 5.9 (3.8) vs. 8.4 (5.4); p=0.001 • 3 months: 3.3 (4.0) vs. 6.3 (3.3) vs. 7.0 (4.3); p=0.0001 Proportion of patients needing medication: • Baseline: 100% for all groups • 1 month: 56% vs. 42% vs. 66%; p=ns • 2 months: 18% vs. 32% vs. 52%; p=0.001 • 3 months: 18% vs. 80% vs. 62%; p=0.0001 Proportion of patients absent from work or social activities: • Baseline: 96% vs. 90% vs. 90%; p=ns • 1 month: 38% vs. 18% vs. 42%; p=0.023 • 2 months: 10% vs. 12% vs. 14%; p=ns • 3 months: 10% vs. 24% vs. 18%; p=ns	Acupuncture showed more pronounced beneficial effects on chronic migraine in comparison with botulinum toxin A injection and sodium valproate. Acupuncture may be the preferred method because of more effectiveness and less side effects.	Authors report no conflict of interest. Funding: Grant through the Research and Technology Vice Chancellorship of Guilan University of Medical Sciences

Author (Year)	Demographics	Results	Author's Conclusions	Comments
	Acupuncture vs. botulinum toxin-A vs. pharmacological treatment			
	Pharmacological treatment (n=50); sodium valproate 500 mg/day for 3 months F/U: 1, 2, and 3 months	Safety: • Nausea and vomiting: similar incidence through 2 months; higher incidence in botulinum toxin-A group after 3 months (p=0.027) • Any side effect: ○ Acupuncture vs. Botulinum toxin-A: 6% (bleeding or subcutaneous hematoma) vs. 22% (ptosis, facial masking or asymmetry), p=0.021 ○ Sodium valproate: asthenia, 10% (5/50); anorexia, 4% (2/50); weight gain, 4% (2/50); tremor, 18% (9/50); somnolence, 18% (9/50); insomnia, 8% (4/50); alopecia, 15% (7/50)		

Appendix Table B2. Study quality (risk of bias) assessment for new RCT

Methodological Principle	Naderinabi 2017
Study design Randomized controlled trial Prospective cohort study Retrospective cohort study Case-control Case-series	■
Random sequence generation*	Unclear
Statement of concealed allocation*	No
Intention to treat*	Yes
Independent or blind assessment	No
Complete follow-up of ≥80%	Yes
<10% difference in follow-up between groups	Unclear
Controlling for possible confounding†	No
Risk of Bias	Moderately High

APPENDIX C. ARTICLES EXCLUDED AT FULL TEXT REVIEW

Table C1. Studies and systematic reviews excluded at full text

	Citation	Reason for exclusion
	From literature search	
1.	[No authors] Clinical and Economic Evaluation of Acupuncture for Migraine. http://www.who.int/trialsearch/Trial2.aspx?TrialID=TCTR20170612002. 2017 PMID: CN-01891463.	Unclear chronicity
2.	Cevoli S, Giannini G, Favoni V, et al. A randomized controlled clinical trial on the efficacy of acupuncture for migraine prophylaxis: the ACUMIGRAN study. Cephalalgia. 2017;37(1):97-. doi: 10.1177/0333102417719573. PMID: CN-01470051.	Abstract
3.	Chen Y, Liu B, Gong W, et al. Auricular acupuncture for migraine: A protocol for systematic review and meta-analysis. Medicine (Baltimore). 2020 Oct 30;99(44):e23036. doi: 10.1097/md.0000000000023036. PMID: 33126394.	Protocol. Likely not relevant as they are including migraine "regardless of degree"
4.	Chen YY, Li J, Chen M, et al. Acupuncture versus propranolol in migraine prophylaxis: an indirect treatment comparison meta-analysis. J Neurol. 2020 Jan;267(1):14-25. doi: 10.1007/s00415-019-09510-x. PMID: 31435770.	Indirect treatment comparison; unclear if chronic
5.	Chu H, Seo J, Kim C, et al. Electroacupuncture for migraine protocol for a systematic review of controlled trials. Medicine (Baltimore). 2018 Apr;97(17):e9999. doi: 10.1097/md.0000000000009999. PMID: 29703068.	Protocol; migraine type unclear, likely not chronic
6.	Dong Y, Guo T, Xu L, et al. Cervicogenic headache treated by acupuncture based on jin theory: study protocol for a randomized controlled trial. Trials. 2019 Jul 10;20(1):418. doi: 10.1186/s13063-019-3478-1. PMID: 31291977.	Protocol; cervicogenic headache
7.	Gao Z, Giovanardi CM, Li H, et al. Acupuncture for migraine: a protocol for a meta-analysis and meta-regression of randomised controlled trials. BMJ Open. 2019 Feb 22;8(11):e022998. doi: 10.1136/bmjopen-2018-022998. PMID: 30798288.	Protocol (relevant; see Appendix G, table G1)
8.	Ishiyama S, Shibata Y, Ayuzawa S, et al. Clinical Effect of C2 Peripheral Nerve Field Stimulation Using Electroacupuncture for Primary Headache. Neuromodulation. 2018 Dec;21(8):793-6. doi: 10.1111/ner.12772. PMID: 29566284.	Case series
9.	Kamavosyan A. Complex Approach to the Chronic Migraine Treatment: connection Between Western and Oriental Medicine. JAMS journal of acupuncture and meridian studies. 2020;13(2):70-1. doi: 10.1016/j.jams.2020.03.010. PMID: CN-02121790.	Case series
10.	Kenan Tastan, Ozlem Ozer Disci, Set T. A Comparison of the Efficacy of Acupuncture and Hypnotherapy in Patients With Migraine. International journal of clinical and experimental hypnosis. 2018;66(4):371-85. doi: 10.1080/00207144.2018.1494444. PMID: CN-01924997.	Comparative observational study
11.	Li YX, Xiao XL, Zhong DL, et al. Effectiveness and Safety of Acupuncture for Migraine: An Overview of Systematic Reviews. Pain Res Manag. 2020;2020:3825617. doi: 10.1155/2020/3825617. PMID: 32269669.	SR of SRs; included SRs checked for applicability – were either published prior to 2016 or from non-peer-reviewed sources.
12.	Liu B. Clinical efficacy of electric acupuncture therapy in the treatment of patients with migraine. China foreign medical	Not chronic (migraine attacks/month = mean 3.9)

	Citation	Reason for exclusion
	treatment [zhong wai yi liao za zhi]. 2016(2):7-9. PMID: CN-01928086.	
13.	Liu L, Zhao LP, Zhang CS, et al. Acupuncture as prophylaxis for chronic migraine: a protocol for a single-blinded, double-dummy randomised controlled trial. BMJ open. 2018;8(5)doi: 10.1136/bmjopen-2017-020653. PMID: CN-01644459.	Protocol (relevant; see Appendix G, table G1)
14.	Lu L, Zheng H, Zheng Q, et al. The long-term effect of acupuncture for patients with chronic tension-type headache: study protocol for a randomized controlled trial. Trials. 2017 Oct 3;18(1):453. doi: 10.1186/s13063-017-2188-9. PMID: 28974247.	Protocol (relevant; see Appendix G, table G1)
15.	Nielsen A. Acupuncture for the Prevention of Tension-Type Headache (2016). Explore: the journal of science and healing. 2017;(no pagination)doi: 10.1016/j.explore.2017.03.007. PMID: CN-01366530.	Commentary on Linde et al 2016
16.	Pokladnikova J, Maresova P, Dolejs J, et al. Economic analysis of acupuncture for migraine prophylaxis. Neuropsychiatr Dis Treat. 2018;14:3053-61. doi: 10.2147/NDT.S174870. PMID: 30519026.	Economic analysis using data from Musli 2018 (above) which does not meet our criteria for chronic
17.	Schiller J, Kellner T, Briest J, et al. The best from East and West? Acupuncture and medical training therapy as monotherapies or in combination for adult patients with episodic and chronic tension-type headache: study protocol for a randomized controlled trial. Trials. 2019 Nov 8;20(1):623. doi: 10.1186/s13063-019-3700-1. PMID: 31703750.	Protocol. Relevant only if they stratify by chronic and episodic – no mention of a plan to do this a priori
18.	Tsai ST, Tseng CH, Lin MC, et al. Acupuncture reduced the medical expenditure in migraine patients: Real-world data of a 10-year national cohort study. Medicine (Baltimore). 2020 Aug 7;99(32):e21345. doi: 10.1097/md.0000000000021345. PMID: 32769867.	Not a formal CE; unclear if chronic
19.	Xu S, Yu L, Luo X, et al. Manual acupuncture versus sham acupuncture and usual care for prophylaxis of episodic migraine without aura: multicentre, randomised clinical trial. BMJ (Clinical research ed.). 2020;368:m697. doi: 10.1136/bmj.m697. PMID: CN-02089900.	Episodic
20.	Yang N, Sung HK. A systemic review about randomized controlled trials of acupuncture treatment for migraine. Journal of alternative and complementary medicine (New York, N.Y.). 2016;22(6):A38-. doi: 10.1089/acm.2016.29003.abstracts. PMID: CN-01743756.	Abstract
21.	Zhang F, Shen Y, Fu H, et al. Auricular acupuncture for migraine: A systematic review protocol. Medicine (Baltimore). 2020 Jan;99(5):e18900. doi: 10.1097/md.0000000000018900. PMID: 32000394.	Protocol. Likely not relevant. No mention of type of migraine.
22.	Zou Y, Tang W, Li X, et al. Acupuncture Reversible Effects on Altered Default Mode Network of Chronic Migraine Accompanied with Clinical Symptom Relief. Neural Plast. 2019;2019:5047463. doi: 10.1155/2019/5047463. PMID: 31011330.	Wrong study design, not RCT; ineligible outcome (MRI-based)
	From list of citations provided by stakeholders	
23.	Biçer, M. (2017). The clinical efficiency of acupuncture in preventing migraine attacks and its effect on serotonin levels. Türkiye Fiziksel Tıp ve Rehabilitasyon Dergisi, 63(1), 59-65. doi:10.5606/tftrd.2017.45578.*	Not chronic (mean 6.9 headache days/month; mean 5.7 attacks/month)*

	Citation	Reason for exclusion
24.	Li, Z., Zeng, F., Yin, T., Lan, L., Makris, N., Jorgenson, K., . . . Kong, J. (2017). Acupuncture modulates the abnormal brainstem activity in migraine without aura patients. Neuroimage Clin, 15, 367-375. doi:10.1016/j.nicl.2017.05.013*	Not chronic (inclusion criteria: ≥1 HA attack per month in last 3 months; frequency of migraine attacks at baseline across all patients: mean 6 per month)*
25.	Li, Z., Liu, M., Lan, L., Zeng, F., Makris, N., Liang, Y., . . . Kong, J. (2016). Altered periaqueductal gray resting state functional connectivity in migraine and the modulation effect of treatment. Sci Rep, 6, 20298. doi:10.1038/srep20298	Same population as Li 2017 above
26.	Mayrink, W. C., Garcia, J. B. S., Dos Santos, A. M., Nunes, J., & Mendonca, T. H. N. (2018). Effectiveness of Acupuncture as Auxiliary Treatment for Chronic Headache. J Acupunct Meridian Stud, 11(5), 296-302. doi:10.1016/j.jams.2018.07.003.*	Mixed headache types, results not stratified and none comprise ≥80% of the total population (65% chronic migraine w/w/o aura, 26% medication overuse headache, 6% chronic daily headache, and 3% chronic TTH)*
27.	Musil F, Pokladnikova J, Pavelek Z, et al. Acupuncture in migraine prophylaxis in Czech patients: an open-label randomized controlled trial. Neuropsychiatric disease and treatment. 2018;14:1221-8. doi: 10.2147/NDT.S155119. PMID: CN-01611066.*	Does meet our criteria for chronic (12 headaches/month; 6 attacks/month)*
28.	Nie, L., Cheng, J., Wen, Y., & Li, J. (2019). The Effectiveness of Acupuncture Combined with Tuina Therapy in Patients with Migraine. Complement Med Res, 26(3), 182-194. doi:10.1159/000496032*	Not chronic (inclusion criteria: average migraine attacks per month between 2 and 6 [including 2 and 6 times)]; frequency of migraine attacks at baseline: mean 4.2 per month)*
29.	Tastan, K., Ozer Disci, O., & Set, T. (2018). A Comparison of the Efficacy of Acupuncture and Hypnotherapy in Patients With Migraine. Int J Clin Exp Hypn, 66(4), 371-385. doi:10.1080/00207144.2018.1494444*	Cannot determine whether migraines are chronic or episodic in nature with the information provided*
30.	Vickers AJ, Vertosick EA, Lewith G, et al. Acupuncture for Chronic Pain: Update of an Individual Patient Data Meta-Analysis. J Pain. 2018 May;19(5):455-74. doi: 10.1016/j.jpain.2017.11.005. PMID: 29198932.*	Individual patient data systematic review; includes conditions beyond headache. "Headache" MAs include migraine, TTH and "both"; included trial either do not define chronic HA in the same way we are defining it or were included in our prior HTA (see Appendix F, table F1 for details)*
31.	Xu, J., Zhang, F. Q., Pei, J., & Ji, J. (2018). Acupuncture for migraine without aura: a systematic review and meta-analysis. J Integr Med, 16(5), 312-321. doi:10.1016/j.joim.2018.06.002.*	Cannot determine with confidence whether migraines are chronic or episodic, some indications that they likely do not meet our criteria for chronic*
32.	Yin, C., Buchheit, T. E., & Park, J. J. (2017). Acupuncture for chronic pain: an update and critical overview. Curr Opin Anaesthesiol, 30(5), 583-592. doi:10.1097/ACO.0000000000000501.	Narrative review; broad range of chronic pain conditions
33.	Zhang, X. T., Li, X. Y., Zhao, C., Hu, Y. Y., Lin, Y. Y., Chen, H. Q., . . . Tian, G. H. (2019). An Overview of Systematic Reviews of Randomized Controlled Trials on Acupuncture Treating Migraine. Pain Res Manag, 2019, 5930627. doi:10.1155/2019/5930627*	Unclear chronicity; SR of SRs*

*Also captured by our search.

APPENDIX D. ARTICLES EXCLUDED AT TITLE ABSTRACT LEVEL FROM LIST OF CITATIONS PROVIDED BY STAKEHOLDERS

Table D1. Citations provided by stakeholder and excluded at title abstract level

	Citation	Reason for exclusion
1.	Allen, J., Deng, Y., & Langland, J. (2016). Treatment of Chronic Refractory Migraine with Acupuncture and Chinese Herbal Medicine: A Case Series. Journal of Chinese Medicine(110), 36-44.*	Case report (n=2)*
2.	Blome, K. (2017). Treatment of Chronic Tension-Type Headache with Balance Acupuncture: A Case Study. Journal of Chinese Medicine(115), 25-29.	Case report (n=1)
3.	Coeytaux, R. R., & Befus, D. (2016). Role of Acupuncture in the Treatment or Prevention of Migraine, Tension-Type Headache, or Chronic Headache Disorders. Headache, 1238-1240.*	Review of SRs/MAs; published prior to our old report*
4.	Fraser, F., Matsuzawa, Y., Lee, Y. S. C., & Minen, M. (2017). Behavioral Treatments for Post-Traumatic Headache. Curr Pain Headache Rep, 21(5), 22. doi:10.1007/s11916-017-0624-x.*	Post-traumatic headache*
5.	Gildir, S., Tuzun, E. H., Eroglu, G., & Eker, L. (2019). A randomized trial of trigger point dry needling versus sham needling for chronic tension-type headache. Medicine (Baltimore), 98(8), e14520. doi:10.1097/MD.0000000000014520*	Trigger point dry needling, not acupuncture*
6.	Hayhoe, S. (2015). Acupuncture for episodic cluster headache: a trigeminal approach. BMJ Case Rep, 2015. doi:10.1136/bcr-2015-211984*	Episodic cluster headache; Case report*
7.	Li, X., Zhang, H., & Cheng, Q. (2019). Analysis of clinical efficacy levels of sibelium combined with acupuncture in the treatment of migraines. Int J Clin Exp Hypn, 12(10), 12384-12389. *	Evaluation of incremental value of combining interventions (acupuncture + sibelium vs. siblelium alone)*
8.	Linde, K., Allais, G., Brinkhaus, B., Fei, Y., Mehring, M., Shin, B. C., . . . White, A. R. (2016). Acupuncture for the prevention of tension-type headache. Cochrane Database Syst Rev, 4, CD007587. doi:10.1002/14651858.CD007587.pub2*	Included/described in previous report (see Table 5 of HTA)*
9.	Linde, K., Allais, G., Brinkhaus, B., Fei, Y., Mehring, M., Vertosick, E. A., . . . White, A. R. (2016). Acupuncture for the prevention of episodic migraine. Cochrane Database Syst Rev(6), CD001218. doi:10.1002/14651858.CD001218.pub3*	Episodic*
10.	Pei, P., Liu, L., Zhao, L., Cui, Y., Qu, Z., & Wang, L. (2016). Effect of electroacupuncture pretreatment at GB20 on behaviour and the descending pain modulatory system in a rat model of migraine. Acupunct Med, 34(2), 127-135. doi:10.1136/acupmed-2015-010840*	Animal study*
11.	Yu, X., & Salmoni, A. (2018). Comparison of the Prophylactic Effect Between Acupuncture and Acupressure on Menstrual Migraine: Results of a Pilot Study. J Acupunct Meridian Stud, 11(5), 303-314. doi:10.1016/j.jams.2018.04.003*	Menstrual migraine*
12.	Zhang, Y., Li, K. S., Liu, H. W., Fu, C. H., Chen, S., Tan, Z. J., & Ren, Y. (2016). Acupuncture treatment modulates the resting-state functional connectivity of brain regions in migraine patients without aura. Chin J Integr Med, 22(4), 293-301. doi:10.1007/s11655-015-2042-4	No outcomes of interest; focus on underlying mechanisms of acupuncture
13.	Zhao, L., Chen, J., Li, Y., Sun, X., Chang, X., Zheng, H., . . . Liang, F. (2017). The Long-term Effect of Acupuncture for Migraine Prophylaxis: A Randomized Clinical Trial. JAMA Intern Med, 177(4), 508-515. doi:10.1001/jamainternmed.2016.9378*	Episodic/not chronic headache (2- 8 episodes/month)*

*Also captured by our search.

APPENDIX E. STUDY PROTOCOLS, ONGOING TRIALS

Appendix Table E1. List of study protocols excluded at full text review that appear to meet inclusion criteria

Studies	Population	Status
Systematic Reviews		
Gao Z, Giovanardi CM, Li H, et al. Acupuncture for migraine: a protocol for a meta-analysis and meta-regression of randomised controlled trials. BMJ Open. 2019 Feb 22;8(11):e022998. doi: 10.1136/bmjopen-2018-022998. PMID: 30798288. PROSPERO registration number CRD42018087270.	Episodic and chronic migraine; sub-analysis planned stratifying by chronic vs. episodic	N/A
RCTs		
Lu L, Zheng H, Zheng Q, et al. The long-term effect of acupuncture for patients with chronic tension-type headache: study protocol for a randomized controlled trial. Trials. 2017 Oct 3;18(1):453. doi: 10.1186/s13063-017-2188-9. PMID: 28974247. Trial ID: NCT03133884.	Chronic tension-type headache	Recruiting: Completed No published results to date
Liu L, Zhao LP, Zhang CS, et al. Acupuncture as prophylaxis for chronic migraine: a protocol for a single-blinded, double-dummy randomised controlled trial. BMJ open. 2018;8(5)doi: 10.1136/bmjopen-2017-020653. PMID: CN-01644459. Trial registration number ISRCTN13563102; Pre-results.	Chronic migraine	Unclear

N/A = not applicable

APPENDIX F. HEADACHE TRIALS INCLUDED IN VICKERS 2018 SR

Appendix Table F1. List of study protocols excluded at FT that appear to meet inclusion criteria

Headache type	Study author, year	Disposition
Migraine	Diener 2006	EXCLUDED FROM PRIOR HTA - Included episodic and chronic migraine, did not stratify; baseline characteristics suggest primarily episodic migraine
	Li 2012	EXCLUDED FROM PRIOR HTA - Included episodic and chronic migraine, did not stratify
	Linde 2005	EXCLUDED FROM PRIOR HTA - Included episodic and chronic migraine, did not stratify
Tension-type headache (TTH)	Coeytaux 2005	EXCLUDE AT TIAB - additive effect of adding 10 acupuncture treatments to medical management vs. medical management alone
	Endres 2007	EXCLUDED FROM PRIOR HTA - >50% episodic tension type headache, did not stratify
	Melchart 2005	EXCLUDED FROM PRIOR HTA - >50% episodic tension type headache, did not stratify
Mixed migraine and TTH	Ferro 2012	EXCLUDE AT TIAB - tanacetum is a herbal treatment; herbal treatments are not FDA approved.
	Jena 2008	EXCLUDED FROM PRIOR HTA- >90% episodic migraine and tension type headache, did not stratify
	Vickers 2004	INCLUDED IN PRIOR HTA

APPENDIX G. PICOTS TABLE FROM PRIOR HTA

Table G1. Summary of inclusion and exclusion criteria from the 2017 HTA

Study Component	Inclusion	Exclusion
Population	Adults with the following chronic headache* of the following types: • Migraine (with or without aura) • Tension-type headache • Chronic daily headache, defined as coexistent chronic migraine and tension-type headache	• Persons <18 years old • Pregnant or breast feeding women • Acute headache or acute migraine attacks • Episodic migraine (migraine occurring <15 days per month) • Menstrual migraine • New daily persistent headache • Hospitalized patients • Patients treated in the emergency department • Other primary headaches (e.g. trigeminal autonomic cephaglias including cluster headache) • Secondary headache types as defined in The International Classification of Headache Disorders, 3rd edition • Acute trauma-related headache • Medication overuse headache/medication rebound headaches as the primary population/study focus • Headache due to malignancy; cancer-related headache • Operative or procedure-related headache • Cervical dystonia • Neuropathic pain • Neck pain not associated with headache
Interventions	• Botulinum toxin injection (Botox, OnabotulinumtoxinA, BoNTA) • Trigger point injection or dry needling • Acupuncture • Transcranial magnetic stimulation (TMS) • Manipulation/manual therapy (e.g. osteopathic, chiropractic) • Massage	• Treatments for acute headache; abortive treatments for acute episodes • Interventions that are not FDA approved and/or are not available in the U.S. • Dysport (abobotulinumtoxinA), incobotulinumtoxinA, RimabotulinumtoxinB) (not FDA approved for use in migraine/headache) • Evaluation of incremental value of combining interventions (e.g. chiropractic manipulation plus physical therapy) • Implantable devices (e.g. spinal cord stimulators, implantable occipital nerve stimulators, implantable catheters) • Nerve block • Biofeedback • TENS • Peripheral nerve decompression surgery • Occipital nerve stimulation • Vagal nerve stimulation (implantable) • Hypothalamic deep brain stimulation • Intranasal sphenopalatine ganglion blocks • Psychological therapies or behavioral interventions (e.g. cognitive behavioral therapy, education, etc.)

Study Component	Inclusion	Exclusion
		• Pharmacological treatment (including oral agents such as opioids, NSAIDS, beta blockers, antiepileptics, calcium channel blockers, calcium channel antagonists, antidepressants, ACE inhibitors, Angiotensin II antagonists, etc.) • Intervention that is part of a multi-modal treatment • Dietary supplements • Exercise/physical activity • Yoga, Tai Chi • Physical therapy • Laser therapy • Ultrasound • Inferential therapy • Hyperbaric oxygen • Surgical treatment (e.g. suborbital nerve decompression, microvascular decompression of the trigeminal nerve) • Laser therapy • Transcranial direct current stimulation • Trager work/Trager approach
Comparator	• Usual treatment(s) (e.g. pharmacological treatment, Psychological therapies or behavioral interventions including biofeedback, conventional physical therapy) • Placebo/Sham† • No treatment • Waitlist	• Comparisons of different forms of the same treatment • Comparisons of timing interventions • Combined pharmacological and procedural interventions • Combined interventions (e.g. chiropractic manipulation plus PT) • Medications that are not FDA approved for use in the United States • Excluded interventions from above except as noted for inclusion
Outcomes	**Primary** Studies must report at least one of the following for inclusion: • Proportion of responders (e.g. at least 50% reduction of headache frequency from baseline for 3-4 months following treatment) • Complete cessation/prevention of headache; reduction in mean number of episodes and/or headache days • Function/disability – focus on validated measures (e.g. BURMIG, burden of migraine; HADLI, Headache Activities of Daily Living Index; HDI, Headache Disability Index (Inventory); HDQ, Headache Disability Questionnaire; HIT-6, Headache Impact Test; MIDAS, Migraine Disability Scale)	• Non-clinical outcomes • Intermediate outcomes • Imaging outcomes

Study Component	Inclusion	Exclusion
	• Harms, treatment-related adverse events, treatment discontinuation due to adverse events **Secondary or intermediate** • Quality of life • Patient satisfaction • Emergency department visits • Loss of working days • Headache intensity • Frequency of analgesic use • Headache scores	
Study Design	Focus will be on studies with the least potential for bias. **Key Questions 1-2:** • High quality systematic reviews of RCTs will be considered if available. • Randomized controlled trials (RCTs) **Key Question 2:** • Randomized controlled trials (RCTs) • Data from non-randomized comparative studies at low risk of bias may be considered for safety if needed to supplement RCT safety data • Case series designed specifically to evaluate harms/adverse events may be considered only for rare events or short or long-term safety in the absence of information from high quality comparative studies **Key Question 3:** • RCTs which stratify on patient or other characteristics and formally evaluate statistical interaction (effect modification) **Key Question 4:** • Only full, formal economic studies (i.e., cost-effectiveness, cost-utility, cost-minimization, and cost-benefit studies) will be considered.	• Indirect comparisons • Non-comparative studies (case series) (except as described to evaluate rare or long-term harms) • Incomplete economic evaluations such as costing studies • Studies with fewer than 10 patients per treatment group • Case reports • Studies in which <80% of patients have a condition or treatment of interest
Publication	• Studies published in English in peer reviewed journals or publically available FDA reports	• Abstracts, editorials, letters • Duplicate publications of the same study which do not report on different outcomes • Single reports from multicenter trials • White papers • Narrative reviews

Study Component	Inclusion	Exclusion
		• Articles identified as preliminary reports when results are published in later versions
Timing	• Focus will be on intermediate (>6 months) and long term (> 12months) for efficacy outcomes, particularly cessation/prevention; any time frame for harms	• Studies with less than 1 week follow-up past intervention

*** While chronic headache is currently defined by the International Classification of Headache Disorders, 3rd edition as 15 or more headache days each month for at least 3 months or more than 180 days a year, older studies may have used varied definitions and timeframes (e.g. 28 day period or 30 day period for a month). Given these variations, studies reporting populations with a mean of ≥12 headache days per month or ≥12 headache episodes or attacks per month or equivalent were considered to meet the criteria for chronic headache.**

† Studies comparing treatments to sham treatments (even those which may be considered "active") as one type of comparator provides valuable information regarding treatment efficacy for pain conditions. Subjective improvement in patients may result from factors other than a given procedure, whether that treatment is an "active" sham or a specified intervention. Some of these factors include the natural course of the condition, the effects of placebo, and measurement error. A placebo effect does not require a physical placebo and reflects a change in a patient's condition attributable to the symbolic importance of a treatment versus specific physiologic or pharmacologic properties.