

Supplemental Table 5: Summary of U.S. randomized controlled trials examining the use of complementary health approaches for severe headache or migraine<sup>a</sup>

Complementary approach	Study	Participants	Methods	Interventions	Primary Measures	Primary Outcomes	Conclusion
Acupuncture	Coeytaux et al. <sup>111</sup> , 2005	74 patients with chronic daily headache; age = 46; gender = 81% women; race not reported; 15 or more headache days in previous month	RCT medical management by neurologist vs. medical management by neurologist plus acupuncture	Medical management as provided by personal healthcare provider and a neurologist at the headache clinic  Series of 10, 30 minute acupuncture treatments over 6 weeks	Change in headache impact test; Daily pain severity and headache related QOL; compared mean differences in outcomes	Acupuncture had mixed results in comparison to usual care. Daily pain severity scores improved in both groups but did not differ between treatment groups; Acupuncture group had a 3.9 reduction in headache impact test scores vs a 0.4 reduction in the medical management only group	Data not clear
Massage therapy	Moraska et al. <sup>112</sup> , 2015	62 patients randomized with tension type headache (International Classification of Headache Disorders); age=33; gender = 86% women; race = 84% white; 2 or more headaches per week	3 arm RCT massage, sham device, or waitlist control	45 minutes of Myofascial trigger point massage twice weekly for 6 weeks; 45 minutes of sham ultrasound twice weekly for 6 weeks; or no intervention	Headache pain frequency calculated as a weekly average, intensity (100mm VAS), and duration in hours and minutes; compared mean differences in outcomes	Massage resulted in improvement in headache frequency compared to sham and waitlist (massage reduced from 3.7 headaches per week to 2.4 at end of treatment vs sham 3.8 to 2.9 and waitlist 3.7 to 3.2) (p=0.026) by treatment group, however no statistically significant reduction in intensity or duration was seen for massage	Data not clear

Omega-3 FA5	Harel et al. <sup>113</sup> , 2002	27 adolescents with frequent migraine; age = 15; gender = 70% female; race not reported; International Headache Society Criteria	Randomized double blind cross-over study to Omega-3 FA or placebo	2 month first intervention, 1 month washout, 2 month second intervention  Omega-3 fish oil 2 1 g capsules per day containing 378 mg EPA and 249 mg DHA, and 2mg tocopherol;  Placebo 2 1g capsules per day of olive oil (691mg oleic acid, 106mg palmitic acid, 62 mg linoleic acid, and 2 mg tocopherol)	10 point visual analog pain scale; 7 point faces pain scale, and 5 point frequency and severity rating scale; compared mean differences in outcomes	No significant difference between fish oil and placebo was found, although frequency before intervention in both fish oil and placebo treated patients reduced headache frequency. Similar improvement with both fish oil and placebo was noted on the 7 point faces pain scale, but no difference between treatments noted.	Does not support use
Omega FA	Ramsden et al. <sup>114</sup> , 2013	67 patients with chronic daily headache; mean age=41; gender = 87% women; race = 86% white; >= 4 hours per day and >=15 days per month for at least 3 months; headache history of >=2 years und care of physician	2 arm RCT Dietary intervention to increase omega-3 fatty acids and lower omega-6 FA; or Dietary intervention to lower omega-6 FA	4 week pre intervention measures; randomized to 12 week food based dietary intervention; food was provided for each diet for 2 meals and 2 snacks per day	Headache Impact Test (HIT-6), headache days per month, and headache hours per day pre and post intervention; analyses compared mean differences in continuous outcomes	The high omega-3 low omega-6 diet produced significantly greater improvement compared to the low omega-6 diet intervention in the HIT score (-7.5 vs -2.1); number of headache days per month (-8.8 vs -4.0); and headache hours per day (-4.6 vs -1.2 hours)	Supports use

Biofeedback and relaxation	Blanchard et al. <sup>115</sup> , 1990	116 patients with vascular headache; age = 39; gender = 78% women; race not reported; Diagnosis by neurologist, at least one migraine per month or at least 3 headache days per week for the last 6 months	4 arm RCT Thermal biofeedback with relaxation training; TBS with cognitive therapy; sham mediation attention control; waitlist headache monitoring	TBF 16 sessions (twice per week for 8 weeks) thermal biofeedback training plus relaxation training with home practice; TBF plus cognitive therapy 16 sessions over 8 weeks 50-100 minutes in duration; sham meditation 16 sessions over 8 weeks 35-40 min per session – body awareness training and mental control; headache monitoring telephone calls and turn in diaries	Headache index was calculated by averaging the daily headache activity (measured 4 times per day); compared mean differences in outcomes	Thermal biofeedback and sham meditation resulted in reductions in the headache index compared to the control headache monitoring condition. Both biofeedback groups had a 1.5 point reduction in the headache index, the sham meditation had a 1.1 point reduction, and the control monitoring group had no reduction.	Supports use
Biofeedback, relaxation, and stress management	Devineni et al. <sup>116</sup> , 2005	139 participants with migraine, tension type headaches or mixed type; age = 42; gender 84% women; race not reported; formal diagnosis by	2 arm RCT Internet delivered behavioral regimen (relaxation, biofeedback, stress management); symptom	1 time a week for 4 weeks of treatment Internet delivered treatment was progressive muscle relaxation plus cognitive stress coping for	Headache Disability Inventory; compared mean differences in outcomes	Relaxation treatment resulted in reduced headache symptoms and headache disability compared to waitlist control. Significant reduction in headache index for the treated group vs the wait list	Supports use

		physician of migraine or chronic tension headache and symptoms for at least a year	monitoring waitlist control	tension type headache or PMR for migraine or mixed headaches		condition (-13.2 vs -4.9)	
Relaxation training	D'Souza et al. <sup>117</sup> , 2008	141 college students with either tension type headache or migraine; age = 21; gender = 86% women; race = 58% Caucasian; 18% African American; moderate or severe headaches more than twice per week; or more than one migraine per month	3 arm RCT Relaxation Training; written emotional disclosure or neutral writing control	Each group given four sessions over 2 weeks, measured at 1 month and 3 month follow up; Written Emotional Disclosure – write about a trauma, upheaval or stressful experience Relaxation-audiotape progressive muscle relaxation, deep breathing Neutral – write about activities of the last week	Headache frequency – number of headache days in the last month; average severity (0 no pain to 10 severe pain); and migraine disability scale; compared mean differences in outcomes	Relaxation training led to greater reductions in headache frequency (decrease by 5 days per month) and disability compared to controls. The written emotional disclosure did not differ from control group on headache frequency, as both had increases in the number of headache days per month (2.3 days disclosure group and 1.6 days control.group). No changes in headache severity was seen between the groups	Data not clear

Relaxation	Holroyd et al. <sup>118</sup> , 2001	203 adults with chronic tension-type headache; age = 37; gender = 76% women; race = 95% white; International Headache Society Criteria	4 arm study: Tricyclic antidepressant; placebo; stress management (relaxation); or relaxation plus antidepressant	8 week treatment duration with stress management delivered at weeks 1, 4, and 8; TCA was amitriptyline or nortriptyline; Stress management 1 hour sessions at 3 visits included relaxation and coping skills	Monthly headache Index Scores (mean of all 11 point rating scale scores for a one month period) and headache disability inventory scores; compared mean differences in outcomes and proportion of participants with 50% improvement	Stress management and tricyclic antidepressant each produced larger reductions in headache activity, analgesic medication use, and headache related disability than placebo; Combined therapy resulted in 64% of participants having 50% reduction in symptoms versus 38% amitriptyline group; 35% in the stress management group and 29% in the placebo group	Data not clear
Biofeedback and stress management	Scharff et al. <sup>119</sup> , 2002	36 children and adolescents with migraine; age = 13; gender = 66% girls  International Headache Society Criteria; at least 1 migraine per week or 5 days per month	3 arm RCT Hand warming biofeedback +stress management; attention control of hand cooling; and waitlist control	Groups received 4 one hour sessions over 6 weeks sessions of biofeedback training Hand warming biofeedback with cognitive behavior stress management training, and progressive muscle relaxation; Hand cooling used imagery of	Headache index calculated as mean headache intensity for a 2 week period before and after treatment; also evaluated number of participants that had 50% reduction in headache index;	Children assigned to hand warming biofeedback were more likely to achieve clinical improvement in migraine immediately after treatment than the hand cooling biofeedback and waitlist control. In the hand warming biofeedback 54% of children had 50% reduction in headache index versus 10% of the hand cooling biofeedback and 0% of the waitlist	Supports use

				cold places and general discussion to control for time and attention; Waitlist tracked symptoms		control.	
Relaxation training	Slavin-Spenny et al. <sup>120</sup> , 2013	147 college students with chronic headaches; age = 22; gender = 88% women; race = 40% Caucasian, 26% African-American; 13.2% Middle Eastern; Headaches several times per month with moderate to severe intensity	3 arm RCT Anger Awareness and Expression Training (AAET); Relaxation Training; Wait-list control	3, 1 hour sessions taught over 2 weeks for group classes: AAET engaged in experiential exercises to help recognize, experience and express anger with homework to practice assertive communication; Relaxation training was progressive muscle relaxation with a CD given to practice daily at home; Waitlist – no intervention provided	Headache frequency as the number of days in the last month with a headache; compared mean differences in outcomes	Both the AAET and Relaxation Training had fewer headaches per month at post-treatment (-3.9 and -2.6 respectively) than did waitlist controls (-1.4), however there was no difference between AAET and RT.	Supports use
Spinal manipulation	Haas et al. <sup>121</sup> , 2010	80 patients with chronic cervicogenic headache (International Headache Society	4 arm RCT dosing study: 8 Spinal Manipulation (SM) treatments and 8 Attention	10 minute sessions Twice weekly treatment with intervention or AC over 8 weeks; SMT=	Modified Von Korff scale pain (average of 3 11 point numerical rating scales for pain today, worst	Improvement over all time points (GEE for longitudinal outcomes) favored SM over Light Massage; adjusted mean difference of -8.1	Supports use

		Criteria); age=36; gender =80% women; race= 85% white; >=5 headaches per month for a minimum of 3 months	control (light massage); 16 SM treatments; 8 light massage, 16 light massage  Follow up at 4 , 8, 12, 16, 20 and 24 weeks	high-velocity low amplitude spinal manipulation of the cervical and upper thoracic spine accompanied by 5 minutes heat and 2 minutes light massage; Light massage receive 5 minutes moist heat and 5 minutes light massage; Attention control 2 minute discussion of condition and 8 minute medical exam (palpation and range of motion)	pain in last 4 weeks, and average pain in last 4 weeks) for cervicogenic headache ; primary analysis was linear models of continuous outcomes; secondary analysis looked a proportion with 50% improvement in outcomes	for the pain scale; Higher dose of SM had greater benefit on the pain scale SMT was more likely to achieve a 50% reduction in symptoms over light massage (adjusted odds ration > 1.8)	
Spinal manipulation	Boline et al. <sup>122</sup> ,1995	150 patients with chronic tension type headache (International Headache Society criteria; age = 41; gender =60% women; at least one headache per week and duration of headaches for at least 3 months	RCT SM vs amitriptyline 10 mg/day first week; 20 mg/day second week; and then 30 mg/day thereafter	SM provided twice weekly for 6 weeks, 20 minute sessions high velocity low amplitude techniques 5-10 min heat and 2 min light massage	Headache intensity score (0-20) was a summary of 4 ratings per day (0 less severe to 5 most severe); headache frequency (0-28 point scale over 2 weeks); medication usage; functional health	SM was as effective as medication with no differences at end of treatment, and significant improvement at 4 week follow; for headache intensity score SM group had a 1.3 point reduction and amitriptyline had 1.8 point reduction; for headache frequency	Data not clear

					status; compared using ANCOVA adjusting for baseline differences	SMT had a 3.8 point reduction and amitriptyline 4.0 point reduction	
Osteopathic manipulation	Hoyt et al. <sup>123</sup> , 1979	22 patients with dull non-throbbing bilateral headaches recurring over months or years (no other details provided about participants)	3 arm RCT Osteopathic manipulation; palpitory exam; no treatment	Osteopathic manipulation and high velocity low amplitude procedures for 10 minutes single session at time of headache	Headache severity (0 less severe to 7 most severe scale), EMG levels on frontalis muscle; compared using one way ANOVA	Significant improvement in headache severity in OMT group (score of 3.9 pretreatment to 2 post treatment) no change in other groups (both remained at ~3.7 pre/post); no changes noted in EMG levels in any of the groups.	Data not clear
Spinal manipulation	Nelson et al. <sup>124</sup> , 1998	218 patients with migraine; age = 38; gender = 79% women; race not reported; International Headache Society Criteria; 4 migraine days per month and symptoms for at least a year	3 arm quasi RCT SMT; amitriptyline; SMT + amitriptyline	SMT 14 treatments over 8 weeks no more than 2 times per week preceded by 5-10 minutes of massage or trigger point therapy	Headache index from diaries calculated as a weekly summary of daily pain rating from 0 no pain to 10 severe pain, summary index maximum of 70; compared mean differences in outcomes	No significant difference between manipulation and medication. No advantage to combining SMT and amitriptyline over the either treatment alone. Study was not powered as a non-inferiority design.	Not relevant

## Footnotes

<sup>a</sup> ABBREVIATIONS

AAET = Anger Awareness and Expression Training



DHA = Docosahexaenoic acid

EPA = Eicosapentaenoic acid

FA = fatty acids

GEE = General estimating equations

OMT= osteopathic manipulative therapy

QOL = Quality of life

RCT = randomized clinical trial

SM = spinal manipulation

VAS = visual analog scale