Supplemental Table 4: Summary of U.S. randomized controlled trials examining the use of complementary health approaches for osteoarthritis of the knee[a]

Complementary approach	Study	Participants	Methods	Interventions	Primary Measures	Primary Outcomes	Conclusion
Acupuncture	Berman et al.[87], 2004	Inclusion criteria: knee OA; KL scores of 2 or more; had to have pain for 6+ months; aged 50 or more. Mean age = 65.5; % female= 64%; OA duration years <5 years = 50%; WOMAC pain score=8.94; WOMAC function score= 31.69	RCT 3 sites N = 570, But lots of drop outs in education control	Acupuncture 9 pts per knee, for 26 weeks, taping number per week (8 wks. of 2/wk.; 2 wks. of 1/wk.; 4 wks. of 1 per 2 wks.; 12wks of 1 per month16 in first two weeks for a total, mean number of session n=23, 20-minute duration – electro at some pints Sham acupuncture – non penetrating but at real points Education control for 6 two hour sessions weeks	WOMAC pain scale WOMAC function scale WOMAC overall index At 8 wks. after start secondary at 26 weeks after start	No difference in WOMAC pain scores between real and sham at 8 wks., but both better than education control. By 14 weeks true better than sham (.89 pts) p<0.01 WOMAC function, S=true better than sham (at 8 wks. (2.9 pts) p=.01) and sham better than education at 8 weeks (2.54) p<0/001. Both these differences remained significant at 26 wks.	Supports use

Acupuncture	Berman et al.[88], 1999	Inclusion criteria: ACR criteria for knee OA, KL scores of 2 or more had to have pain for 6+ months Aged 50 or more, were taking analgesics or anti-inflammatory drugs for at least one month. Exclusions: corticosteroid inject in knee or knee surgeries within 4 weeks. Mean age=65; % female = 60%; White= 85%; BMI = 32; WOMAC total =49.9; WOMAC pain = 9.75; WOMAC disability = 34.35; Pain duration= 7 years	RCT, one site N=73	Acupuncture – 9 per knees, electro at two points, 16 treatments over 8 weeks, 20 min duration Standard care control, asked to remain on current meds	WOMAC pain scale WOMAC function scale WOMAC overall index	Acupuncture significantly better than standard care on WOMAC scales. Difference scores between groups at 8 wks., for WOMAC total (19.85 pts) p<.001) WOMAC dysfunction (14.2 pts) P<0.001 and WOMAC pain (3.92 pts) p<0.001	Supports use
Acupuncture	Chen et al.[89], 2013	Inclusion criteria: Knee OA radiologically confirmed as KL score of 2 or 3. At least 40+, and with pain in one or both knees for 6+ months and VAS of 4+ in the	RCT 3 sites N= 214	Acupuncture 1-2/wk., for 12 total treatments nine pts based on literature Sham- Streiberger non-penetrating needle at same acupuncture point	WOMAC total change?36% Secondary BPI	No difference between real and sham acupuncture on primary measure no secondary outcomes were different	Does not support use

		last week. Exclusions included other Rheumatology diseases, previous acupuncture. Mean age 60.45; % female=51.6%; % white = 29%; % black = 66%; BMI=32.9; Pain duration 10.5 years; WOMAC pain = 45.8		as real.			
Acupuncture	Suarez-Almazoret al.[90], 2010	Inclusion criteria: Knee OA according to Am Coll Rheum., including radiologic diagnosis, pain in knee >=10, no prior acupuncture, non-intra-articular injections in previous two months. Female=64.1%; Mean age = 64.5; white = 67.9%; Duration of knee pain yrs. = 9.2 yrs.; WOMAC pain = 44.7; VAS pain = 57.2	RCT with nested design to compare treatment vs control and impact of patient provider interactions Total N= 560 randomized, but 527 actually completed Single site	Electro acupuncture standardized to 8 pts, 2/wk. for 6 weeks Sham acupuncture same number of pts not relevant to kneed and less deeply inserted and thinner than standard needles, tens de vice attached to needles but not turned on Wait list control also	Primary – joint specific multi-dimensional assessment of pain, WOMAC pain subscale	No difference was seen between real and sham acupuncture for any of the outcome measures, but both of these groups were substantially better than wait list controls. E.g.-<VAS score for real and sham were 3.3 and 3.4 vs sham 4.2 p<0.0003 For WOMACP pain, 30.8 and 31.0 vs 42.4, p<.0002 For VAS pain 36.2and 36.7 vs 54.3 p<.0001. however both real and sham improved on all measures vs	Supports use

						baseline	
Glucosamine and/or chondroitin	Clegg et al.[91], 2006	Inclusion criteria: Radiographic evidence of OA, KL score of 2 or 3 Aged 40+ Knee pain for at least 6 months and the majority of days during the past 30 days WOMAC kneed index of 125-400 And ARA functional class I-III. Allowed to take up to 4000 mg acetaminophen daily; Female=64.1%; Mean age 58.6; BMI = 31.7; White = 78.3%; Black = 14%; During of OA = 10 yrs.; ARA functional class 1=25%; ARA functional class	RCT, multicenter (16 sites) Total N=1583	Double dummy scheme Five groups 1) 500 mg of glucosamine hydrochloride 3/day 2) 400 mg of sodium chondroitin sulfate 3/day 3) glucosamine plus chondroitin as above 4) 200 mg celecoxib (Celebrex) dialy5) placebo	Primary outcome was response to treatment, defined as 20% decreased in the summed score for WOMAC pain scale from baseline to week 25. Secondary WOMAC stiffness and functions scales OMERACT-OARSI RESPONSE= Improvement in pain or function of at least 50 and a decrease of at least 20mm on VAS pain or function scale	No difference was seen between Glucosamine HCl and placebo. For primary outcome no difference between glucosamine and chondroitin, alone or combined compared to placebo Glucaosmine3.9 pts better (higher) p=.17, Chondroitin =5.3 pts better p=.30 Combined = 6.5 pts, p=0.09 In the subgroup with moderate to serve OA (based on joint gap) For primary outcome, Glucosamine and Chondroitin combined better than	Does not support use

		2 = 57.5%; KL grade 2 = 55.3%; WOMAC pain = 235.9; WOMAC function = 772.4; WOMAC stiffness= 106.4;				placebo. Difference of 19 pts., p=0.002 OMERACT-OARSI RESPONSE TOTAL SAMPLE: Glucosamine = 14 pts better (higher) p=.35, Chondroitin = 24 pts better p=.09 Combined = 30 pts, p=0.02 In the subgroup with moderate to serve OA (based on joint gap) Glucosamine and Chondroitin combined better than placebo; 20 pt. difference, p=0.001	
Glucosamine and/or chondroitin	Frestedt et al.[92], 2008	Inclusion criteria: Aged 25-70, diagnosed with moderate to serve OA according to ACR criteria and had WOMAC index score <= 75. Exclusion include other rheumatologic diseases, required RX for pain control,	RCT, single site, N=70	12 weeks, 3 capsules three time a day (9 total /day). four groups: Aquamin; glucosamine sulfate; aquamin and glucosamine placebo	WOMAC global and pain, function and stiffness subscales	Glucosamine sulfate was significantly better than placebo for pain. Only WOMAC pain was significant difference with mean difference score = 9.7. p=.0003	Supports use

		corticosteroid injection within 4 weeks, intra articular injections of corticosteroids within 2 months, inter-articular hyaluronic acid within 4 months. Mean age= 59.2; Female = 52.8%; BMI=31.9; WOMAC pain= 58.5; WOMAC composite= 65.5; WOMANC function= 57.2; WOMAC stiffness = 48.2					
Glucosamine and/or chondroitin	Leffler et al.[93], 1999	Inclusion criteria: US navy active duty. Knee or low back pain for most days in last 3 months, corresponding degenerative changes in X-ray. Exclusions – state 4 radiographic disease, inflammatory arthritis, referred for surgery, articular injection in last month, currently deployed. Mean age knee pain group = 45.2; Radiographic stage =	RCT N= 34 (including back pain) N=21 for OA Single site	1) Cosamine (glucosamine HCL 1500 mg/day + chondroitin sulfate 1200 mg /day and manganese acerbate (228 mg /day) for 8 wks., patients then crossed over to the placebo for 8 weeks (washout period included) Placebo for 8 weeks, then crossed over to active for 9 weeks	Primary – overall summary score that added the following: Lequesne index of knee OA severity, physician assessment of severity: 'VAS pan 0-10; Patients assessment of handicap; Tenderness of the knee; Time to run 100	Cosamine was significantly better than placebo for the overall summary score. Overall summary score = 16.3, p,0.05; Secondary outcomes; VAS pain mean difference score 26.6 p, 0.05; Patient assessment of treatment mean difference .89, p<0.05; Physical examination – mean difference	Supports use

		1=9 subjects; 2=9 subjects; Males=100%; Participants allowed to use acetaminophen during the study. Patients continued other non-drug treatments such as exercise		9washout period included	yards; Physical examination including tenderness, decreased range of motion, Knee active range of motion; Patents assessment of treatment; Primary outcome was summary score based on all of the above	43.3 p<0.01; Disability frequencies – no difference; 1000 yard run, no difference, range of motion, no difference; Physician assessment of severity no difference; Stair climbing times no difference.	
Glucosamine and/or chondroitin	McAlindon et al.[94], 2004	Inclusion criteria: Radiographic evidence of OA, ACR criteria for OA Age 45+ Excluded – knee injections within 60 days; arthroplasty in in the study knee current use of glucosamine or chondroitin. Aged <=54=33% Aged 55-65=35% Female=63% White = 89% Used NSAIDS = 80%	Single site RCT; N=205	Glucosamine hydrochloride 1.5 grams/day for 12 weeks Two makes of glucosamine: Roota pharm (New Jersey) and Physiologics (Colorado) Placebo	WOMAC pain subscale WOMAC stiffness scale	No difference was seen between Glucosamine HCl and placebo. Pain = mean between difference = .5; Overall WOMAC = 0.6 Subgroup – looked at those with severe OA and non-severe OA; Severe OA mean difference in pain WOMAC score = 1.4; Non severe = 0.3 Subgroup by pharm	Does not support use

		Severe OA (based on total joint space loss) = 82% BMI=32.6				company: Mean difference score for WOMAC pain vs. Roota Pharm. = 2.5 (p=.05) but favored placebo Mean difference score for WOMAC pain vs. Physcioligics Pharm. = 0.2	
Glucosamine and/or chondroitin	Messier et al.[95], 2007	Inclusion criteria: Aged 50+ with a Kellgren-Lawrence grade of 2 or 3, who met ACR criteria for arthritis. Exclusion criteria included dementia, other severe chronic diseases, unwilling to go off current arthritis medication, recent knee surgery, knee injections, severe lower extremity disability. Mean age = 72 Mean baseline BMI = 29, Female = 70.7% White = 73% Black = 15.7%	RCT, single site total n=89	Combination of glucosamine HCl (1500 mg /day) and chondroitin sulfate (1200 mg day) for 6 months vs. placebo Then identical exercise program added to both groups for 6 months with subjects continuing the same treatment as in the first 6 months	Primary outcome was WOMAC function subscale Secondary measures included WOMAC pain subscale, distance walked in 6 min Two times periods analyzed, 6 months and 12 months	No difference was seen between Glucosamine/Chondroitin and placebo. Mean WOMAC function scores did not vary between groups at either 6 or 12 months The WOMAC pain scores did not vary between groups at either 6 or 12 months	Does not support use

Glucosamine and/or chondroitin	Rindone et al.[96], 2000	Inclusion criteria: Radiographic evidence of OA, KL grade of 1 or more Mean age= 64, duration of OA = 13 yrs. % female = 5% only VAS pain = 3.75 33% were taking NSAIDS and 18% were taking acetaminophen – participants told to continue their use throughout study	RCT ,single site N= 98	Glucosamine 500 mg (unknown whether sulfate or chloride) 3 times daily for two months Placebo 3 times daily. For two months,	VAS pain scale 0-10 at baseline, 30 days, 60 days	No difference between glucosamine and placebo; mean difference score at 60 days was 0.1	Does not support use
Glucosamine and/or chondroitin	Rubin et al.[97], 2001	Inclusion criteria: OA but not defined 50% were female; age range 36-50	RCT n=10 Single site	1.5 g of POLY-Nag per day for 6 weeks (glucosamine bound to polymer for sustained release) Placebo one a day for 6 weeks	Osteoarthritis severity index	While placebo group had no change in severity index, glucosamine group improved their score. Data in table, no statistics or standard errors	Unknown
Glucosamine and/or chondroitin	Zenk et al.[98], 2002	Inclusion criteria: Physician diagnosed OA aged 19+ Daily joint pain, stiffness or immobility. Exclusions were patient who could not go off of meds for OA or were non ambulatory due to OA.	RCT single site N=42	3 groups glucosamine sulfate 500 mg twice a day Milk protein condensate (MPC) or placebo	WOMAC global, l	Glucosamine Sulfate was significantly better than placebo for global WOMAC score; improvement by 2 weeks (16.2 pts; $p<0.05$) this was maintained at 4 a but seems to disappear at 6 weeks	Supports use

		Mean age = 58.3 Female = 86% WOMAC global =63.9 WOMAS pain = 65.0 WOMAS function = 64.9					
Massage therapy	Perlman et al.[99], 2012	Inclusion criteria: Radiographically established OSA of Knee, 35+ years old and VAS pain score of 40 to 90 knee replacement was and exclusion as were recent knee arthroscopy, or use of oral or intra articular corticosteroids or hyaluronate. Mean age = 64. Female= 70% 85% white; 11% black; mean WOMAC global = 52; mean pain VAS=61.7 Female= 70%	RCT stratified by BMI. Two sites Total N=125. With 25 per intervention group, followed 8 wks.	Five groups: 1) usual care, 2)30 minutes of massage/ wk., 8 wks., 3) 30 min 2/wk. 4 wks., then 1/wk. for 4 wks., 4) 60 min/wk. 8 wks., 5) 60 min 2/wk. 4 wks. 60 1/wk. 4 wks. Swedish Massage manualized – allowed for some individualized massage	Primary - Change in WOMAC arthritis index from baseline to end of intervention (8 wks.) Secondary change in VAS pain score Secondary Change in joint flexibility	Both 60 minute per session of massage groups were significantly better than usual care for WOMAC score. Primary outcome: both 60 min groups differed for Usual Care at 8 wks. 30 min groups not diff from usual care ($p<0.05$) Secondary ($p<0.05$). 60 min groups reduced pain vs usual care, 30 min groups not diff. Joint Stiff – no diff between any groups. WOMAS functional subscale – 60 min groups better than Usual care; Dose response seen – as minutes of	Supports use

						massage increased so did improvement of primary outcome up to 480 min/wk.	
Massage therapy	Perlman et al.[100], 2006	Inclusion criteria: Radiographically established OA of the knew who met Am. Coll. Rheum. criteria, aged 35+, score of 40-90 on WOMAS OA index and on VAS pain scale, worst pain ever, 40-90 Exclusions other rheumatologic conditions, intra articular knee injects in past 3 months, or articular hyaluroate with 6 months, or knee injury with 6 months. 4 weeks. Mean age =68.3 Mean BMI = 28.55, Female=77.5%, white=85% Baseline WOMAC global= 51.25, WOMAC pain=46.35, WOAC	RCT, one site, total N=68	Swedish full body massage standardized for study. Sessions were 1-hour long. 2/wk. for first 4 weeks, then 1/wk. for next 4 weeks Wait list Usual care, included pain meds, exercise and or hot and cold therapy	WOMAC global score, Secondary; VAS for pain,	Massage significantly better than wait list for the WOMAC scales. At 8 wks. Massage group saw significant improvement ($p<0.05$) in WOMAC global (different of 16.6 pts), also in WOMAC pain (20.11), WOMAC Function (15.48); WOMAC Stiffness (17.31), and VAS pain (20.62)	Supports use

		function=52.15 VAS pain = 65					
MSM	Kim et al.[102], 2006	Inclusion criteria: age >40, and knee OA according to ACR criteria. Including Kellgren-Lawrence grades of 2-3 and arthritis pain for most days in the last 3 months. Exclusions included other types of rheumatic disease, other chronic pain conditions, arthroscopy or intra-articular injects in the last 3 months, use of anti-coagulate drugs, corticosteroids or narcotic pain killers, or BMI >45. Mean age = 56.1; Female= 62.5%; Arthritis duration=5.8 years; Baseline Pain VAS= 56.6	Single site RCT, total N=50	6 grams/day of MSM for 12 weeks. Placebo control	Primary outcome: WOMAC pain, function and stiffness subscales. The secondary measures include patient and physician global assessment of arthritis disease	MSM was significantly better than placebo for pain and function. Individuals randomized to MSM saw greater improvements in the WOAMC pain scale (by 13.2%, p=.41) and function (16.7%, p=0.45). No differences were seen either the patient or physician global assessment of disease status.	Supports use

SAMe	Najm et al.[103], 2004	At least 40+, OA of kneed based on ACR criteria. Exclusion criteria included, serious chronic diseases, use of narcotic analgesics. Mean age 52.9; Female= 70%; BMI = 41.4	RCT, crossover design with a one-week washout, single sit\re total N=61	SAMe- 600 mg 2/day for 8 weeks Celecoxib (Celebrex) 100 mg twice a day for 8 weeks	VAS pain scale; Rowland Morris activity scale Clinical assessment of knee OR – tenderness, fluid swelling WOMAC pain subscale, WOMAC function subscales, WOMAC stiffness subscale	No difference seen between Celebrex and SAMe on any outcome measure. However, study underpowered to determine equivalency.	Unknown
Tai chi	Brismee et al.[104], 2007	Inclusion criteria: Aged 50+. Confirmed OA of the knee based on American Rheumatism Association criteria. Exclusions included knee trauma or keen injection within on months; bilateral total knee arthroplasties or MMSE<=23. Mean age = 69.9 Female = 84% mean Baseline VAS pain =4.4 Overall WOMAC = 62.3 Pain WOMAC =	RCT 12 weeks with 6 week follow-up Total N = 41	24-form Yang style tai chi – 3 classes/wk. for six weeks followed by 6/wks. of practice with home video Attention control – three 40 min sessions /wk. for six weeks; Nothing for second 6 weeks	Primary Knee pain using 0-10 VAS Secondary WOMAC overall score, WOMAC pain subscales WOMAC stiffness subscale WOMAC function subscales	Tai Chi significantly better than the attention control group for pain. After the 12-week intervention Tai chi better on VAS pain (less. 1.0) ($p < 0.05$)), WOMAC function (less 4.7) ($p =< 0.05$. No other difference was seen at either 12 or 18 weeks	Supports use

		16.67 WOMAC function = 40.4 WOMAC stiffness = 5.4 BMI= 27.8					
Tai chi	Hartman et al.[105], 2000	Inclusion criteria: Documented diagnosis of OA in spine, lower joints, hips knees ankles or foot. It was OK to have undergone major joint surgery and to have multiple joint involvements. Total N= 33. mean age 68; female=84% White = 94% Tai chi group had OA form more years than controls – e.g., 50% of tai chi had OA for >10 years vs. 13% of controls.	RCT two group single site	Tai chi one hour 2/wk. for 12 weeks. 9-form Yang style routine care and were invited to 3 group meetings to have a mean, socials and share experiences, contacted every 2 weeks to discuss issues related to OA	Arthritis Self Efficacy (ASE) scales and Arthritis Impact Measurement Scale – primary not identified	Tai chi was significantly better than Routine Care for the ASE score. Tai chi had better total ASE score (11 pts higher) than controls p=.043, but no difference on pain subscale	Supports use

Tai chi	Tsai et al.[106], 2013	Inclusion criteria: >60 years of age; MMSE score of 18-28 (mild to moderate cognitive impairment); diagnose of knee OA confirmed by medical records. Mean age = 79, 73% women, 93% white, mean MMSE= 25.5. Exclusion: WOMAC pain <3, too high or low M<SSSE, participation in another exercise program, other comorbid pain	RCT. Four sites, total n=55. Followed for 21 wks.	12 form Sun tai chi. Three times / wk. for 20-40 minutes (increased over time). Attentional control – health education, group social activities equal time a tai chi	Primary WOMAC pain subscale, Secondary measures: physical function sub scale WOMAS stiffness scale	Tai chi was significantly better than the attention control for the WOMAC pain score. Primary change in score of 2.2.8 pts between groups p=0.006 at 21 weeks differ started at week 9, p=0.026 Secondary measures: phys. function different of 5.98 lower for tai chi at 21 week p=.0071 and WOMAC stiffnes1.3 lower for tai chi t 21 weeks p=0.001	Supports use
Tai chi	Wang et al.[107], 2009	A Inclusion criteria: ge >= 55, BMI=40, WOMAC pain scale>40, Kellgen Lawrence grade >=2. Exclusions: those with prior tai chi or yoga, steroid injections into joints <=3 months; surgery of knee or intra-articular hyaluronate >= 6 months; MMSE<24. 75% female;	RCT, single site	60 min tai chi 2/wk. for 12 wks. classic Yang style 10 forms after 24 session participant told to practice at home with DVD until the 48-week follow-up. Attention control - wellness education and stretching program 60 min 2/wk. for 12 weeks.	Primary – WOMAC pain scale at 12 weeks. Secondary measures: WOMCAC function and WOMAC stiffness	Tai Chi was significantly better than the attention control for the WOMAC pain score. Primary tai chi lower WOMAC pain at 12 weeks by 118, p=.00005. WOMAC function, tai chi lowered score by 324, p. <001. No different on WOMAC stiffness	Supports use

		70% white; mean age 65; 98% had at least HS education; BMI = 29.9 KL grade 2 = 18%; KL grade 3 =2 5%; KL grade4 = 58%; WOMAC pain = 214.8; WOMAC phys. Function = 767 WOMAC stiffness = 113 VAS pain = 4.5					
Yoga	Park et al.[108], 2011	Inclusion criteria: Have OA (not defined); having pain for at least 15 days in last month with VAS score of >=4; 55+ years old; Exclusions: use of narcotic analgesics. Mean age=80; Female=31.3%; White=100%; Self-reported health status = 62.3% very good or excellent	Quasi-experimental trial. Participants randomized to either yoga or reiki, but education control group not randomized N=21	Chair based Yoga – 2/wk. for 45 minutes for 8 wks. Education/discussion control – 1.5 hrs. Every other week for 8 wks.	WOMAC physical function subscale	Yoga was significantly better than education control group for function. Yoga had greater improvement on WOMAN function scale then Reiki or control. Yoga vs control mean difference score = 19.5 p<.02	Supports use

Footnotes

[a] Abbreviations

ARA = American Rheumatology Association

ASE= Arthritis Self Efficacy

BMI = Body Mass Index

KL = Kellgren-Lawrence

MSM = Methylsulfonylmethane

NSAID = Nonsteroidal anti-inflammatory drugs

OA = Osteoarthritis

RCT =– Randomized, controlled trial

SAMe = S-Adenoysl methionine

VAS = Visual analog scale

WOMAC = The Western Ontario and McMaster Universities