**Table C1. Evidence table for all included studies**

| **Study** | **Participants** | **Inclusion Criteria** | **Exclusion Criteria** | **Intervention(s)** | **Relevant Outcomes Reported** |
| --- | --- | --- | --- | --- | --- |
| Abbott, 2015[65](#_ENREF_65)  Study design: RCT  Trial name: None  Study Location: New Zealand  Health care setting: Academic orthopedic surgery clinic/department, Physical therapy outpatient clinic  Single Site | Total n = 75  Mean Age: 64  Arm 1, Mean Age: 64(10) BMI: 29.2(6.1) Arm 2, Mean Age: 65(10) BMI: 30.2(5.6) Arm 3, Mean Age: 61(12) BMI: 27.6(4.7) Arm 4, Mean Age: 64(10.2) BMI: 29.8(6.6)  Female: 62%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Subtype: NR  Diagnosis: ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 40  ACR: NA | Surgery knee limb in prior previous hip or knee replacement of the affected joint or any other surgical procedure in the previous 6 months month(s)  Pending surgery  Analgesics use in the previous Injected opioid or analgesic use in the previous 30 days month(s)  Injected corticosteroids in the prior 30 days, hip or knee month(s)  RA  Physical impairments that would prevent participation  Inability to comprehend study instructions or to attend and complete the sessions and follow-up | Arm 1: Land-based exercise n = 19 Placebo/ Dose: 45 minutes per session Frequency: 12 sessions per 9 weeks Duration: 9 weeks Method of Blinding: NA Co-Intervention: none  Arm 2: Land-based exercise n = 19 Dose: 45 minutes per session Frequency: 8 sessions in 9 weeks, 2 booster sessions at 5 months, 1 session at 8 months, 1 session at 11 months Duration: 11 months Method of Blinding: NA Co-Intervention: Booster sessions at 5, 8, and 11 months  Arm 3: Land-based exercise + manipulation n = 18 Dose: 45 minutes per exercise session and 30-45 minutes per manual therapy session Frequency: 12 sessions exercise and manual therapy each in 9 weeks Duration: 9 weeks Method of Blinding: NA Co-Intervention: Manual therapy  Arm 4: Land-based exercise plus manipulation n = 19 Dose: 45 minutes per exercise session and 30-45 minutes per manual therapy session Frequency: 12 sessions exercise and manual therapy each in 9 weeks plus 2 booster sessions at 5 months, 1 session at 8 months, 1 session at 11 months Duration: 11 months Method of Blinding: NA Co-Intervention: Booster sessions plus manual therapy | TUG (s):  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-2.58, 0.58)  Comparator: Arm 3 vs Arm 1 , MD : 0.00 95% CI: (-1.42, 1.42)  Comparator: Arm 4 vs Arm 1 , MD : -0.10 95% CI: (-2.02, 1.82)  WOMAC total:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -56.10 95% CI: (-92.70, -19.50)  Comparator: Arm 3 vs Arm 1 , MD : -39.20 95% CI: (-69.38, -9.02)  Comparator: Arm 4 vs Arm 1 , MD : -8.30 95% CI: (-41.90, 25.30)  Pain intensity score:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-3.84, -0.16)  Comparator: Arm 3 vs Arm 1 , MD : -2.30 95% CI: (-4.07, -0.53)  Comparator: Arm 4 vs Arm 1 , MD : 0.20 95% CI: (-1.86, 2.26) |
| Acosta-Olivo, 2014[26](#_ENREF_26)  Study design: RCT  Trial name: None  Study Location: Mexico  Health care setting: Academic orthopedic surgery clinic/department  Single Site | Total n = 42  Age Range: NR  Arm 1, Mean Age: NR BMI: NR Arm 2, Mean Age: NR BMI: NR  Female: NR  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: K-L: Grade I  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 3 months  Minimum Age: 40  Able to sign Consent  Without previous treatment  NR | Surgery knee limb in prior 2 months month(s)  Prior experience with the intervention of interest  Use of anticoagulants  Varus-valgus deformities  Prior arthritis in the knee  Autoimmune disorders  Cerebrovascular diseases; hemoglobin <11; drug or alcohol abuse; active infections | Arm 1: Control n = 21 Dose: 1g paracetamol Frequency: 3 times per day Duration: 1 month  Arm 2: Cell-based therapies n = 21 Dose: 5 ml plasma per injection Frequency: 2 doses per month Duration: 1 month | KOOS:  Follow-Up Time: 4 months : Comparator: Arm 2 vs Arm 1 , MD : -9.00 95% CI: (-18.11, 0.11)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -6.90 95% CI: (-18.29, 4.49) |
| Atamaz, 2012[87](#_ENREF_87)  Study design: RCT  Trial name: None  Study Location: NR  Health care setting: NR  Multiple Sites: 4 | Total n = 203  Total # of knees = NR  Age Range: NR  Arm 1, Mean Age: 60.7 (SD 6.5) BMI: 29.0 (SD 4.1) Arm 2, Mean Age: 61.9 (SD 6.9) BMI: 28.4 (SD 3.5)  Female: 82.3%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2&3, ~Symptomatic with at least 40mm or 4cm severity of pain on the VAS for at least 6 months, ACR  Analgesic Use: Yes, Patients were asked to discontinue any pretreatment with NSAIDs drugs 7 days before the start of the study. If the patient required analgesic medication for knee pain, paracetamol use was permitted and noted. | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 6 months  Minimum Age: 51  Maximum Age:79  Otherwise Healthy  K-L: 2&3  ACR: confirmed knee OA | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 1 month(s)  Prior experience with the intervention of interest  Diagnosis of joint infection, a specific condition (neoplasm, diabetes mellitus, paresis, osteonecrosis, recent trauma, etc.), ascertained/suspected pregnancy or lactation, and poor general health status that would interfere with the functional assessments  History of any contraindication for electrotherapy  Received corticosteroid therapy or chondroprotective agents during the 30 days prior to the study or viscosupplementation treatment within 6 months prior to the study  Undergone previous major surgery, such as joint replacement or arthroscopy, within 6 months prior to the study | Arm 1: Sham n = 37, Placebo/Sham TENS, Dose: 20 minutes, Frequency: 5 times per week, Duration: 3 weeks Method of Blinding: All patients, investigators, and analysts were blinded, with the exception of members of the data and safety monitoring board Co-Intervention: Exercise program in groups of 4-5 patients led by a physiotherapist 3x/week for 3 weeks, included 5- to 6-minutes of jogging, stretching exercises (approx. 10min), isometric quadriceps exercises (10–15 repetitions) in the seated position were performed for 10 seconds with 10-second breaks, and chair lift and mini squats exercises (10–15 reps). At the end of 3 weeks, the physiotherapist prescribed a home-based training program (3x/week) as well as group exercise. Before the treatments, all patients participated in a single education group session of approximately 1-hour duration.  Arm 2: Neuromuscular electrical stimulation n = 37, Dose: 80Hz with 10- to 30-mA intensity for 20 minutes, Frequency: 5 times per week, Duration: 3 weeks Method of Blinding: All patients, investigators, and analysts were blinded, with the exception of members of the data and safety monitoring board Co-Intervention: Exercise program in groups of 4-5 patients led by a physiotherapist 3x/week for 3 weeks, included 5- to 6-minutes of jogging, stretching exercises (approx. 10min), isometric quadriceps exercises (10–15 repetitions) in the seated position were performed for 10 seconds with 10-second breaks, and chair lift and mini squats exercises (10–15 reps). | VAS pain:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : 4.30 95% CI: (-5.99, 14.59)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (-11.23, 11.63)  WOMAC function:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -2.50 95% CI: (-8.66, 3.66)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.50 95% CI: (-9.73, 4.73)  WOMAC pain:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -1.40 95% CI: (-3.69, 0.89)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.30 95% CI: (-3.89, 1.29) |
| Atamaz, 2012[87](#_ENREF_87) -Continued |  |  |  | At the end of 3 weeks, the physiotherapist prescribed a home-based training program (3x/week) as well as group exercise. Before the treatments, all patients participated in a single education group session of approximately 1-hour duration.  Arm 3-6 : Not of Interest |  |
| Atkins, 2013[122](#_ENREF_122)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: Wellness center  Single Site | Total n = 40  Total # of knees = NR  Age Range: NR  Arm 1, Mean Age: NR BMI: NR Arm 2, Mean Age: NR BMI: NR  Female: NR  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: Written diagnosis of knee OA by participants' health care provider  Analgesic Use: NR | Minimum Age: 50  Ambulatory  Willingness to attend 75% of scheduled self-massage sessions  No limitations that prevented mobility of the knee  Knee pain, pain on most days of the prior month, and morning stiffness lasting less than 30 minutes  Crepitus on motion and bony enlargement at affected joints  Agreement to practice no new exercise or stretching program and commitment to receiving no other mas sage therapy during the study | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Surgery knee limb in prior 6 month(s)  Injected corticosteroids in the prior 3 month(s)  Active rheumatoid arthritis or other serious medical conditions  Intra-articular knee injection of a steroid within the previous 3 months  Surgical procedure on either lower extremity within the past 6 months | Arm 1: Control n = 19 Placebo/Control, wait list Dose: NA Frequency: NA Duration: 12 weeks Method of Blinding: None Co-Intervention: Usual care only and received optional future dates for the knee self-massage training  Arm 2: Massage n = 21 Dose: Supervised sessions were 1 hour, including 20 minutes of the intervention. During the unsupervised weeks, participants were encouraged to continue their twice-weekly practice of self-massage. Frequency: 2 times per week Duration: 12 weeks Method of Blinding: None Co-Intervention: Usual care | WOMAC function:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.80 95% CI: (NC, NC)  WOMAC pain:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.65 95% CI: (NC, NC)  WOMAC total:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.70 95% CI: (NC, NC) |
| Atukorala, 2016[128](#_ENREF_128)  Study design: Single arm trial  Trial name: Healthy weight for life  Study Location: Australia  Health care setting: internet and phone-based program  Multiple Sites: NR (internet-based) | Total n = 1383  Mean Age(SD): Mean age 64.0(8.7)  Arm 1, Mean Age: 64(8.7) BMI: 34.4(5.2)  Female: 70.9%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: K-L: not specified, Mean KOOS pain 56.3(6.8)  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  BMI>28  Referral to orthopedist for KR  Enrollment in OAHWFL program  Radiographic or arthroscopy: NR | Exclusion : NR | Arm 1: Weight loss and exercise n = 1383 Dose: NA Frequency: NA Duration: 18 weeks | KOOS function:  Follow-Up Time: 18 weeks : Comparator: >10% weight change (post-pre) , MD : 17.40 95% CI: (15.9, 18.9)  Comparator: 7.6-10% weight change (post-pre) , MD : 13.60 95% CI: (11.9, 15.3)  Comparator: 5.1-7.5% weight change (post-pre) , MD : 12.00 95% CI: (10.2, 13.8)  Comparator: 2.5-5% weight change (post-pre) , MD : 8.90 95% CI: (7.0, 10.8)  Comparator: <2.5% weight change (post-pre) , MD : 7.80 95% CI: (4.8, 10.8)  KOOS pain:  Follow-Up Time: 18 weeks : Comparator: >10% weight change (post-pre) , MD : 16.70 95% CI: (15.2, 18.2)  Comparator: 7.6-10% weight change (post-pre) , MD : 13.30 95% CI: (11.6, 15.0)  Comparator: 5.1-7.5% weight change (post-pre) , MD : 12.00 95% CI: (10.2, 13.8)  Comparator: 2.5-5% weight change (post-pre) , MD : 9.90 95% CI: (7.7, 12.1)  Comparator: <2.5% weight change (post-pre) , MD : 6.10 95% CI: (3.2, 9.0) |
| Avelar, 2011[93](#_ENREF_93)  Study design: RCT  Trial name: None  Study Location: NR  Health care setting: NR  Site size: NR | Total n = 23  Total # of knees = NR  Age Range: NR  Arm 1, Mean Age: 71 (SD 4) BMI: NR Arm 2, Mean Age: 75 (SD 5) BMI: NR  Female: 86.96%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: bilateral 34.8% (of 21), unilateral 56.5% (of 21)  Subtype: NR  Diagnosis: K-L: 1-4, Knee OA in at least 1 knee clinical and radiographic criteria according to ACR  Analgesic Use: NR | Minimum Age: 60  Ambulatory  Able to sign Consent  Not requiring a walking aid  Any cognitive deficit as determined by the Mini-Mental Status Examination | Concomitant medical problems that prevent participation  Concomitant or prior use of other meds  Prior acute injury to the knee  Not having suffered any recent knee injury  Any orthopedic, neurological, respiratory, or acute cardiac diseases that would preclude the study  Not having been submitted to any rehabilitation procedure in the previous 3 months  Not having used glucocorticoids for at least 2 months prior the study | Arm 1: Control n = 11 Placebo/Control Dose: NA Frequency: NA Duration: 12 weeks Method of Blinding: Blinded, not otherwise described Co-Intervention: Squatting exercises, for each repetition, individuals were instructed to perform 3 seconds of isometric flexion of the quadriceps to 60 degrees and 3 seconds of isometric flexion of the quadriceps to 10 degrees. Prior to the squatting exercises, both groups warmed-up on an ergometric bicycle at 70% of the predicted maximum heart rate for age for 10 minutes  Arm 2: Vibrating platform (whole body vibration) n = 12 Dose: Frequency of 35Hz–40Hz, amplitude of 4mm, and acceleration that ranged from 2.78G to 3.26G Frequency: 3 times per week Duration: 12 weeks Method of Blinding: Blinded, not otherwise described Co-Intervention: Squatting exercises, for each repetition, individuals were instructed to perform 3 seconds of isometric flexion of the quadriceps to 60 degrees and 3 seconds of isometric flexion of the quadriceps to 10 degrees. Prior to the squatting exercises, both groups warmed-up on an ergometric bicycle at 70% of the predicted maximum heart rate for age for 10 minutes | 6 min walk (meter):  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -27.62 95% CI: (-76.92, 21.68)  TGUG (s):  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.02 95% CI: (-0.93, 0.97)  WOMAC function:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -59.00 95% CI: (-373.43, 255.43)  WOMAC pain:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 24.00 95% CI: (-60.64, 108.64) |
| Azlin, 2011[116](#_ENREF_116)  Study design: RCT  Trial name: None  Study Location: Malaysia  Health care setting: Physiotherapy unit in academic medical center  Single Site | Total n = 13  Age Range: 40  Arm 1, Mean Age: 59.7(4.9) BMI: 26.2 Arm 2, Mean Age: 63.1 (10.8) BMI: 28.5  Female: 85%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: bilateral 85%, unilateral 15%  Subtype: NR  Diagnosis: By orthopedic specialist  Analgesic Use: Yes, Continued normal medications | Diagnosis of osteoarthritis of the knee: By orthopedic specialist  Ambulatory  Ascend and descend at least a flight of stair  Willingness to be randomized  Sub-acute or chronic OA  Number of knees >=1 | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Prior acute injury to the knee  Acute inflammation or contracture  Cognitive problem (MMSE<20)  Pain during exercise | Arm 1: Control n = 6 Placebo/Conventional physical therapy Frequency: Twice a week Duration: 4 weeks  Arm 2: Passive joint mobilization n = 7 Frequency: Twice a week Duration: 4 weeks Co-Intervention: Conventional physiotherapy (exercises followed by thermal therapy with hot pack) | VAS pain stairs:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.99 95% CI: (-21.54, 15.56) |
| Bagnato, 2016[92](#_ENREF_92)  Study design: RCT  Trial name: None  Study Location: Italy  Health care setting: Academic rheumatology clinic/department  Single Site | Total n = 66  Age Range: >=40  Arm 1, Mean Age: 66.9 (10) BMI: 27.1 (4.1) Arm 2, Mean Age: 68.6 (11.9) BMI: 27.7 (4.6)  Female: 72%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: A diagnosis of primary OA of the knee according to the ACR criteria, including radiological evidence of OA  Analgesic Use: Yes, 43% of total used analgesics; 40% of tx group and 46% of control group | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >=6 months  Minimum Age: >=40  Persistent pain despite receiving the maximal tolerated doses of conventional medical therapy, including acetaminophen and/or an NSAID, with persistent pain defined as a minimal mean score of 40 mm on the VAS for global pain  Daily pain during the month prior to study enrolment  Ability to attend follow-up appointments  No change in pain medication during the last month  ACR: a diagnosis of primary OA of the knee according to the ACR criteria, including radiological evidence of OA | Concomitant medical problems that prevent participation  Concomitant or prior use of other meds  Injected corticosteroids in the prior month(s)  Patients affected by secondary causes of OA, DIP joint OA, local or systemic infection, secondary FM, diabetes mellitus, systemic arthritis, coagulopathy, patients on anticoagulant therapy and patients who had received previous intra-articular steroid injection or with avascular necrosis of bone were excluded. | Arm 1: Sham PEMF n = 33 Placebo/Sham Dose: 12 hours Frequency: Daily Duration: 4 weeks Method of Blinding: Double blind  Arm 2: Pulsed electromagnetic fields (PEMF) n = 33 Dose: 12 hours Frequency: Daily Duration: 4 weeks Method of Blinding: Double bind | SF-36 mental health:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -0.20 95% CI: (-2.32, 1.92)  SF-36 physical health:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -2.70 95% CI: (-5.81, 0.41)  VAS pain:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -11.30 95% CI: (-19.17, -3.43)  WOMAC function:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -8.00 95% CI: (-26.32, 10.32)  WOMAC pain:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -5.20 95% CI: (-9.72, -0.68)  WOMAC total:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -14.70 95% CI: (-36.83, 7.43) |
| Barduzzi, 2013[59](#_ENREF_59)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: NR  Site size: NR | Total n = 15  Arm 1, Mean Age: 70.8(6.3) BMI: NR Arm 2, Mean Age: 71.6(7.0) BMI: NR Arm 3, Mean Age: 66.4(5.1) BMI: NR  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: bilateral 60%  Subtype: NR  Diagnosis: ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 60  Maximum Age:79  Able to sign Consent  ACR: NA | Concomitant medical problems that prevent participation  Pending surgery  Physical Therapy or Rehab or exercise in the previous 3 months month(s)  Use of assistive walking devices  Neurological dysfunction that promoted cognitive changes | Arm 1: Control n = 5 Dose: NA Frequency: NA Duration: NA  Arm 2: Water based physical therapy n = 5 Dose: 60 minutes per session (2-4 sets, 20-25 repetitions) Frequency: 3 sessions per week Duration: 4 months (45 day break between 12th and 13th session) 24 sessions total  Arm 3: Land-based physical therapy n = 5 Dose: 60 minutes per session (2-4 sets, 20-25 repetitions) Frequency: 3 sessions per week Duration: 4 months (45 day break between 12th and 13th session) 24 sessions total | Walking speed:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -1.18 95% CI: (-5.39, 3.03)  Comparator: Arm 3 vs Arm 1 , MD : -0.29 95% CI: (-4.77, 4.19)  Follow-Up Time: 4.5 months : Comparator: Arm 3 vs Arm 2 , MD : 4.03 95% CI: (-0.51, 8.57) |
| Bartels, 2014[68](#_ENREF_68)  Study design: Single arm trial  Trial name: CAROT  Study Location: Denmark  Health care setting: NR  Site size: NR | Total n = 192  Total # of knees = NR  Mean Age(SD): 62.6 (SD 6.3) (for 175 who  Arm 1, Mean Age: 62.6 (SD 6.3) BMI: 37.1 (SD 4.4)  Female: NR  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: ACR primary knee OA  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 51  BMI >= 30 kg/m 2  ACR: Primary knee OA  NR: Clinical symptoms and radiographic verification of the diagnosis | Exclusion : NR | Arm 1: Weight loss, self-management n = 192 Dose: 8-week formula weight loss diet 415-810 kcal/day, followed by 8 weeks on a hypo-energetic 1200 kcal/day diet of normal food and formula products Frequency: Diet was daily. Weekly sessions (1.5 h/week) by a dietician giving nutritional instructions and behavioral therapy Duration: 16 weeks Method of Blinding: NA Co-Intervention: NR | KOOS function:  Follow-Up Time: 16 weeks : Comparator: post-pre , MD : 12.10 95% CI: (10.0, 14.2)  KOOS pain:  Follow-Up Time: 16 weeks : Comparator: post-pre , MD : 10.70 95% CI: (8.5, 12.9)  Weight (kg):  Follow-Up Time: 16 weeks : Comparator: pre-post , MD : 14.00 95% CI: (13.3, 14.7) |
| Bellare, 2014[30](#_ENREF_30)  Study design: RCT  Trial name: None  Study Location: India  Health care setting: Orthopedic clinics  Multiple Sites: 3 | Total n = 117  Age Range: >=50  Arm 1, Mean Age: 60.70 (8.31) BMI: 27.68 (3.03) Arm 2, Mean Age: 59.98 (8.81) BMI: 27.36 (3.71)  Female: 23%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: ACR  Analgesic Use: Yes | Diagnosis of osteoarthritis of the knee: ACR | Exclusion : NR | Arm 1: Diet therapy n = 56 Dose: 1200-1400 kcal/d Duration: 1 year  Arm 2: Diet therapy + Glucosamine-chondroitin n = 61 Dose: Glucosamine 1500mg/day; Chondroitin 1200mg/day Frequency: Twice daily (G 750mg+C 600mg) Duration: 1 year | Lequesne Index Score:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -3.20 95% CI: (-3.86, -2.54)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.56 95% CI: (-3.35, -1.77)  VAS score:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -1.70 95% CI: (-1.99, -1.41)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.08 95% CI: (-2.40, -1.76)  WOMAC function:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -7.90 95% CI: (-10.06, -5.74)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.86 95% CI: (-6.16, -1.56)  WOMAC pain:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -3.10 95% CI: (-3.69, -2.51)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.59 95% CI: (-2.31, -0.87) |
| Bennell, 2011[109](#_ENREF_109)  Study design: RCT  Trial name: None  Study Location: Australia  Health care setting: NR  Site size: NR | Total n = 200  Age Range: >=50  Arm 1, Mean Age: 65.0 (7.9) BMI: 30.4 (5.6) Arm 2, Mean Age: 63.3 (8.1) BMI: 28.1 (4.2)  Female: 58%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Medial 100%  Diagnosis: Radiological evidence  Analgesic Use: Yes, Not specified | Diagnosis of osteoarthritis of the knee  Minimum Age: 50  Able to sign Consent  Pain on walking>=3  Radiological knee alignment <=185 degrees  X-ray: Osteophytes or joint space narrowing in medial compartment | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Surgery knee limb in prior 6 month(s)  Concomitant or prior use of other meds  Injected corticosteroids in the prior 6 month(s)  Prior experience with the intervention of interest  K-L: 1 or 4  Predominant patellofemoral joint symptoms  Systemic arthritic conditions | Arm 1: Control Insoles n = 97 Placebo/No-wedging insoles Frequency: All day every day Duration: 12 months  Arm 2: Wedge Insoles n = 103 Frequency: All day every day Duration: 12 months | Pain numerical rating scale:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-0.65, 0.65)  Quality of life:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-0.06, 0.06)  WOMAC function:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.70 95% CI: (-2.79, 4.19)  WOMAC pain:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (-0.75, 1.15) |
| Bennell, 2015[53](#_ENREF_53)  Study design: RCT  Trial name: None  Study Location: Australia  Health care setting: Academic sports medicine clinic/department  Single Site | Total n = 222  Mean Age: 63  Arm 1, Mean Age: 62.7 (7.9) BMI: 31.5 (5.9) Arm 2, Mean Age: 63.0 (7.9) BMI: 30.8 (6.4) Arm 3, Mean Age: 64.6 (8.3) BMI: 31.0 (6.0)  Female: 60%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 73%, unilateral 27%  Diagnosis: K-L: 30% Grade II; 21% grade III; 23% grade IV  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: knee pain >=3 months  Minimum Age: 50  Average pain >=40/100mm on VAS in preceding week  At least moderate difficulty with daily functioning (WOMAC physical function \_ 25/68 units)  ACR Criteria: NA | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 months month(s)  Pending surgery  Injected corticosteroids in the prior 3 months month(s)  Physical Therapy or Rehab or exercise in the previous 6 months month(s)  Prior experience with the intervention of interest  Systemic arthritis  Self-reported history of serious mental illness, such as schizophrenia, or self reported diagnosis of current clinical depression; neurological condition such as Parkinson’s disease, multiple sclerosis or stroke  Walking exercise for >30 minutes continuously daily; participating in a regular (more than twice a week) structured and/or supervised exercise program such as attending exercise classes in a gym or use of a personal trainer | Arm 1: Land-based Exercise strength/resistance training n = 75 Dose: 25 minutes exercise Frequency: 10 sessions per 12 weeks plus home practice Duration: 12 weeks  Arm 2: Self-management n = 74 Dose: NR Frequency: 10 sessions per 12 weeks plus home practice Duration: 12 weeks  Arm 3: Self-management plus Land-based exercise: strength training n = 73 Dose: 25 minute exercise sessions plus educational session Frequency: 10 sessions per 12 weeks plus home practice Duration: 12 weeks | AQoL-6D:  Follow-Up Time: 12 weeks : Comparator: Arm 3 vs Arm 2 , MD : -0.02 95% CI: (-0.07, 0.03)  Follow-Up Time: 52 weeks : Comparator: Arm 3 vs Arm 2 , MD : -0.03 95% CI: (-0.07, 0.01)  TUG (s):  Follow-Up Time: 12 weeks : Comparator: Arm 3 vs Arm 2 , MD : -1.10 95% CI: (-1.97, -0.23)  Follow-Up Time: 52 weeks : Comparator: Arm 3 vs Arm 2 , MD : -1.10 95% CI: (-1.84, -0.36)  VAS overall pain:  Follow-Up Time: 12 weeks : Comparator: Arm 3 vs Arm 2 , MD : -6.80 95% CI: (-13.73, 0.13)  Follow-Up Time: 52 weeks : Comparator: Arm 3 vs Arm 2 , MD : -3.10 95% CI: (-10.78, 4.58)  VAS walking:  Follow-Up Time: 12 weeks : Comparator: Arm 3 vs Arm 2 , MD : -8.20 95% CI: (-15.41, -0.99)  Follow-Up Time: 52 weeks : Comparator: Arm 3 vs Arm 2 , MD : -4.90 95% CI: (-13.21, 3.41) |
| Bennell, 2015[53](#_ENREF_53) -Continued |  |  | Inability to walk unaided  Inadequate written and spoken English; inability to comply with the study protocol such as inability to attend physical therapy sessions or attend assessment appointments at the University |  | WOMAC function:  Follow-Up Time: 12 weeks : Comparator: Arm 3 vs Arm 2 , MD : -8.10 95% CI: (-11.46, -4.74)  Follow-Up Time: 52 weeks : Comparator: Arm 3 vs Arm 2 , MD : -5.30 95% CI: (-8.82, -1.78)  WOMAC pain:  Follow-Up Time: 12 weeks : Comparator: Arm 3 vs Arm 2 , MD : -1.50 95% CI: (-2.50, -0.50)  Follow-Up Time: 52 weeks : Comparator: Arm 3 vs Arm 2 , MD : -0.60 95% CI: (-1.70, 0.50) |
| Bliddal, 2011[126](#_ENREF_126)  Study design: RCT  Trial name: None  Study Location: Denmark  Health care setting: Home, NR  Site size: NR | Total n = 96  Age Range: 36-90  Arm 1, Mean Age: 64.1 (10.5) BMI: 35.2 (4.5) Arm 2, Mean Age: 61.1 (11.1) BMI: 35 (5.5)  Female: 89%  Racial/Ethnic Distribution: NR  Living Situation: NR  Subtype: NR  Diagnosis: K-L: 2&3, ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 18  Overweight was defined as a body mass index (BMI) \_28 kg/m2. Only patients who explicitly expressed a clear, unequivocal desire for weight loss  Fluent in Danish  ACR | Concomitant medical problems that prevent participation  History of other rheumatic diseases possibly responsible for secondary OA, diabetes mellitus or other endocrine disorders, and substantial abnormalities in haematological, hepatic, renal or cardiac function | Arm 1: Conventional diet program n = 45 Placebo/Control Dose: 1200 calories/day Frequency: Daily Duration: 52 weeks Method of Blinding: Single-blinded  Arm 2: Low-energy diet n = 44 Dose: 810-1200 cal/day Frequency: Daily Duration: 52 weeks Method of Blinding: Single-blinded | WOMAC disability:  Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.60 95% CI: (-9.14, 1.94)  WOMAC pain:  Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.20 95% CI: (-13.30, -1.10)  WOMAC total:  Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.30 95% CI: (-9.57, 0.97)  Weightloss, kg:  Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.30 95% CI: (-9.52, -5.08) |
| Bokaeian, 2016[99](#_ENREF_99)  Study design: RCT  Trial name: None  Study Location: Iran  Health care setting: NR  Site size: NR | Total n = 28  Age Range: 35-76  Arm 1, Mean Age: 54.0 (3.9) Arm 2, Mean Age: 51.8 (8.3)  Female: 93%  Racial/Ethnic Distribution: NR  Living Situation: NR  Subtype: Tibiofemoral 100%  Diagnosis: K-L: mild to moderate chronic osteoarthritis of unilaterally or bilaterally tibiofe moral joint according to the method of Kellgren & Lawrence  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >1 month  Minimum Age: >35  Maximum Age:76  Ambulatory  K-L: mild to moderate | Concomitant medical problems that prevent participation  Surgery knee limb in prior 3 months month(s)  Injected hyaluronic acid in the past or during the past 3 months month(s)  Injected corticosteroids in the prior 3 months month(s)  Other dis eases such as: diabetes, diseases of musculoskeletal, neuromuscular, cardiovascular, respiratory,  Having an artificial hip or knee joints,  Medication  History of trauma to knee joint during last week  Performing regular professional exercise and extreme physical weakness | Arm 1: Strength training alone n = 13 Placebo/Strength training alone Dose: approx.11 min Frequency: 3 times a week Duration: 8 weeks Method of Blinding: Single-blind  Arm 2: Whole body vibration + strength training n = 15 Dose: 30-70s, 6-9 sets Frequency: 3 times a week Duration: 8 weeks Method of Blinding: Single-blind Co-Intervention: Strength training | VAS pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.50 95% CI: (-0.80, 3.80)  WOMAC quality of life:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.80 95% CI: (-3.29, 4.89) |
| Brosseau, 2012[39](#_ENREF_39)  Study design: RCT  Trial name: None  Health care setting: Physical therapy outpatient clinic  Single Site | Total n = 222  Mean Age(SD): Mean age 63.4(8.6)  Arm 1, Mean Age: 62.3(6.8) BMI: 29.9(5.3) Arm 2, Mean Age: 63.9(10.3) BMI: 29.4(5.4)  Female: 69%  Racial/Ethnic Distribution: African American 2.3%, Asian 4.5%, Caucasian 88.7%, Hispanic 3.6%, 0.5% American Indian, 0.5% Other  Living Situation: Community Dwelling  Location of OA: bilateral 23%, unilateral 77%  Subtype: NR  Diagnosis: Mild to moderate according to ACR clinical and radiographic criteria  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: pain for at least 3 months  Ambulatory  Expected medications to change during study period  Demonstrated ability to walk for a minimum of 20 minutes with minimal pain (<=3/10 on VAS)  Able to be treated as outpatients  Available 3 times a week for 12 months  mild to moderate according to ACR clinical and radiographic criteria: NR | Injected hyaluronic acid in the past or during the past 12 months month(s)  Injected corticosteroids in the prior 12 months month(s)  Physical Therapy or Rehab or exercise in the previous regular activity program 2 or more times per week for more than 20 minutes per session during previous 6 months or rehab treatment within prior 12 months month(s)  Severe OA of the knee or other weight bearing joints of the lower extremity  Pain at rest or at night  Any other treatment for knee OA besides analgesic for prior 12 months  Uncontrolled HTN or other condition, such as rheumatoid arthritis that would make participation difficult  Significant cognitive deficits, inability to communicate in English, intention to move within the year, unwillingness to sign consent | Arm 1: Control n = 74 Placebo/Educational materials (pamphlet) Dose: NA Frequency: NA Duration: 12 months Method of Blinding: NA  Arm 2: Walking n = 79 Dose: 45 minutes walking and 20 minutes warm-up/cool down per session Frequency: 3 sessions per week Duration: 12 months Method of Blinding: NA Co-Intervention:  Arm 3: Walking + Co-Intervention: behavioral intervention adapted from Program for Arthritis Control through Education and Exercise program: education and behavioral counseling | 6 min walk (meter):  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 47.44 95% CI: (4.45, 90.43)  Comparator: Arm 3 vs Arm 1 , MD : 40.20 95% CI: (-1.29, 81.69)  SF-36 pain:  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 2.40 95% CI: (-5.89, 10.69)  Comparator: Arm 3 vs Arm 1 , MD : 6.28 95% CI: (-1.94, 14.49)  SF-36 physical function:  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 7.54 95% CI: (-1.57, 16.64)  Comparator: Arm 3 vs Arm 1 , MD : 12.44 95% CI: (2.30, 22.58)  TUG (s):  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.53 95% CI: (-0.35, 1.41)  Comparator: Arm 3 vs Arm 1 , MD : 0.52 95% CI: (-0.23, 1.27)  WOMAC function:  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : -1.20 95% CI: (-8.35, 5.95)  Comparator: Arm 3 vs Arm 1 , MD : 4.75 95% CI: (-2.94, 12.44)  WOMAC pain:  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-7.32, 7.52)  Comparator: Arm 3 vs Arm 1 , MD : 2.66 95% CI: (-5.35, 10.67) |
| Brosseau, 2012[39](#_ENREF_39) -Continued |  |  |  |  | WOMAC total:  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-7.54, 6.34)  Comparator: Arm 3 vs Arm 1 , MD : 4.68 95% CI: (-2.80, 12.16) |
| Bruce-Brand, 2012[44](#_ENREF_44)  Study design: RCT  Trial name: None  Study Location: Ireland  Health care setting: Academic orthopedic surgery clinic/department  Single Site | Total n = 26  Mean Age: 64  Arm 1, Mean Age: 65.2 ± 3.1 BMI: 31.7 ± 4.1 Arm 2, Mean Age: 63.4 ± 5.9 BMI: 33.9 ± 8.3 Arm 3, Mean Age: 63.9 ± 5.8 BMI: 33.7 ± 5.6  Female: 42%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 3&4, Moderate-to-severe, Outerbridge Scale 3-4  Analgesic Use: Yes, Subjects in all 3 groups were advised to maintain any pre-existing treatment of their OA such as pharmacologic therapy. | Diagnosis of osteoarthritis of the knee  Minimum Age: 55  Maximum Age:74  Ambulatory  Wait list for arthroplasty  K-L: 3&4  Outerbridge scale: 3-4 | Surgery knee limb in prior 3 month(s)  Pending surgery  Physical Therapy or Rehab or exercise in the previous 6 months month(s)  Prior experience with the intervention of interest  Medical co-morbidities precluding participation in an exercise program  Implanted electrical devices  Neurological disorders, inflammatory arthritis  Significant cognitive impairment  Anticoagulant therapy | Arm 1: Standard care n = 6 Placebo/OA education, weight loss, pharmacologic therapy, and physical therapy Dose: not applicable Frequency: not applicable Duration: 6 weeks  Arm 2: Strength/resistance training n = 10 Dose: 30 minutes Frequency: 3 sessions per week Duration: 6 weeks  Arm 3: NMES n = 10 Dose: 20 minutes per session Frequency: 5 sessions per week Duration: 6 weeks | SF-36 mental:  Follow-Up Time: 14 weeks : Comparator: Arm 2 vs Arm 1 , MD : 5.20 95% CI: (-18.46, 28.86)  Comparator: Arm 3 vs Arm 1 , MD : 5.10 95% CI: (-14.55, 24.75)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.64 95% CI: (-23.41, 20.13)  Comparator: Arm 3 vs Arm 1 , MD : -5.67 95% CI: (-27.62, 16.28)  SF-36 physical:  Follow-Up Time: 14 weeks : Comparator: Arm 2 vs Arm 1 , MD : 14.63 95% CI: (-8.68, 37.94)  Comparator: Arm 3 vs Arm 1 , MD : 20.23 95% CI: (1.63, 38.83)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 6.00 95% CI: (-15.16, 27.16)  Comparator: Arm 3 vs Arm 1 , MD : 5.50 95% CI: (-13.19, 24.19)  WOMAC function:  Follow-Up Time: 14 weeks : Comparator: Arm 2 vs Arm 1 , MD : 9.83 95% CI: (-7.73, 27.39)  Comparator: Arm 3 vs Arm 1 , MD : 9.83 95% CI: (-7.20, 26.86)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 7.80 95% CI: (-4.79, 20.39)  Comparator: Arm 3 vs Arm 1 , MD : 7.77 95% CI: (-4.54, 20.08)  WOMAC pain:  Follow-Up Time: 14 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.27 95% CI: (-2.88, 5.42)  Comparator: Arm 3 vs Arm 1 , MD : 0.17 95% CI: (-3.50, 3.84) |
| Bruce-Brand, 2012[44](#_ENREF_44) -Continued |  |  |  |  | Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 2.45 95% CI: (-1.37, 6.27)  Comparator: Arm 3 vs Arm 1 , MD : 0.55 95% CI: (-2.85, 3.95) |
| Bruyere, 2008[33](#_ENREF_33)  Study design: Post-hoc analysis  Trial name: None  Study Location: Belgium, Czech Republic  Health care setting: Academic orthopedic surgery clinic/department, Institute of Rheumatology  Multiple Sites: 2 | Total n = 275  Age Range: 63.2  Arm 1, Mean Age: 63.6 BMI: 26.6 Arm 2, Mean Age: 62.9 BMI: 26.6  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Inclusion : NR  ACR | Exclusion : NR | Arm 1: Placebo n = 131 Placebo/Tablets packets Dose: Frequency: Once daily Duration: 12 months  Arm 2: Glucosamine sulfate use n = 144 Dose: 1500mg Frequency: Once daily Duration: 12 months | Total knee replacement:  Follow-Up Time: 5 years : Comparator: Arm 2 vs Arm 1 , RR : 0.43 95% CI: (0.20, 0.92) |
| Cakir, 2014[79](#_ENREF_79)  Study design: RCT  Trial name: None  Study Location: Turkey  Health care setting: Department of Physical Medicine and Rehabilitation  Single Site | Total n = 60  Age Range: 40-80  Arm 1, Mean Age: 57.1 (7.8) BMI: 29.5 (5.9) Arm 2, Mean Age: 56.9 (8.8) BMI: 27.9 (4.4) Arm 3, Mean Age: 58.2 (9.9) BMI: 30.9 (4.0)  Female: 15.5%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2&3, ACR  Analgesic Use: Yes, Paracetamol up to 2000 mg/day | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 6 months  Minimum Age: 40  Maximum Age:79  K-L: 2&3 | Concomitant medical problems that prevent participation  Concomitant or prior use of other meds  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 1 month(s)  Physical Therapy or Rehab or exercise in the previous month(s)  Prior experience with the intervention of interest  Joint infection, neoplasm, diabetes mellitus, paresis, osteonecrosis, recent trauma, ascertained/suspected pregnancy or lactating and poor general health status | Arm 1: Control n = 20 Placebo/Sham procedure Frequency: 5 times a week Duration: 12 months Co-Intervention: Isometric exercise, strengthening, stretching  Arm 2: Continuous Ultrasound n = 20 Dose: Frequency of 1 MHz with intensity of 1 W/cm2 Frequency: 5 times a week Duration: 12 months Co-Intervention: Isometric exercise, strengthening, stretching  Arm 3: Pulse Ultrasound n = 20 Dose: Frequency of 1 MHz with intensity of 1 W/cm2 Frequency: 5 times a week Duration: 12 months Co-Intervention: Isometric exercise, strengthening, stretching | VAS pain at rest:  Follow-Up Time: 6.5 months : Comparator: Arm 2 vs Arm 1 , MD : -0.90 95% CI: (-11.14, 9.34)  Comparator: Arm 3 vs Arm 1 , MD : -2.10 95% CI: (-10.99, 6.79)  VAS pain on movement:  Follow-Up Time: 6.5 months : Comparator: Arm 2 vs Arm 1 , MD : 0.60 95% CI: (-13.56, 14.76)  Comparator: Arm 3 vs Arm 1 , MD : -0.60 95% CI: (-16.69, 15.49)  WOMAC function:  Follow-Up Time: 6.5 months : Comparator: Arm 2 vs Arm 1 , MD : -2.90 95% CI: (-9.15, 3.35)  Comparator: Arm 3 vs Arm 1 , MD : 1.60 95% CI: (-2.94, 6.14)  WOMAC pain:  Follow-Up Time: 6.5 months : Comparator: Arm 2 vs Arm 1 , MD : -1.60 95% CI: (-3.25, 0.05)  Comparator: Arm 3 vs Arm 1 , MD : 0.20 95% CI: (-1.32, 1.72) |
| Callaghan, 2015[100](#_ENREF_100)  Study design: RCT  Trial name: None  Study Location: UK  Health care setting: NR  Single Site | Total n = 126  Age Range: 40-70  Arm 1, Mean Age: 56.4 (8.1) BMI: 30.5 (5.1) Arm 2, Mean Age: 54.5 (6.7) BMI: 31.4  Female: 57.1  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Patellofemora 100%  Diagnosis: K-L: 2&3  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 3 months; >=4 on VAS scale  Taking same medication for past 3 months  K-L: 2&3  Patellofemoral OA: PL OA is present and greater than tibiofemoral OA | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Injected corticosteroids in the prior 1 month(s)  Initiating new treatment | Arm 1: No brace n = 63 Placebo/Control Duration: 6 weeks Method of Blinding: Single-blind  Arm 2: Brace n = 63 Duration: 6 weeks Method of Blinding: Single-blind | Koos pain subscale:  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.70 95% CI: (-10.76, -0.64)  VAS:  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.30 95% CI: (-2.01, -0.59) |
| Campos, 2015[106](#_ENREF_106)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Hospital-outpatient  Single Site | Total n = 58  Mean Age: 64.3  Arm 1, Mean Age: 63.3 (7.5) BMI: 30.3 (5.1) Arm 2, Mean Age: 65.2 (9.6) BMI: 30.8 (6.1)  Female: 63.8  Racial/Ethnic Distribution: African American 10.3%, Asian 3.4%, Caucasian 74.1%, 12.1% Mixed  Living Situation: NR  Location of OA: NR  Subtype: Medial 100%  Diagnosis: K-L: 1-4, ACR  Analgesic Use: Yes, Unlimited | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 6 months of usual care treatment  Able to sign Consent  ACR | Concomitant medical problems that prevent participation  Pending surgery  Concomitant or prior use of other meds | Arm 1: Neutral insole n = 29 Placebo/Sham Dose: 5-10 hrs/day Frequency: Daily Duration: 6 months Method of Blinding: Unblinded  Arm 2: Wedged insole n = 29 Dose: 5-10 hrs/day Frequency: Daily Duration: 6 months Method of Blinding: Unblinded | Lequesne index:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.10 95% CI: (-1.19, 3.39)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.00 95% CI: (-1.02, 3.02)  VAS:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.20 95% CI: (-14.34, 9.94)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-11.99, 11.39)  WOMAC pain:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.10 95% CI: (-2.30, 2.10)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.70 95% CI: (-2.64, 1.24)  WOMAC total:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.70 95% CI: (-13.38, 7.98)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-11.04, 9.04) |
| Carlos, 2012[80](#_ENREF_80)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Physical therapy outpatient clinic  Single Site | Total n = 30  Arm 1, Mean Age: 62.7(8.7) BMI: 31.1(3.2) Arm 2, Mean Age: 63.4(4.6) BMI: 27.8(3.8) Arm 3, Mean Age: 63.9(6.3) BMI: 31.8(4.1)  Female: 70%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: bilateral 86.7%, unilateral 13.3%  Subtype: NR  Diagnosis: K-L: Grade I1-4 on at least one knee  Analgesic Use: No | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 3 months  Minimum Age: 50  Maximum Age:75  K-L:-grade I1-4 | Concomitant medical problems that prevent participation  Continued Use of Analgesics  Diabetes, uncontrolled hypertension, morbid obesity  Dementia  OA of the hip  Use of anti-inflammatory or anxiolytic drugs during the past 6 months | Arm 1: Exercise n = 10 Dose: 45 minutes (2 sets of 30 reps) Frequency: 3 sessions per week Duration: 8 weeks  Arm 2: Ultrasound n = 10 Dose: 2.5W/cm2, 20%, 100Hz Frequency: 3 sessions per week for 4 weeks Duration: 8 weeks (4 weeks US, 4 weeks exercise) Co-Intervention: strength/resistance training 3 sessions per week for 4 weeks  Arm 3: Ultrasound n = 10 Dose: Frequency: 3 sessions per week for 4 weeks Duration: 8 weeks (4 weeks US, 4 weeks exercise) Co-Intervention: strength/resistance training 3 sessions per week for 4 weeks | VAS movement:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.05 95% CI: (-0.23, 0.14)  Comparator: Arm 3 vs Arm 1 , MD : 0.03 95% CI: (-0.08, 0.14)  VAS rest:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.42 95% CI: (0.13, 0.71)  Comparator: Arm 3 vs Arm 1 , MD : 0.17 95% CI: (-0.17, 0.50)  WOMAC function:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.38 95% CI: (0.16, 0.60)  Comparator: Arm 3 vs Arm 1 , MD : 0.31 95% CI: (0.08, 0.54)  WOMAC pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.42 95% CI: (0.25, 0.59)  Comparator: Arm 3 vs Arm 1 , MD : 0.32 95% CI: (0.09, 0.55)  WOMAC total:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.43 95% CI: (0.15, 0.71)  Comparator: Arm 3 vs Arm 1 , MD : 0.28 95% CI: (-0.01, 0.57) |
| Cheawthamai, 2014[117](#_ENREF_117)  Study design: RCT  Trial name: None  Study Location: Thailand  Health care setting: Academic physical therapy department  Single Site | Total n = 43  Age Range: 65.3  Arm 1, Mean Age: 64.1(7.9) BMI: 27.1(3.6) Arm 2, Mean Age: 66.6(8.8) BMI: 27.0(4.6)  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 51%, unilateral 48%  Subtype: NR  Diagnosis: ACR  Analgesic Use: Yes, Participants were instructed to continue any current medication and not to start any new medication | Diagnosis of osteoarthritis of the knee  Female  ACR: NR | Surgery knee limb in prior 1.5 months month(s)  Injected corticosteroids in the prior 1month month(s)  Systemic joint disease, cerebrovascular disease, Parkinson's  Back and limb surgery in the prior 1.5 months | Arm 1: Home-exercise program n = 22 Placebo/Home-exercise Dose: Customized Frequency: Daily Duration: 12 weeks  Arm 2: Manipulation/manual therapy n = 21 Dose: Customized Frequency: Daily Duration: 12 weeks Co-Intervention: home-based exercise | 6 min walk (meter):  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 5.00 95% CI: (NC, NC)  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 10.00 95% CI: (NC, NC)  VAS pain:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (-1.29, 1.69)  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.90 95% CI: (0.41, 3.39) |
| Cherian, 2015[101](#_ENREF_101)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: NR  Single Site | Total n = 52  Age Range: 41-80  Arm 1, Mean Age: 54 Arm 2, Mean Age: 59  Female: 48.1%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 3&4  Analgesic Use: Yes, Both treatment and the matched cohorts were not prohibited from receiving previously prescribed NSAIDs. However, we instructed patients to remain taking the same dosage of NSAIDs medication throughout the study, and that if increase or change of dosage was needed, this would only occur after their three month follow-up appointment. In addition, no patients in the study were started on new pain medications at the time of enrollment and throughout the trial period by our institution. The rationale behind our choices for a corticosteroid injection/ physical therapy and to allow the use of NSAID as the matching cohort was to compare the use of the brace to the current initial standard of care at our institution. | Diagnosis of osteoarthritis of the knee  Minimum Age: 41  Maximum Age:79  Able to sign Consent  Medial or lateral OA  Persistent pain beyond treatment  Ability to comply with treatment  K-L: 3&4 | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Injected corticosteroids in the prior 3 month(s)  Equal medial/lateral OA  History of traumatic onset of knee pain | Arm 1: Usual care n = 26 Placebo/Usual care Dose: 1 mL Kenalog 40 mg and 4 mL of 1% lidocaine (corticosteroids); unspecified length of time (physical therapy) Frequency: Unspecified (corticosteroids); gait training three times a week for six weeks, self-directed physical therapy every other day (physical therapy) Duration: 3 months Method of Blinding: Single-blinded  Arm 2: Brace n = 26 Dose: 3+ hrs per day Frequency: Daily Duration: 3 months Method of Blinding: Single-blinded | SF-36 mental:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -2.30 95% CI: (NC, NC)  SF-36 physical:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : 5.90 95% CI: (NC, NC)  TUG (s):  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -3.10 95% CI: (NC, NC)  VAS:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -2.30 95% CI: (-3.66, -0.94) |
| Cheung, 2014[71](#_ENREF_71)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: Home, NR  Site size: NR | Total n = 36  Mean Age: 72  Arm 1, Mean Age: 71.9 (69.3, 74.6) 95% CI BMI: 29.1 (26.7, 31.7) 95% CI Arm 2, Mean Age: 71.9 (69.0, 75.0) 95% CI BMI: 28.8 (26.0, 31.7) 95% CI  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 6 months  Minimum Age: 65  Maximum Age:89  ACR | Concomitant medical problems that prevent participation  Surgery knee limb in prior 24 month(s)  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 3 month(s)  Prior experience with the intervention of interest  Not currently participating in a supervised exercise program  Cognitive/mental impairment  Symptoms of joint locking; in stability indicated by chronic use of a knee brace, cane, walker, or wheelchair  Prior joint replacement  : a) uncontrolled high blood pressure or existing heart condition; and b) other comorbid condition with overlapping symptoms (i.e. fibromyalgia, rheumatoid arthritis) were also be excluded. | Arm 1: Wait list control n = 18 Placebo/Wait list Duration: 8 weeks Method of Blinding: Single-blind  Arm 2: Hatha yoga n = 18 Dose: 60 minutes Frequency: Weekly Duration: 8 weeks Method of Blinding: Single-blind | SF-12 mental component:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 2.00 95% CI: (-1.33, 5.33)  SF-12 physical component:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.70 95% CI: (-2.04, 3.44)  WOMAC function:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.20 95% CI: (-10.58, 2.18)  WOMAC pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.50 95% CI: (-4.36, -0.64)  WOMAC total:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -8.30 95% CI: (-16.62, 0.02) |
| Christensen, 2015[62](#_ENREF_62)  Study design: RCT  Trial name: CAROT  Study Location: Denmark  Health care setting: Home, Hospital-outpatient, Dietary unit  Site size: NR | Total n = 192  Total # of knees = NR  Age Range: NR  Arm 1, Mean Age: 61.7 (SD 6.8) BMI: NR Arm 2, Mean Age: 63.0 (SD 6.5) BMI: NR Arm 3, Mean Age: 62.9 (SD 5.8) BMI: NR  Female: 80.7%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: bilateral 89%, unilateral 11%  Subtype: NR  Diagnosis: Confirmed knee OA based on clinical symptoms, including pain, and on standing radiographs in at least 1 joint compartment  Analgesic Use: Yes, Participants were asked not to change any medication or nutritional supplements during the study | Diagnosis of osteoarthritis of the knee  Minimum Age: 50  BMI >= 30 kg/m2  NR: Confirmed knee OA based on clinical symptoms, including pain, and on standing radiographs in at least 1 joint compartment | Pending surgery  Lack of motivation to lose weight  Inability to speak Danish  Planned antiobesity surgery, total knee alloplasty (TKA), or receiving pharmacologic therapy for obesity | Arm 1: Control n = 64 Placebo/Control Dose: NA Frequency: NA Duration: 68 weeks (16 on co-intervention, 52 on control) Method of Blinding: NR Co-Intervention: Initial 16-week intensive dietary therapy  Arm 2: Weight loss n = 64 Dose: 1 hour sessions Frequency: Weekly sessions for 52 weeks Duration: 68 weeks (16 on co-intervention, 52 on additional weight loss intervention) Method of Blinding: NR Co-Intervention: Initial 16-week intensive dietary therapy  Arm 3: Home exercise program; strength/resistance training n = 64 Dose: 60 minutes per session Frequency: 3 days per week Duration: 68 weeks (16 on co-intervention, 52 on additional exercise intervention) Method of Blinding: NR Co-Intervention: Initial 16-week intensive dietary therapy | 6 min walk (meter):  Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -14.63 95% CI: (-35.67, 6.41)  Comparator: Arm 3 vs Arm 1 , MD : -15.59 95% CI: (-36.63, 5.45)  KOOS pain:  Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.10 95% CI: (-4.13, 6.33)  Comparator: Arm 3 vs Arm 1 , MD : 1.90 95% CI: (-3.33, 7.13)  SF-36 mental health:  Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.60 95% CI: (-1.09, 4.29)  Comparator: Arm 3 vs Arm 1 , MD : 1.20 95% CI: (-1.49, 3.89)  SF-36 physical component:  Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.10 95% CI: (-3.86, 1.66)  Comparator: Arm 3 vs Arm 1 , MD : 0.60 95% CI: (-2.16, 3.36)  VAS pain:  Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-7.67, 6.47)  Comparator: Arm 3 vs Arm 1 , MD : -0.10 95% CI: (-7.17, 6.97)  Change in BMI:  Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.10 95% CI: (-2.09, -0.11)  Comparator: Arm 3 vs Arm 1 , MD : 0.60 95% CI: (-0.39, 1.59) |
| Christensen, 2015[62](#_ENREF_62) -Continued |  |  |  |  | Weightloss, kg:  Follow-Up Time: 68 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.73 95% CI: (-5.37, -0.09)  Comparator: Arm 3 vs Arm 1 , MD : 1.99 95% CI: (-0.65, 4.63) |
| Claes, 2015[130](#_ENREF_130)  Study design: Single arm trial  Trial name: Osteoarthritis Chronic CAre Program (OACCP)  Study Location: Australia  Health care setting: Hospital-outpatient  Multiple Sites: 11 | Total n = 203  Arm 1, Mean Age: 67.3(9.7) BMI: 31.3(6.6)  Female: 64.5  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: VAS >=4/10 at initial assessment; waiting list for TKR or orthopaedic referral | VAS>=4/10 at recruitment visit  Pain associated with affected joint on most days of prior month | Exclusion : NR | Arm 1: Weight loss n = 203 Placebo/NA Dose: NA Frequency: NA Duration: 1 year Method of Blinding: NA Co-Intervention: NA | 6-minute walk test (m):  Follow-Up Time: 12 weeks : Comparator: post-pre , MD : 36.70 95% CI: (27.2, 46.2)  Follow-Up Time: 26 weeks : Comparator: post-pre , MD : 44.00 95% CI: (31.5, 56.5)  BMI:  Follow-Up Time: 12 weeks : Comparator: pre-post , MD : 0.50 95% CI: (0.3, 0.7)  Follow-Up Time: 26 weeks : Comparator: pre-post , MD : 0.80 95% CI: (0.5, 1.1)  KOOS pain:  Follow-Up Time: 12 weeks : Comparator: post-pre , MD : 5.00 95% CI: (2.0, 7.9)  Follow-Up Time: 26 weeks : Comparator: post-pre , MD : 5.60 95% CI: (1.6, 9.6)  TUG (s):  Follow-Up Time: 12 weeks : Comparator: pre-post , MD : 1.40 95% CI: (1.1, 1.7)  Follow-Up Time: 26 weeks : Comparator: pre-post , MD : 2.00 95% CI: (1.4, 2.6)  VAS pain:  Follow-Up Time: 12 weeks : Comparator: pre-post , MD : 1.00 95% CI: (0.7, 1.3)  Follow-Up Time: 26 weeks : Comparator: pre-post , MD : 0.90 95% CI: (0.4, 1.4) |
| Claes, 2015[130](#_ENREF_130) -Continued |  |  |  |  | Weight (kg):  Follow-Up Time: 12 weeks : Comparator: pre-post , MD : 1.40 95% CI: (0.8, 2.0)  Follow-Up Time: 26 weeks : Comparator: pre-post , MD : 2.10 95% CI: (1.2, 3.0) |
| Coleman, 2012[133](#_ENREF_133)  Study design: RCT  Trial name: Osteoarthritis of the Knee Self Management Program  Study Location: Australia  Health care setting: Community venue  Site size: NR | Total n = 146  Total # of knees = NR  Mean Age(SD): 65 (SD 8)  Arm 1, Mean Age: 65 (SD 8.7) BMI: NR Arm 2, Mean Age: 65 (SD 7.9) BMI: NR  Female: 74.7%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: X-ray or clinical diagnosis of OA  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 18  English-speaking  Referral from general practitioner or specialist  Able to meet program requirements  NR: X-ray or clinical diagnosis of OA | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Coexisting inflammatory arthritis  Serious comorbidity  Knee replacement scheduled in < 6 months  Cannot meet program time points | Arm 1: Control group n = 75 Placebo/Control Dose: NA Frequency: NA Duration: 6 weeks Method of Blinding: Patients were not blind, physiotherapists performing the assessments were blind to group allocation Co-Intervention: NR  Arm 2: Self-management program n = 71 Dose: 2.5 hours Frequency: Once per week Duration: 6 weeks Method of Blinding: Patients were not blind, physiotherapists performing the assessments were blind to group allocation Co-Intervention: NR | SF-36 body pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -6.00 95% CI: (-11.96, -0.04)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.20 95% CI: (-12.47, -1.93)  SF-36 physical function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -5.70 95% CI: (-10.97, -0.43)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.60 95% CI: (-9.48, -1.72)  TUG (s):  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-1.55, -0.45)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-1.55, -0.45)  WOMAC function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-6.14, -0.86)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.30 95% CI: (-7.24, -3.36)  WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.43, 0.23)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-2.33, -0.67)  WOMAC total:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -4.10 95% CI: (-7.43, -0.77) |
| Coleman, 2012[133](#_ENREF_133) -Continued |  |  |  |  | Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.20 95% CI: (-9.97, -4.43)  Number with MCII SF36 pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.81 95% CI: (0.54, 1.21)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.73 95% CI: (0.43, 1.24)  Number with MCII SF36 physical function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.73 95% CI: (0.52, 1.02)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.57 95% CI: (0.38, 0.84)  Number with MCII TUG:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.68 95% CI: (0.47, 0.99)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.32 95% CI: (0.20, 0.52)  Number with MCII VAS Pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.20 95% CI: (0.08, 0.49)  Number with MCII WOMAC physical function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.56 95% CI: (0.33, 0.95)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.24 95% CI: (0.11, 0.51) |
| Cortes, 2014[118](#_ENREF_118)  Study design: RCT  Trial name: None  Study Location: Spain  Health care setting: NR  Site size: NR | Total n = 18  Total # of knees = NR  Age Range: 67-91  Arm 1, Mean Age: NR BMI: NR  Female: NR  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: Radiologic evidence and/or clinical signs of knee OA  Analgesic Use: Yes, No changes in drug administration, including NSAIDs, during the study | Able to sign Consent  Knee pain most days within the last month  Disabling knee pain during at least one of the following activities: going down stairs or upstairs; walking at a pace of 0.4 km; and standing up or sitting down on the toilet or bed  No changes in drug administration, including NSAIDs, during the study | Concomitant medical problems that prevent participation  Surgery knee limb in prior 12 month(s)  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 6 month(s)  Rheumatoid arthritis or other inflammatory joint disease  Intra-articular injection within the last 6 months  Cognitive impairment that may bias the research | Arm 1: Control n = 9 Placebo/Control Dose: NA Frequency: NA Duration: 6 weeks Method of Blinding:  Arm 2: Massage | TUG (s):  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : 3.94 95% CI: (-4.01, 11.89)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : 2.84 95% CI: (-4.61, 10.29)  VAS pain:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : 3.10 95% CI: (0.76, 5.44)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : 2.28 95% CI: (0.44, 4.12)  WOMAC total:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : 21.42 95% CI: (9.79, 33.05)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : 14.04 95% CI: (4.71, 23.37) |
| da Silva, 2015[58](#_ENREF_58)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Physical therapy outpatient clinic  Single Site | Total n = 30  Mean Age: 59  Arm 1, Mean Age: 60 ± 7.76 BMI: 29.29 ± 5.00 Arm 2, Mean Age: 57 ± 6.01 BMI: 29.37 ± 4.10  Female: 87%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: Lequesne, ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 18  Pain within the past year; on most days for at least 3 months  Stable doses of NSAIDs  ACR: NA  Lequesne Index: 5-13 | Concomitant medical problems that prevent participation  Prior experience with the intervention of interest  Other cause of pain in the lower limb  Refusal to continue  Two consecutive or 3 non-consecutive absences | Arm 1: Control n = 15 Duration: 8 weeks Co-Intervention: Pre-randomization self-management program  Arm 2: Land-based exercise program n = 15 Dose: 45 minutes per session Frequency: 2 sessions per week Duration: 8 weeks Co-Intervention: Pre-randomization self-management program plus weekly educational sessions | 6 min walk:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -50.40 95% CI: (-94.26, -6.54)  Lequesne Index Function:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.83 95% CI: (-1.84, 0.18)  SF-36 bodily pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -14.80 95% CI: (-27.39, -2.21)  SF-36 physical function:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -14.00 95% CI: (-26.24, -1.76)  SF-36 role physical:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -53.33 95% CI: (-76.10, -30.56)  TUG (s):  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.05 95% CI: (-3.12, -0.98) |
| de Rooij, 2016[66](#_ENREF_66)  Study design: RCT  Trial name: None  Study Location: Netherlands  Health care setting: Secondary outpatient rehabilitation center  Single Site | Total n = 126  Arm 1, Mean Age: 63.9 (12.4) BMI: 35 (7.6) Arm 2, Mean Age: 63.2 (8.4) BMI: 36 (6.8)  Female: 77% T, 73% C  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 19%, unilateral 81%  Subtype: NR  Diagnosis: K-L: 0-IV, ACR  Analgesic Use: Yes, 79.4% T/76.2% C use pain meds | Diagnosis of osteoarthritis of the knee  Presence of coronary disease, HF, type 2 diabetes, COPD, or obesity,  Primary treatment goal related to OAK  ACR: diagnosis of OAK | Concomitant medical problems that prevent participation  Pending surgery  Prior experience with the intervention of interest  Insufficient knowledge of Dutch  Psych distress necessitating treatment  Dementia; MMSE>25  Expected to be lost at follow up (i.e. moving)  Refusal to sign informed consent | Arm 1: Usual care / waitlist n = 63 Placebo/Usual care / waitlist Duration: 32 weeks on waitlist  Arm 2: Exercise therapy n = 63 Dose: 30-60 min Frequency: Twice a week Duration: 20 weeks | 6MWT:  Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : -17.20 95% CI: (-56.64, 22.24)  Follow-Up Time: 20 weeks : Comparator: Arm 2 vs Arm 1 , MD : -31.50 95% CI: (-71.82, 8.82)  Follow-Up Time: 32 weeks : Comparator: Arm 2 vs Arm 1 , MD : -42.30 95% CI: (-82.63, -1.97)  NRS pain:  Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.40 95% CI: (-1.17, 0.37)  Follow-Up Time: 20 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-2.26, -0.74)  Follow-Up Time: 32 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-2.26, -0.74)  SF-36 physical health:  Follow-Up Time: 20 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.90 95% CI: (-3.62, -0.18)  Follow-Up Time: 32 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.50 95% CI: (-4.26, -0.74)  TUG:  Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.90 95% CI: (-2.32, 0.52)  Follow-Up Time: 20 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.10 95% CI: (-2.57, 0.37)  Follow-Up Time: 32 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.40 95% CI: (-2.69, -0.11) |
| de Rooij, 2016[66](#_ENREF_66) -Continued |  |  |  |  | WOMAC function:  Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.50 95% CI: (-6.67, 1.67)  Follow-Up Time: 20 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.10 95% CI: (-9.81, -0.39)  Follow-Up Time: 32 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.90 95% CI: (-12.78, -3.02)  WOMAC pain:  Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.70 95% CI: (-1.92, 0.52)  Follow-Up Time: 20 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.90 95% CI: (-3.28, -0.52)  Follow-Up Time: 32 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-3.37, -0.63) |
| Dundar, 2015[91](#_ENREF_91)  Study design: RCT  Trial name: None  Study Location: Turkey  Health care setting: Academic Physical Medicine and Rehabilitation Department  Single Site | Total n = 40  Total # of knees = NR  Age Range: NR  Arm 1, Mean Age: 57.6 BMI: 31.2 Arm 2, Mean Age: 56.8 BMI: 31.7  Female: 72.5%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: bilateral 100%  Subtype: NR  Diagnosis: K-L: 2&3, Bilateral knee OA diagnosis according to ACR criteria  Analgesic Use: Yes, Patients were not allowed to change the dosage of their routine pain medication or begin a new pain medication during the study. | Inclusion : NR | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 6 month(s)  Pregnant  Not allowed to change dosage of their routine pain medication  Not allowed to begin new pain medication | Arm 1: Sham Procedure n = 20 Placebo/Sham Procedure Dose: NR Frequency: 5 times per week Duration: 4 weeks Method of Blinding: The WOMAC questionnaire and VAS for pain were performed by a physiatrist who was blind to the patient’s treatment protocol. Another clinician blinded to the patient’s clinical and treatment data, performed the ultrasound. Co-Intervention: Both groups received 20 sessions (5 sessions in a week, each lasting 60 min) of physical therapy, including hot pack, ultrasound, TENS and isometric knee exercise  Arm 2: Neuromuscular electrical stimulation n = 20 Dose: frequency of 50Hz, intensity 100 microT for 20 minutes Frequency: 5 times per week Duration: 4 weeks Method of Blinding: The WOMAC questionnaire and VAS for pain were performed by a physiatrist who was blind to the patient’s treatment protocol. Another clinician blinded to the patient’s clinical and treatment data, performed the ultrasound. Co-Intervention: Both groups received 20 sessions (5 sessions in a week, each lasting 60 min) of physical therapy, including hot pack, ultrasound, TENS and isometric knee exercise | Total WOMAC:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 7.00 95% CI: (NC, NC)  VAS pain:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-15.49, 15.49)  WOMAC pain:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 7.00 95% CI: (NC, NC) |
| Dwyer, 2015[120](#_ENREF_120)  Study design: RCT  Trial name: None  Study Location: US, South Africa  Health care setting: Chiropractic university-based outpatient teaching clinics  Multiple Sites: 2 | Total n = 78  Total # of knees = 85  Age Range: 38-80  Arm 1, Mean Age: 60.9 (10.3) BMI: 28.6 (5.2) Arm 2, Mean Age: 63.5 (10.9) BMI: 28.6 (5.2) Arm 3, Mean Age: 62.2 (11.8) BMI: 30.6 (7.6)  Female: 63  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 91%, unilateral 9%  Subtype: NR  Diagnosis: K-L: 0-3,  of three clinical criteria involving knee pain, crepitus, morning stiffness, and bony enlargement  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >=1 year  Minimum Age: 38  Maximum Age:79  Ambulatory  K-L: 0-3  1 of three clinical criteria involving knee pain, crepitus, morning stiffness, and bony enlargement: 1 of 3 criteria | Surgery knee limb in prior 6 month(s)  Prior experience with the intervention of interest  >=720/2400 on WOMAC | Arm 1: Rehabilitation n = 26 Placebo/Usual care Dose: 20 min Frequency: 6 times Duration: 4 weeks Method of Blinding: Unblinded  Arm 2: Manual and manipulative therapy (MMT) n = 26 Dose: 20 minutes Frequency: 12 times Duration: 4 weeks Method of Blinding: Unblinded  Arm 3: Rehabilitation + Manual and manipulative therapy (MMT) n = 26 Dose: 20-40 minutes Frequency: 6 session ß- 3 with extra training Duration: 4 weeks Method of Blinding: Unblinded Co-Intervention: Rehab or MMT | WOMAC function:  Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -22.00 95% CI: (-162.58, 118.58)  Comparator: Arm 3 vs Arm 1 , MD : -32.80 95% CI: (-191.40, 125.80)  WOMAC pain:  Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -26.90 95% CI: (-68.88, 15.08)  Comparator: Arm 3 vs Arm 1 , MD : -31.50 95% CI: (-72.40, 9.40)  WOMAC total:  Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -80.50 95% CI: (-281.64, 120.64)  Comparator: Arm 3 vs Arm 1 , MD : -63.20 95% CI: (-273.72, 147.32) |
| Elboim-Gabyzon, 2013[85](#_ENREF_85)  Study design: RCT  Trial name: None  Study Location: Israel  Health care setting: Physical therapy outpatient clinic  Single Site | Total n = 63  Mean Age(SD): 68.9 (SD 7.7)  Arm 1, Mean Age: NR BMI: NR Arm 2, Mean Age: NR BMI: NR  Female: 82.5%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: >=2, Diagnosis of idiopathic knee OA  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: Knee pain at least 3 months, with pain presenting at least three days a week during the last month  Minimum Age: 51  Ambulatory  Ability to follow instructions  K-L: >=2  ACR: Compliance with the classification of ACR  NR: Diagnosis of idiopathic knee OA | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 6 month(s)  Existence of a pacemaker  History of cardiovascular, neurological or orthopedic problems that could affect functional performance or previous knee surgery other than arthroscopy  Inability to tolerate electrical stimulation at a level of current sufficient to elicit full knee extension  Change in pain medication in the previous month  Injections to the knee joint during the previous six months | Arm 1: Control n = 30, Placebo/Control, Dose: NA, Frequency: NA, Duration: NA Method of Blinding: Assessor was blind to treatment allocation only at the initial assessment. Physical therapists leading group exercise program were familiar with the study protocol were not aware of treatment allocation. Co-Intervention: Group exercise program consisting of 12 45-minute sessions, biweekly for six weeks, with 6–8 subjects in each group led by one of 3 physical therapists. To be included in final analysis, subjects had to complete the 12 sessions within 8 weeks. The program included: range of motion exercises; knee and lower extremity muscle-strengthening exercises; functional activities; and balance training. Sessions also included patient education on self-management; activity and exercise planning, and discussion of pain-coping strategies.  Arm 2: Neuromuscular electrical stimulation n = 33, Dose: 75 Hz frequency; 2s ramp-up time; 10s on time; 2s off time; amplitude to tolerance (max 100mA); 10 contractions, Frequency: Biweekly, Duration: 6 weeks Method of Blinding: Assessor was blind to treatment allocation only at the initial assessment. Physical therapists leading group exercise program were familiar with the study protocol were not aware of treatment allocation. Co-Intervention: Group exercise program consisting of 12 45-minute sessions, biweekly for six weeks, with 6–8 subjects in each group led by one of 3 physical therapists. To be included in final analysis, subjects had to complete the 12 sessions within 8 weeks. | TUG (s):  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (-1.60, 2.00)  VAS pain:  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.70 95% CI: (-2.98, -0.42)  WOMAC total:  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -23.20 95% CI: (-49.20, 2.80) |
| Elboim-Gabyzon, 2013[85](#_ENREF_85) -Continued |  |  |  | The program included: range of motion exercises; knee and lower extremity muscle-strengthening exercises; functional activities; and balance training. Sessions also included patient education on self-management; activity and exercise planning, and discussion of pain-coping strategies. |  |
| Erhart, 2010[113](#_ENREF_113)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: NR  Site size: NR | Total n = 79  Total # of knees = NR  Age Range: >=60.2  Arm 1, Mean Age: 62.1 BMI: 27.4 Arm 2, Mean Age: 61.4 BMI: 27.6  Female: 51.39%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: Medial 100%  Diagnosis: Osteoarthritic changes based on MRI (cartilage thinning and/or osteophytes)  Analgesic Use: NR | Minimum Age: 40  Maximum Age:79  Ambulatory  Able to sign Consent | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Concomitant or prior use of other meds  Prior acute injury to the knee  BMI >35 kg/m2  Use of shoe insert or hinged knee brace  Narcotic pain medication use  Intraarticular joint injection in previous 2 months  Nerve or muscle disease associated with walking difficulty, Gout or recurrent pseudogout, and Diagnosed or symptomatic osteoarthritis in other lower extremity joints, and Serious injury to foot, ankle, back, or hips | Arm 1: Control n = 26 Placebo/Control shoes Dose: NA Frequency: Suggested minimum wear time 4hr/day, average monthly reports 7.9-9.5h/day Duration: 6 months Method of Blinding: Subjects were blinded to the shoe type, researcher was not blinded Co-Intervention: NR  Arm 2: Variable-stiffness shoes n = 34 Dose: NA Frequency: Suggested minimum wear time 4hr/day, average monthly reports 6.9-8.0h/day Duration: 6 months Method of Blinding: Subjects were blinded to the shoe type, researcher was not blinded Co-Intervention: NR | WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.70 95% CI: (-10.08, 2.68)  WOMAC total:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -10.00 95% CI: (-36.46, 16.46)  Clinically significant on WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.49 95% CI: (0.31, 0.79) |
| Erhart-Hledik, 2012[114](#_ENREF_114)  Study design: RCT  Trial name: None  Study Location: NR  Health care setting: NR  Site size: NR | Total n = 79  Total # of knees = NR  Mean Age(SD): 60.2 (SD 9.8)  Arm 1, Mean Age: 61.0 (SD 12.0) BMI: NR Arm 2, Mean Age: 57.3 (SD 8.5) BMI: NR  Female: 46.8%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: Medial 100%  Diagnosis: Symptomatic medial compartment knee OA, osteoarthritic changes based on MRI/radiograph  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: Persistent medial compartment knee joint pain  Minimum Age: 40  Maximum Age:80  Ambulatory  Able to sign Consent  NR: Symptomatic medial compartment knee OA  NR: Osteoarthritic changes based on MRI/radiograph | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Concomitant or prior use of other meds  Injected hyaluronic acid in the past or during the past 2 month(s)  Injected corticosteroids in the prior 2 month(s)  Prior acute injury to the knee  BMI > 35 kg/m2  Total knee replacement  Intraarticular joint injection in previous 2 months  Use of shoe insert or hinged knee brace or narcotic pain medication  Nerve or muscle disease associated with walking difficulty; serious injury to foot, ankle, back, or hips; gout or recurrent pseudogout; or OA in other lower extremity joint | Arm 1: Control n = 39 Placebo/Control, constant-stiffness shoe Dose: Instructed to use their assigned shoes as their main walking shoes, a minimum 4 h of wear per day Frequency: Daily Duration: 12 months Method of Blinding: Patients were blinded to their shoe type. The researcher performing the gait analysis was not blinded to shoe type. Co-Intervention: NR  Arm 2: Orthotics/shoes n = 40 Dose: Instructed to use their assigned shoes as their main walking shoes, a minimum 4 h of wear per day Frequency: Daily Duration: 12 months Method of Blinding: Patients were blinded to their shoe type. The researcher performing the gait analysis was not blinded to shoe type. Co-Intervention: NR | WOMAC pain:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (NC, NC) |
| Fioravanti, 2012[72](#_ENREF_72)  Study design: RCT  Trial name: None  Study Location: Italy  Health care setting: Academic rheumatology clinic/department, health spa  Single Site | Total n = 60  Mean Age: 70.5  Arm 1, Mean Age: 72.45±7.14 BMI: 26.53±4 Arm 2, Mean Age: 69.33±7.63 BMI: 27.52±3  Female: 50%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 100%  Subtype: NR  Diagnosis: ACR  Analgesic Use: Yes, Patients in both groups were advised to continue their established pharmacological and non-pharmacological treatments, with the exception of analgesic drugs (500 mg acetaminophen tablets) and NSAIDs (150 mg Diclofenac tablets, 20 mg Piroxicam tablets, 750 mg Naproxen tablets, 200 mg Aceclofenac), which were to be consumed as required and noted daily in a diary. | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >+3 months  Minimum Age: 50  Maximum Age:75  ACR: NA  VAS: >30mm  K-L: 1-3 | Concomitant medical problems that prevent participation  Injected hyaluronic acid in the past or during the past 6 months month(s)  Injected corticosteroids in the prior 3 months month(s)  Physical Therapy or Rehab or exercise in the previous thermal treatments in the previous 6 months month(s)  Severe comorbidity of the heart, lungs, liver, cerebrum or kidney, varices, systemic blood disease, neoplasm  Acute illness  Type 1 diabetes  Pregnancy or nursing  Arthroscopy with or without joint lavage in the previous 6 months, chondroprotective agents in the previous 6 months | Arm 1: Control n = 30 Duration: NA  Arm 2: Balneotherapy n = 30 Dose: 20 minutes per treatment Frequency: 12 treatments per 2 weeks Duration: 2 weeks | Lequesne index:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -7.50 95% CI: (-9.57, -5.43)  SF-36 mental component:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -17.00 95% CI: (-25.14, -8.86)  SF-36 physical component:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -32.60 95% CI: (-49.62, -15.58)  VAS pain:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -42.50 95% CI: (-53.67, -31.33)  WOMAC total function score:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -37.47 95% CI: (-46.61, -28.33)  WOMAC total pain score:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -25.70 95% CI: (-34.06, -17.34) |
| Fioravanti, 2015[75](#_ENREF_75)  Study design: RCT  Trial name: None  Study Location: Italy  Health care setting: Spa resort  Single Site | Total n = 103  Age Range: 40-80  Arm 1, Mean Age: 69.66 (11.1) BMI: 28.01 (4.18) Arm 2, Mean Age: 68.49 (9.01) BMI: 28.58 (4.01)  Female: 72  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 100%  Subtype: NR  Diagnosis: K-L: 1-3, ACR  Analgesic Use: Yes, Allowed but washout of concomitant acetaminophen or NSAIDs was required for an entire week before randomization and 24 h before every assessment. | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 6  Minimum Age: 40  Maximum Age:79  VAS: >=30mm in last 3 months  K-L: 1-3 | Concomitant medical problems that prevent participation  Injected hyaluronic acid in the past or during the past 3 month(s)  Injected corticosteroids in the prior 3 month(s)  Prior experience with the intervention of interest  Symptomatic Slow Acting Drugs for OA (SYSADOA) in last 3 months | Arm 1: Usual care n = 50 Duration: 2 weeks Method of Blinding: Unblinded  Arm 2: Mud-bath therapy n = 53 Dose: 35 minutes Frequency: 12 sessions Duration: 2 weeks Method of Blinding: Unblinded | EQ-5D:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -0.10 95% CI: (NC, NC)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.24 95% CI: (NC, NC)  EQ-5D-VAS:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -22.09 95% CI: (-31.75, -12.43)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -14.35 95% CI: (-24.01, -4.69)  SF-12 mental component:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 2.71 95% CI: (-6.95, 12.37)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 1.92 95% CI: (-7.74, 11.58)  SF-12 physical component:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -11.85 95% CI: (-21.51, -2.19)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -12.46 95% CI: (-22.12, -2.80)  VAS:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -10.00 95% CI: (-21.31, 1.31)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -15.00 95% CI: (-25.63, -4.37) |
| Fioravanti, 2015[75](#_ENREF_75) -Continued |  |  |  |  | WOMAC function:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -5.50 95% CI: (-10.81, -0.19)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -10.00 95% CI: (-15.00, -5.00) |
| Fitzgerald, 2011[55](#_ENREF_55)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: NR  Single Site | Total n = 183  Mean Age(SD): 64.5 (8.7)  Arm 1, Mean Age: 65 (8.6) BMI: 30 (6.1) Arm 2, Mean Age: 63.8 (8.9) BMI: 29.8 (6.3)  Female: 65%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Tibiofemoral  Diagnosis: K-L: >=2, ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 40  ACR: meet criteria for OAK  K-L: >=2 | Concomitant medical problems that prevent participation  Prior surgery on one or both knees | Arm 1: Strength training; agility training; aerobic exercise n = 84 Placebo/Control Dose: N/A Frequency: Twice a week Duration: 6 weeks Method of Blinding: Unblinded  Arm 2: Standard exercise + agility and perturbation training n = 75 Dose: N/A Frequency: Twice a week Duration: 6 weeks Method of Blinding: Unblinded | WOMAC physical function score:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.30 95% CI: (-3.59, 4.19)  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -2.40 95% CI: (-5.87, 1.07)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-7.32, 0.32)  WOMAC total:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.40 95% CI: (-4.98, 5.78)  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -3.00 95% CI: (-7.74, 1.74)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -4.50 95% CI: (-9.61, 0.61)  Get up and go test score (s):  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 1.40 95% CI: (-0.13, 2.93)  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-0.94, 0.34)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-0.75, 0.15)  Knee pain:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-0.89, 1.09)  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.38, 0.18)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.45, 0.25) |
| Fitzgerald, 2016[67](#_ENREF_67)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: Hospital-outpatient, Academic physical therapy department, private hospital and military hospital  Multiple Sites: 3 | Total n = 300  Age Range: >=40  Arm 1, Mean Age: 58.3 (10.0) BMI: 30.1 (6.5) Arm 2, Mean Age: 58.4 (8.7) BMI: 31.4 (7.2) Arm 3, Mean Age: 58 (9.8) BMI: 31.1 (5.7) Arm 4, Mean Age: 58.5 (9.4) BMI: 31.7 (5.6)  Female: 66%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 60%  Subtype: NR  Diagnosis: ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: >= 40 years  ACR: diagnosis of OAK | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Prior TKA  Prior total arthoplasty of any lower extremity joint  Have back or leg pain in other areas besides your knee that affects your ability to perform physical activities  History of neurological disorders that would affect lower extremity function (stroke, peripheral neuropathy, Parkinson's disease, multiple sclerosis) | Arm 1: Exercise therapy + no booster n = 75 Placebo/Usual care Dose: 45-60 min Frequency: 12 sessions Duration: 9 weeks Method of Blinding: Single-blind  Arm 2: Exercise therapy + booster n = 76 Dose: 45-60 min Frequency: Participants receiving booster sessions completed eight sessions in the first 9 weeks, two booster sessions at 5 months, and one booster session at 8 and 11 months. Duration: 11 months Method of Blinding: Single-blind Co-Intervention: Booster  Arm 3: Manual therapy + exercise therapy + no booster n = 75 Dose: 45-60 min Frequency: 9 sessions Duration: 12 weeks Method of Blinding: Single-blind Co-Intervention: Exercise therapy  Arm 4: Manual therapy + exercise therapy + booster n = 74 Dose: 45-60 min Frequency: Participants receiving booster sessions completed eight sessions in the first 9 weeks, two booster sessions at 5 months, and one booster session at 8 and 11 months. Duration: 11 months Method of Blinding: Single-blind Co-Intervention: Exercise therapy + booster | Knee pain rating:  Follow-Up Time: 1 year : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-0.78, -0.42)  Comparator: Arm 3 vs Arm 1 , MD : -0.20 95% CI: (-0.36, -0.04)  Comparator: Arm 4 vs Arm 1 , MD : -0.70 95% CI: (-0.90, -0.50)  Follow-Up Time: 9 week : Comparator: Arm 2 vs Arm 1 , MD : 0.60 95% CI: (0.42, 0.78)  Comparator: Arm 3 vs Arm 1 , MD : 0.10 95% CI: (-0.06, 0.26)  Comparator: Arm 4 vs Arm 1 , MD : 0.00 95% CI: (-0.20, 0.20)  TUG:  Follow-Up Time: 1 year : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-0.78, -0.42)  Comparator: Arm 3 vs Arm 1 , MD : -0.30 95% CI: (-0.46, -0.14)  Comparator: Arm 4 vs Arm 1 , MD : 0.00 95% CI: (-0.21, 0.21)  Follow-Up Time: 9 week : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-0.48, -0.12)  Comparator: Arm 3 vs Arm 1 , MD : -0.20 95% CI: (-0.36, -0.04)  Comparator: Arm 4 vs Arm 1 , MD : -0.30 95% CI: (-0.51, -0.09)  WOMAC total:  Follow-Up Time: 1 year : Comparator: Arm 2 vs Arm 1 , MD : -3.40 95% CI: (-7.74, 0.94)  Comparator: Arm 3 vs Arm 1 , MD : 2.00 95% CI: (-2.16, 6.16)  Comparator: Arm 4 vs Arm 1 , MD : -5.80 95% CI: (-10.76, -0.84)  Follow-Up Time: 9 week : Comparator: Arm 2 vs Arm 1 , MD : 6.60 95% CI: (2.26, 10.94)  Comparator: Arm 3 vs Arm 1 , MD : -4.50 95% CI: (-8.66, -0.34)  Comparator: Arm 4 vs Arm 1 , MD : -6.00 95% CI: (-10.96, -1.04) |
| Foroughi, 2011[52](#_ENREF_52)  Study design: RCT  Trial name: None  Study Location: Australia  Health care setting: NR  Single Site | Total n = 54  Age Range: >=40  Arm 1, Mean Age: 64 (8) BMI: 33.2 (8.1) Arm 2, Mean Age: 64 (7) BMI: 31.9 (5.2)  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Medial 74%, Lateral 26%  Diagnosis: ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: >40  ACR | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 6 month(s)  Prior acute injury to the knee  Secondary OA  Men | Arm 1: Sham exercise n = 28 Placebo/Sham Dose: approx.40 minutes ( ) Frequency: Daily Duration: 6 months Method of Blinding: Single-blinded  Arm 2: Progressive resistance training (PRT) n = 26 Dose: approx.60 minutes Frequency: Daily Duration: 6 months Method of Blinding: Single-blinded | WOMAC function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -7.49 95% CI: (-15.08, 0.10)  WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.67 95% CI: (-3.71, 0.37)  WOMAC total:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -10.40 95% CI: (-20.56, -0.24) |
| Fransen, 2014[31](#_ENREF_31)  Study design: RCT  Trial name: LEGS  Study Location: Australia  Health care setting: NR  Site size: NR | Total n = 605  Age Range: 45-75  Arm 1, Mean Age: 60.6 (8.1) BMI: 29.1 (5.8) Arm 2, Mean Age: 61.2 (7.7) BMI: 28.4 (4.7) Arm 3, Mean Age: 60.7 (8.4) BMI: 28.8 (6.0) Arm 4, Mean Age: 59.5 (8.0) BMI: 29.6 (5.4)  Female: 56%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Medial 100%  Diagnosis: K-L: <2  Analgesic Use: Yes, Not restricted | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 6 months  Pain >=4/10  Radiographs: Reduced joint space in medial tibial-femoral compartment but > 2mm | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Pending surgery  Injected hyaluronic acid in the past or during the past 3 month(s)  Injected corticosteroids in the prior 3 month(s)  Rheumatoid arthritis  Unstable diabetes  Allergy to shellfish  Bilateral knee replacement | Arm 1: Placebo n = 151 Placebo/Capsules Frequency: Once daily Duration: 2 years Method of Blinding: Double dummy  Arm 2: Glucosamine n = 152 Dose: 1500 mg Frequency: Once daily Duration: 2 years Method of Blinding: Double dummy  Arm 3: Glucosamine–chondroitin n = 151 Dose: 1500mg Glucosamine+ 800 mg Chondroitin Frequency: Once daily Duration: 2 years Method of Blinding: Double dummy  Arm 4: Chondroitin n = 151 Dose: 800 mg Frequency: Once daily Duration: 2 years Method of Blinding: Double dummy | SF-12 mental:  Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-3.99, 0.99)  Comparator: Arm 3 vs Arm 1 , MD : -3.00 95% CI: (-5.19, -0.81)  Comparator: Arm 4 vs Arm 1 , MD : -2.00 95% CI: (-4.45, 0.45)  SF-12 physical:  Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : 0.30 95% CI: (-2.04, 2.64)  Comparator: Arm 3 vs Arm 1 , MD : 1.60 95% CI: (-0.83, 4.03)  Comparator: Arm 4 vs Arm 1 , MD : 0.10 95% CI: (-2.27, 2.47)  WOMAC function:  Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-3.23, 3.23)  Comparator: Arm 3 vs Arm 1 , MD : 0.00 95% CI: (-3.29, 3.29)  Comparator: Arm 4 vs Arm 1 , MD : -0.40 95% CI: (-3.62, 2.82)  WOMAC pain:  Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : -0.10 95% CI: (-0.98, 0.78)  Comparator: Arm 3 vs Arm 1 , MD : 0.10 95% CI: (-0.79, 0.99)  Comparator: Arm 4 vs Arm 1 , MD : -0.20 95% CI: (-1.08, 0.68)  Pain:  Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : -0.17 95% CI: (-0.80, 0.46)  Comparator: Arm 3 vs Arm 1 , MD : -0.45 95% CI: (-1.09, 0.19)  Comparator: Arm 4 vs Arm 1 , MD : -0.27 95% CI: (-0.92, 0.38) |
| Ghroubi, 2008[123](#_ENREF_123)  Study design: RCT  Trial name: None  Study Location: Tunisia  Health care setting: Physical therapy outpatient clinic  Single Site | Total n = 56  Mean Age: 41  Arm 1, Mean Age: 42.4(9.8) BMI: 39.2 (3.7) Arm 2, Mean Age: 39.8(13.1) BMI: 37.1(5.7) Arm 3, Mean Age: 41.4(3.9) BMI: 37.45(3.68) Arm 4, Mean Age: 41.5(11.7) BMI: 38.74(6.15)  Female: NR  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: K-L: mean 2.25, Mild to moderate  Analgesic Use: Yes, Patients who changed their medication use during the study were excluded. | Diagnosis of osteoarthritis of the knee  Minimum Age: 18  BMI>=35 or 30-35 with at least one chronic health risk factor  Pain in the knee several days per week and having functional difficulties due to the OA, such as walking>1km, climbing stairs, housework, doing errands, lifting heavy load  K-L: I=III | Prior surgery on one or both knees  Prior acute injury to the knee  An orthopedic problem that would prevent walking on a treadmill  Treatment for another form of arthritis  Contraindication to exercising  Precursors to CVD or prior recent MI  Serious psychiatric disorders | Arm 1: Control n = 14 Placebo/No diet or exercise Dose: NA Frequency: NA Duration: 2 months  Arm 2: Land-based exercise n = 13 Dose: 60 minutes aerobic and strength training per session Frequency: 3 sessions per week Duration: 2 months  Arm 3: Diet and exercise n = 15 Dose: 60 minutes per session Frequency: 3 sessions per week Duration: 2 months  Arm 4: Diet only n = 14 Dose: NA Frequency: NA Duration: 2 months | 6 min walk:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -39.00 95% CI: (-46.47, -31.53)  Comparator: Arm 3 vs Arm 1 , MD : -53.00 95% CI: (-59.33, -46.67)  Comparator: Arm 4 vs Arm 1 , MD : 2.00 95% CI: (-6.51, 10.51)  Lequesne Index:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.41 95% CI: (-3.52, -1.30)  Comparator: Arm 3 vs Arm 1 , MD : -3.73 95% CI: (-4.65, -2.81)  Comparator: Arm 4 vs Arm 1 , MD : -2.23 95% CI: (-3.30, -1.16)  VAS:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.90 95% CI: (-4.52, -1.28)  Comparator: Arm 3 vs Arm 1 , MD : -4.56 95% CI: (-5.82, -3.30)  Comparator: Arm 4 vs Arm 1 , MD : -2.10 95% CI: (-3.32, -0.88)  WOMAC function:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.09 95% CI: (-4.46, -1.72)  Comparator: Arm 3 vs Arm 1 , MD : -4.01 95% CI: (-5.56, -2.46)  Comparator: Arm 4 vs Arm 1 , MD : -2.34 95% CI: (-3.71, -0.97)  Number with significant improvement in WOMAC:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.23 95% CI: (0.02, 2.23)  Comparator: Arm 3 vs Arm 1 , RR : 0.16 95% CI: (0.02, 1.39)  Comparator: Arm 4 vs Arm 1 , RR : 0.33 95% CI: (0.03, 3.43) |
| Gormeli, 2015[24](#_ENREF_24)  Study design: RCT  Trial name: None  Study Location: Turkey  Health care setting: NR  Site size: NR | Total n = 182  Age Range: 53.5  Arm 1, Mean Age: 52.8 (12.8) BMI: 29.5 (3.2) Arm 2, Mean Age: 53.8 (13.4) BMI: 28.4 (4.4) Arm 3, Mean Age: 53.7 (13.1) BMI: 28.7 (4.8) Arm 4, Mean Age: 53.5 (14) BMI: 29.7 (3.7)  Female: 55.6%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: Tibiofemoral 100%  Diagnosis: K-L: 1-4  Analgesic Use: Yes, Paracetamol was prescribed for discomfort. | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: > 4 months  K-L: 1-4 | Surgery knee limb in prior month(s)  Systemic disorders (diabetes, rheumatic diseases, severe cardiovascular diseases, haematological diseases, infections)  Generalized OA,  Undergoing anticoagulant or antiaggregant therapy  Use of NSAIDs in the 5 days before injection  Hemoglobin values < 11 g/dL and platelet values < 150,000/mm3 | Arm 1: Control n = 40 Frequency: One time treatment  Arm 2: PRP1 n = 44 Frequency: One time treatment  Arm 3: PRP3 n = 39 Frequency: One time treatment  Arm 4: HA n = 39 Frequency: One time treatment | EQ-VAS:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 14.00 95% CI: (11.56, 16.44)  Comparator: Arm 3 vs Arm 1 , MD : 23.40 95% CI: (19.66, 27.14)  Comparator: Arm 4 vs Arm 1 , MD : 12.80 95% CI: (10.04, 15.56)  EuroQol-VAS:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -14.00 95% CI: (-16.44, -11.56)  Comparator: Arm 3 vs Arm 1 , MD : -23.40 95% CI: (-27.14, -19.66)  Comparator: Arm 4 vs Arm 1 , MD : -12.80 95% CI: (-15.56, -10.04) |
| Gschiel, 2010[86](#_ENREF_86)  Study design: RCT  Trial name: None  Study Location: Germany  Health care setting: Academic pain clinic  Single Site | Total n = 45  Mean Age: 58  Arm 1, Mean Age: 57.7(3.5) BMI: 29.6 Arm 2, Mean Age: 58.4(2.4) BMI: 27  Female: 75%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: NR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 18  Maximum Age:79  Body weight 50-100kg  Chronic pain (at least 4/11 NRS)  radiologically verified diagnosis: NR | Concomitant medical problems that prevent participation  Prior experience with the intervention of interest  CVD  Permanent pacemaker  Neurologic disease  Inflammatory joint disease  Cancer | Arm 1: Placebo n = 20 Dose: 30 minutes per treatment session Frequency: two sessions per day Duration: 3 weeks  Arm 2: TENS n = 25 Dose: 30 minutes per treatment session Frequency: two sessions per day Duration: 3 weeks | WOMAC Pain:  Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (-2.85, 0.85)  WOMAC total:  Follow-Up Time: 5 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.20 95% CI: (-18.43, 10.03) |
| Hatef, 2014[105](#_ENREF_105)  Study design: RCT  Trial name: None  Study Location: Iran  Health care setting: NR  Site size: NR | Total n = 150  Arm 1, Mean Age: 48.6 (10) at end line Arm 2, Mean Age: 48.21 (12) at end line  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: Medial 100%, Tibiofemoral 100%  Diagnosis: Mild-to-moderate, ACR  Analgesic Use: Yes, Unrestricted? Not detailed | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: Pain on a daily basis for at least 1 month during the previous 3 months  K-L: >2  Clinical diagnosis: Medial femoro-tibial OA | Concomitant medical problems that prevent participation  Injected corticosteroids in the prior 1 month(s)  Knee joint lavage within the previous 3 months  Tibial osteotomy within the previous 5 years  Drug treatment for OA within the previous week  Greater or similar reduction in lateral than medial femoro-tibial joint space width  Secondary knee or hip OA | Arm 1: Neutral insoles n = 75 Placebo/Sham Duration: 2 months Method of Blinding: Double-blinded  Arm 2: Lateral wedged insoles n = 75 Duration: 2 months Method of Blinding: Double-blinded | VAS:  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -23.05 95% CI: (-28.34, -17.76)  VAS - number pain mild (21-40):  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , RR : 0.13 95% CI: (0.05, 0.36)  VAS - number pain none to scant (0-20):  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , RR : 0.23 95% CI: (0.03, 2.03) |
| Henriksen, 2014[56](#_ENREF_56)  Study design: RCT  Trial name: None  Study Location: Denmark  Health care setting: Hospital-outpatient  Single Site | Total n = 60  Age Range: >=40  Arm 1, Mean Age: 62.3 (7.1) BMI: 28.2 (4.6) Arm 2, Mean Age: 65 (8.9) BMI: 28.9 (4.1)  Female: 80%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Tibiofemoral 100%  Diagnosis: Diagnosis of tibiofemoral OA confirmed by radiography  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: >=40  Body mass index between 20 and 35  clinical diagnosis of tibiofemoral OA confirmed by radiography | Concomitant medical problems that prevent participation  Physical Therapy or Rehab or exercise in the previous 3 month(s)  Systemic inflammatory and autoimmune disease  Significant cardiovascular, neurologic, or psychiatric disease, cervical or lumbar nerve root compression syndromes, and wide spread or regional pain syndromes (e.g., fibromyalgia)  Lower extremity joint replacement | Arm 1: Control n = 23 Placebo/Control Duration: 12 weeks  Arm 2: Exercise therapy n = 25 Dose: 1 hour Frequency: 3 times a week Duration: 12 weeks | KOOS function:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.80 95% CI: (-9.02, 3.42)  KOOS pain:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -6.80 95% CI: (-12.18, -1.42)  KOOS quality of life:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -6.10 95% CI: (-14.16, 1.96) |
| Herrero-Beaumont, 2016[32](#_ENREF_32)  Study design: RCT  Trial name: None  Study Location: Spain  Health care setting: Academic orthopedic surgery clinic/department, Academic rheumatology clinic/department  Multiple Sites: 9 | Total n = 158  Arm 1, Mean Age: 65 (8) BMI: 28.5 (3.4) Arm 2, Mean Age: 67 (8) BMI: 27.9 (3.2)  Female: 85% T, 81% C  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2&3, ACR  Analgesic Use: Yes, Another confounding factor is the analgesic effect due to pain killer rescue medication allowed in all OA clinical trials. | Diagnosis of osteoarthritis of the knee  Were required to complain of moderate-severe pain as defined by a score of 40 80 mm in Visual Analog Scale (VAS)  ACR: primary symptomatic OAK  K-L: 2&3 | Concomitant medical problems that prevent participation  . Exclusion criteria included obesity [body mass index (BMI) \_ 35 kg/m2], concurrent arthritic conditions, or any coexisting disease that could preclude successful completion of the stud | Arm 1: Chondroitin sulfate + glucosamine sulfate n = 80 Placebo/Placebo Dose: 1200mg CS + 1500mg GS Frequency: Once daily Duration: 6 months Method of Blinding: Double blind  Arm 2: Placebo n = 78 Frequency: Once daily Duration: 6 months Method of Blinding: Double blind | VAS pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 8.70 95% CI: (7.95, 9.45)  WOMAC function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 5.30 95% CI: (4.68, 5.92)  WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 6.90 95% CI: (6.21, 7.59)  WOMAC total:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 5.90 95% CI: (5.28, 6.52) |
| Hochberg, 2008[134](#_ENREF_134)  Study design: RCT  Trial name: GAIT  Study Location: US  Health care setting: Academic rheumatology clinic/department  Multiple Sites: 16 | Total n = 1583  Total # of knees = NR  Age Range: NR  Arm 1, Mean Age: 58(10) BMI: 31.9(7.3) Arm 2, Mean Age: 59(10) BMI: 31.8(6.8) Arm 3, Mean Age: 58(10) BMI: 32.0(7.6) Arm 4, Mean Age: 59(11) BMI: 31.5(6.6) Arm 5, Mean Age: 59(11) BMI: 31.5(7.1)  Female: 64%  Racial/Ethnic Distribution: African American 14%, Asian NR, Caucasian 78%, NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2&3, WOMAC pain scores 125-400 out of 500, Functional class I, II, or III  Analgesic Use: Yes, Patients were allowed to take up to 4000 mg of acetaminophen (Tylenol, McNeil) daily, except during the 24 hours before a clinical evaluation for joint pain. Otheranalgesics, including narcotics and NSAIDs, were not permitted. | Diagnosis of osteoarthritis of the knee  Minimum Age: 40  Ambulatory  Knee pain for at least six months and on the majority of days during the preceding month  K-L: 2&3  ACR: 1, II, or III  WOMAC: 125-400mm | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Prior acute injury to the knee  Concurrent medical or arthritic conditions that could confound evaluation of the index joint  Concurrent use of analgesics other than acetominophen, including NSAIDs or narcotics  Predominant patellofemoral disease  A history of clinically significant trauma or surgery to the index knee | Arm 1: Placebo n = 313 Dose: NA (not applicable) Frequency: 3 times a day Duration: 24 weeks Method of Blinding: NR  Arm 2: Glucosamine n = 317 Dose: 500mg Frequency: three times a day Duration: 24 weeks Method of Blinding: NA  Arm 3: Chondroitin sulfate n = 318 Dose: 400 mg Frequency: three times a day Duration: 24 weeks Method of Blinding: NA  Arm 4: Glucosamine+chondroitin sulfate n = 317 Dose: 500 mg G + 400 mg CS Frequency: three times a day Duration: 24 weeks Method of Blinding: NA  Arm 5: Celecoxib n = 318 Dose: 200 mg Frequency: once a day Duration: 24 weeks Method of Blinding: NA | WOMAC pain (% with 20% or better improvement in pain:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.94 95% CI: (0.83, 1.06)  Comparator: Arm 3 vs Arm 1 , RR : 0.92 95% CI: (0.81, 1.04)  Comparator: Arm 4 vs Arm 1 , RR : 0.90 95% CI: (0.80, 1.02)  Comparator: Arm 5 vs Arm 1 , RR : 0.86 95% CI: (0.76, 0.96) |
| Hochberg, 2015[29](#_ENREF_29)  Study design: RCT  Trial name: MOVES  Study Location: France, Germany, Poland and Spain  Health care setting: NR  Multiple Sites: 42 | Total n = 606  Age Range: >=40  Arm 1, Mean Age: 63.2 (9.0) BMI: 30.9 (18.0) Arm 2, Mean Age: 62.2 (8.8) BMI: 31.1 (5.8)  Female: 83.9%  Racial/Ethnic Distribution: Caucasian 98.7%, 1.3%  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2&3, ACR  Analgesic Use: Yes, Up to 3 g/day of acetaminophen except during the 48 h before clinical evaluation | Diagnosis of osteoarthritis of the knee: ACR  Duration of Symptoms: 1 month  Minimum Age: 40  Otherwise Healthy  Able to sign Consent  No clinical or significant laboratory abnormalities  Negative pregnancy test and use of birth control  Not participating in another clinical trial  Agree to attend all study-related visits  K-L: 2&3  WOMAC: >301 | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Surgery knee limb in prior 6 month(s)  Pending surgery  Concomitant or prior use of other meds  Known allergy to chondroitin, glucosamine, celecoxib, sulphonamides, aspirin, lactose, NSAIDs, Allergy to shellfish Intolerance to acetaminophen  History of systemic diseases (heart attack or stroke, DM, hypertension, chronic liver/kidney diseases, infections); history of psychiatric disorders, alcohol/drug abuse  Active malignancy or history of a malignancy within the past 5 years  Concurrent arthritic disease, pain in other parts of the body, fibromyalgia | Arm 1: Celecoxib n = 282 Dose: 200mg Frequency: Once daily Duration: 6 months Method of Blinding: Matching capsules  Arm 2: Glucosamine-chondroitin n = 286 Dose: 500 mg Glucosamine+400 mg Chondroitin Frequency: Three time daily Duration: 6 months | % clinically significant on WOMAC pain:  Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , RR : 1.00 95% CI: (0.85, 1.17)  EuroQol-5D mobility:  Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-0.00, 0.00)  EuroQol-5D pain/discomfort:  Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (0.10, 0.10)  WOMAC function:  Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , MD : 21.20 95% CI: (-44.99, 87.39)  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : 71.50 95% CI: (NC, NC)  WOMAC pain:  Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , MD : 1.10 95% CI: (-19.76, 21.96)  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : 25.00 95% CI: (5.05, 44.95)  Clinically significant on WOMAC function:  Follow-Up Time: 180 days : Comparator: Arm 2 vs Arm 1 , RR : 1.02 95% CI: (0.86, 1.21) |
| Hsieh, 2012[78](#_ENREF_78)  Study design: RCT  Trial name: None  Study Location: Taiwan  Health care setting: NR  Single Site | Total n = 72  Mean Age(SD): Mean: 60.3 (10.4)  Arm 1, Mean Age: 61.3 (12) BMI: 26 (4.5) Arm 2, Mean Age: 61.1 (9.4) BMI: 26.4 (5.0)  Female: 86%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: II+ in both knees, ACT  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  K-L: II+ in both knees  ACR | Concomitant medical problems that prevent participation  Surgery knee limb in prior Ever month(s)  Pregnant or planning to become pregnant, and those who had a self-reported history of malignancy, vertigo, or stroke. | Arm 1: Sham monochromatic infrared energy (MIRE) n = 35 Placebo/Sham Dose: 40 minutes Frequency: 3 times a week Duration: 2 weeks Method of Blinding: Double-blind  Arm 2: Monochromatic infrared energy (MIRE) n = 37 Dose: 40 minutes Frequency: 3 times a week Duration: 2 weeks Method of Blinding: Double-blind | KOOS pain:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.70 95% CI: (-7.74, 4.34)  KOOS quality of life:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-6.39, 6.59)  OAQOL:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-2.70, 2.10)  WHOQOL-BREF physical:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.80 95% CI: (-8.48, 4.88)  WHOQOL-BREF psychological:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.40 95% CI: (-11.19, 2.39) |
| Imoto, 2012[48](#_ENREF_48)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Academic rheumatology clinic/department  Single Site | Arm 1, Mean Age: 58.78 (9.60) BMI: 30.00 (5.05) Arm 2, Mean Age: 61.50 (6.94) BMI: 29.72 (4.11)  Female: 92%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 26%, unilateral 74%  Subtype: NR  Diagnosis: K-L: 92% Grade II, 5% Grade III, 3% Grade IV, NRS pain 7.2  Analgesic Use: Yes, Patients were allowed to continue their medications, but paracetamol, diacerein, and chloroquin were used | Diagnosis of osteoarthritis of the knee  Minimum Age: 50  Maximum Age:75  Knee pain  Less than 30 minutes morning stiffness and crepitation in active movement and osteophytes  ACR  K-L: 2 or above in past 12 months | Physical therapy more than twice a week  Inability to pedal a bike  Unstable heart condition  Fibromyalgia  Prior knee arthroplasty | Arm 1: Control n = 50 Placebo/Educational manual and 2 phone calls Dose: NA Frequency: NA Duration: 8 weeks Method of Blinding: NR  Arm 2: Land-based strength training n = 50 Dose: 30-40 minutes per session Frequency: two sessions per week Duration: 8 weeks Method of Blinding: NR Co-Intervention: Orientation manual | Numerical Rating Scale for pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.47 95% CI: (-2.71, -0.23)  SF-36 functional capacity:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.83 95% CI: (-18.92, 3.26)  SF-36 pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.98 95% CI: (-13.94, 7.98)  SF-36 physical aspects:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -13.47 95% CI: (-33.97, 7.03)  TUG (s):  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.80 95% CI: (-2.97, -0.63) |
| Imoto, 2013[84](#_ENREF_84)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Hospital-outpatient  Single Site | Total n = 100  Mean Age: 59.7  Arm 1, Mean Age: 58.8 (9.6) BMI: 30 (5) Arm 2, Mean Age: 60.6 (6.7) BMI: 30 (4)  Female: 93%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 72% (96% for NMES group)  Subtype: NR  Diagnosis: K-L: 93% grade II, 4% grade III, 3% grade IV  Analgesic Use: Yes, Patients' continued medications during intervention but paracetamol, diacerein, and chloroquine were prescribed | Diagnosis of osteoarthritis of the knee  Minimum Age: 50  Maximum Age:75  ACR: NA  K-L: Grade 2 or more in the prior 12 months | Use of pacemaker, unstable cardiac status,  Attendance in a physical activity program more than twice a week  Inability to ride a stationary bike, or to walk  Previous arthroplasty | Arm 1: Control group n = 50 Placebo/Educational materials Dose: NA Frequency: NA Duration: 8 weeks Method of Blinding: NR  Arm 2: NMES n = 50 Dose: 40 minutes per session Frequency: NR Duration: 8 weeks Method of Blinding: NR Co-Intervention: Educational guide | Lequesne Index:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.81 95% CI: (-4.53, -1.09)  NRS:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.44 95% CI: (-2.65, -0.23)  TUG (s):  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.45 95% CI: (-3.42, -1.48) |
| Inal, 2016[89](#_ENREF_89)  Study design: RCT  Trial name: None  Study Location: Turkey  Health care setting: NR  Site size: NR | Total n = 93  Arm 1, Mean Age: 64.6 (1.88) BMI: 33.6 (0.77) Arm 2, Mean Age: 64.4 (1.7) BMI: 34.2 (0.87) Arm 3, Mean Age: 64.1 (0.99) BMI: 31.7 (0.92)  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: I1-4, ACR  Analgesic Use: No | Diagnosis of osteoarthritis of the knee  ACR: symptomatic knee OA | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Concomitant or prior use of other meds  Injected hyaluronic acid in the past or during the past 3 month(s)  Injected corticosteroids in the prior 3 month(s)  Prior acute injury to the knee  Had received TENS in the previous six months and had cardiac pace-maker,  Complaints linked to lower extremities such as radiculopathy or pain on ankle  Used non-steroidal anti-inflammatory drugs and chondroprotective agents in the last month  Uncontrolled co-morbid chronic disease such as diabetes mellitus and hypertension, a poor general health status, definite/suspected pregnancy, dementia or cognitive impairment, neurological disorders such as multiple sclerosis, Parkinson’s and Alzheimer’s diseases, major trauma in last 6 months | Arm 1: Sham TENS + physical therapy n = 30 Placebo/Sham Dose: 20 minutes Frequency: 5 times per week Duration: 2 weeks (TENS) / 4 weeks (home exercise) Method of Blinding: Double blind  Arm 2: Low frequency TENS + physical therapy n = 30 Dose: 20 minutes Frequency: 5 times per week Duration: 2 weeks (TENS) / 4 weeks (home exercise) Method of Blinding: Double blind  Arm 3: High frequency TENS + physical therapy n = 30 Dose: 20 minutes Frequency: 5 times per week Duration: 2 weeks (TENS) / 4 weeks (home exercise) Method of Blinding: Double blind | VAS pain in motion:  Follow-Up Time: 6 weeks : Comparator: Arm 3 vs Arm 1 , MD : 0.02 95% CI: (-1.82, 1.86)  VAS pain in rest:  Follow-Up Time: 6 weeks : Comparator: Arm 3 vs Arm 1 , MD : 0.26 95% CI: (-1.62, 2.14)  WOMAC function:  Follow-Up Time: 6 weeks : Comparator: Arm 3 vs Arm 1 , MD : -0.95 95% CI: (-8.46, 6.55)  WOMAC pain:  Follow-Up Time: 6 weeks : Comparator: Arm 3 vs Arm 1 , MD : -0.62 95% CI: (-3.01, 1.78)  WOMAC total:  Follow-Up Time: 6 weeks : Comparator: Arm 3 vs Arm 1 , MD : -1.73 95% CI: (-10.83, 7.37) |
| Inoshi, 2016[128](#_ENREF_128)  Study design: Single arm trial  Trial name: Healthy weight for life  Study Location: Australia  Health care setting: internet and phone-based program  Multiple Sites: NR (internet-based) | Total n = 1383  Mean Age(SD): Mean age 64.0(8.7)  Arm 1, Mean Age: 64(8.7) BMI: 34.4(5.2)  Female: 70.9%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: K-L: not specified, Mean KOOS pain 56.3(6.8)  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  BMI>28  Referral to orthopedist for KR  Enrollment in OAHWFL program  Radiographic or arthroscopy: NR | Exclusion : NR | Arm 1: Weight loss and exercise n = 1383 Dose: NA Frequency: NA Duration: 18 weeks | KOOS function:  Follow-Up Time: 18 weeks : Comparator: >10% weight change (post-pre) , MD : 17.40 95% CI: (15.9, 18.9)  Comparator: 7.6-10% weight change (post-pre) , MD : 13.60 95% CI: (11.9, 15.3)  Comparator: 5.1-7.5% weight change (post-pre) , MD : 12.00 95% CI: (10.2, 13.8)  Comparator: 2.5-5% weight change (post-pre) , MD : 8.90 95% CI: (7.0, 10.8)  Comparator: <2.5% weight change (post-pre) , MD : 7.80 95% CI: (4.8, 10.8)  KOOS pain:  Follow-Up Time: 18 weeks : Comparator: >10% weight change (post-pre) , MD : 16.70 95% CI: (15.2, 18.2)  Comparator: 7.6-10% weight change (post-pre) , MD : 13.30 95% CI: (11.6, 15.0)  Comparator: 5.1-7.5% weight change (post-pre) , MD : 12.00 95% CI: (10.2, 13.8)  Comparator: 2.5-5% weight change (post-pre) , MD : 9.90 95% CI: (7.7, 12.1)  Comparator: <2.5% weight change (post-pre) , MD : 6.10 95% CI: (3.2, 9.0) |
| Jones, 2012[115](#_ENREF_115)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Academic rheumatology clinic/department  Single Site | Total n = 64  Arm 1, Mean Age: 62.56 (5.88) BMI: 29.54 (3.42) Arm 2, Mean Age: 61.75 (5.92) BMI: 29.01 (2.83)  Living Situation: Community Dwelling  Diagnosis: VAS 5.56/10, WOMAC 51.0/96  Analgesic Use: Yes, Stable use of analgesics | Diagnosis of osteoarthritis of the knee  Stable doses of anti-inflammatory drugs  No regular physical exercise in the month before the study  ACR: NA  VAS: 3-7/10 | Injected hyaluronic acid in the past or during the past 3 months month(s)  Injected corticosteroids in the prior 3 months month(s)  Physical Therapy or Rehab or exercise in the previous physical therapy in the previous 6 months or rehab in the previous 3 months month(s)  Prior experience with the intervention of interest  Symptomatic heart disease  Symptomatic disease of the lower limbs (other than knee osteoarthritis) or upper limb that would secure the cane  Symptomatic lung disease; severe systemic disease; severe psychiatric illness  Regular physical exercise; (three or more times per week for at least 3 months)  Inability to walk; geographic inaccessibility | Arm 1: Control n = 32 Duration: 2 months  Arm 2: Braces or Canes n = 32 Dose: NA Frequency: NA Duration: 2 months Co-Intervention: usual therapy | 6 min walk with cane (m):  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : 83.28 95% CI: (62.38, 104.18)  6 min walk without cane (m):  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -6.50 95% CI: (-24.86, 11.86)  Lequesne:  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -2.53 95% CI: (-4.34, -0.72)  SF-36 bodily pain:  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -14.16 95% CI: (-24.30, -4.02)  SF-36 physical function:  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -9.06 95% CI: (-17.81, -0.31)  SF-36 role physical:  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -16.75 95% CI: (-31.69, -1.81)  VAS pain:  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -2.11 95% CI: (-2.83, -1.39)  WOMAC total:  Follow-Up Time: 60 days : Comparator: Arm 2 vs Arm 1 , MD : -1.06 95% CI: (-8.87, 6.75) |
| Jorge, 2015[49](#_ENREF_49)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: NR  Site size: NR | Total n = 60  Age Range: 40-70  Arm 1, Mean Age: 59.9 (7.5) BMI: 31.4 (4.42) Arm 2, Mean Age: 61.7 (6.4) BMI: 30.6 (5.75)  Female: 100  Racial/Ethnic Distribution: Caucasian 69% T, 71% C  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: ACR  Analgesic Use: Yes, All subjects were instructed to take 750 mg of acetaminophen every eight hours when experiencing pain. When pain exceeded a 7 on the visual analog scale, the subject could take 50 mg of diclofenac every eight hours. Both groups received a chart to record the doses of drugs taken during the study period for the purposes of analysis. | Diagnosis of osteoarthritis of the knee  Minimum Age: >=40  Maximum Age:69  Pain at rest between 3 and 8 out of 10 on the visual analog scale for one or both knees  ACR: meets criteria | Concomitant medical problems that prevent participation  Injected hyaluronic acid in the past or during the past 3 month(s)  Injected corticosteroids in the prior 3 month(s)  Inflammatory conditions or any medical condition that prevented physical activity  Travel plans for the subsequent 12 weeks  Regular physical activity at the time | Arm 1: Waitlist n = 31 Placebo/Waitlist Duration: 12 weeks Method of Blinding: Single-blind  Arm 2: Progressive resistance exercise n = 29 Dose: 2 set of 8 reps w/ 1 min rest period between sets Frequency: Twice a week Duration: 12 weeks Method of Blinding: Single-blind | 6MWT:  Follow-Up Time: 45 days : Comparator: Arm 2 vs Arm 1 , MD : -15.60 95% CI: (-45.14, 13.94)  Follow-Up Time: 90 days : Comparator: Arm 2 vs Arm 1 , MD : -26.40 95% CI: (-55.73, 2.93)  SF-36 mental health:  Follow-Up Time: 45 days : Comparator: Arm 2 vs Arm 1 , MD : -16.10 95% CI: (-26.66, -5.54)  Follow-Up Time: 90 days : Comparator: Arm 2 vs Arm 1 , MD : -16.90 95% CI: (-27.00, -6.80)  SF-36 physical health:  Follow-Up Time: 45 days : Comparator: Arm 2 vs Arm 1 , MD : -8.80 95% CI: (-17.26, -0.34)  Follow-Up Time: 90 days : Comparator: Arm 2 vs Arm 1 , MD : -19.00 95% CI: (-28.93, -9.07)  VAS pain:  Follow-Up Time: 45 days : Comparator: Arm 2 vs Arm 1 , MD : -1.10 95% CI: (-2.02, -0.18)  Follow-Up Time: 90 days : Comparator: Arm 2 vs Arm 1 , MD : -2.30 95% CI: (-3.55, -1.05)  WOMAC function:  Follow-Up Time: 45 days : Comparator: Arm 2 vs Arm 1 , MD : -4.00 95% CI: (-9.04, 1.04)  Follow-Up Time: 90 days : Comparator: Arm 2 vs Arm 1 , MD : -9.40 95% CI: (-15.17, -3.63) |
| Jorge, 2015[49](#_ENREF_49) -Continued |  |  |  |  | WOMAC pain:  Follow-Up Time: 45 days : Comparator: Arm 2 vs Arm 1 , MD : -3.40 95% CI: (-5.10, -1.70)  Follow-Up Time: 90 days : Comparator: Arm 2 vs Arm 1 , MD : -4.60 95% CI: (-6.50, -2.70)  WOMAC total:  Follow-Up Time: 45 days : Comparator: Arm 2 vs Arm 1 , MD : -8.20 95% CI: (-14.78, -1.62)  Follow-Up Time: 90 days : Comparator: Arm 2 vs Arm 1 , MD : -14.20 95% CI: (-22.03, -6.37) |
| Ju, 2015[57](#_ENREF_57)  Study design: RCT  Trial name: None  Study Location: Korea  Health care setting: NR  Site size: NR | Total n = 14  Age Range: NR  Arm 1, Mean Age: 65.1 ± 2.9 BMI: Average weight: 60.6 ± 7.69 kg, average height 153.1 ± 4.5 cm and Arm 2, Mean Age: 65.7 ± 3.5 BMI: average weight of 64.7 ± 2.3 kg, height 152.4 ± 5.1 cm and an  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: ACR  Analgesic Use: NR | Minimum Age: 60 | Exclusion : NR | Arm 1: Control n = 7 Duration: NR  Arm 2: Agility-type exercise n = 7 Dose: 20 minutes (3 sets of 10 repetitions per exercise) per session Frequency: 3 sessions per week Duration: 8 weeks | VAS pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.00 95% CI: (-5.32, -2.68) |
| Kahan, 2009[38](#_ENREF_38)  Study design: RCT  Trial name: None  Study Location: US, France, Belgium, Switzerland, Austria  Health care setting: Hospital-outpatient  Multiple Sites: 35 | Total n = 622  Age Range: 45-80  Arm 1, Mean Age: 61.8(0.5) BMI: 28.8 Arm 2, Mean Age: 62.9(0.5) BMI: 28.5  Female: 68.5%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: Medial 100%  Diagnosis: ACR  Analgesic Use: Yes, Acetaminophen in 500-mg tablets (maximum dosage 4 gm/day); NSAIDs were allowed in cases of acute pain. | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 3 months  Minimum Age: 45  Maximum Age:79  ACR  VAS: >= 30 mm  JSW: >= 1 mm | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Concomitant or prior use of other meds  Injected hyaluronic acid in the past or during the past 3 month(s)  Injected corticosteroids in the prior 3 month(s)  Prior acute injury to the knee  K-L: 4  Isolated lateral tibiofemoral OA; isolated patellofemoral OA  A history or the active presence of other rheumatic diseases that could be responsible for secondary OA  A history of hip OA or hip surgery | Arm 1: Placebo n = 313 Placebo/Sachet Frequency: Once daily  Arm 2: Chondroitins sulfate n = 309 Dose: 800 mg Frequency: Once daily | VAS pain last 48 hours:  Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : 0.50 95% CI: (-2.27, 3.27)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -4.00 95% CI: (-8.16, 0.16)  WOMAC pain score last 48 hours:  Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-6.16, 2.16)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-7.66, 0.66)  Responder: reduction in pain score of at least 40% WOMAC:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.83 95% CI: (0.68, 1.02)  Responder: reduction in pain score of at least 40mm:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.68 95% CI: (0.51, 0.91)  Responder: reduction in pain score of at least 60mm:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , RR : 0.44 95% CI: (0.23, 0.85) |
| Kapci, 2015[81](#_ENREF_81)  Study design: RCT  Trial name: None  Study Location: Turkey  Health care setting: NR  Site size: NR | Total n = 90  Age Range: 40-65  Arm 1, Mean Age: 57.76 (7.15) BMI: 30.91 (4.33) Arm 2, Mean Age: 56.13 (6.61) BMI: 32.31 (5.23) Arm 3, Mean Age: 54.63 (6.53) BMI: 31.15 (4.68)  Female: 83%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 100%  Subtype: NR  Diagnosis: K-L: 2&3  Analgesic Use: NR |  | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 6 month(s)  Secondary knee OA; active synovitis; symptomatic hip, foot, and ankle disease; neurologic deficits in a lower extremity; recent knee trauma  Application of physical treatment to the knee in the last 3 months | Arm 1: Sham ultrasound n = 30 Placebo/Sham Dose: 5 min Frequency: 5 days a week Duration: 2 weeks US / 8 weeks exercise Method of Blinding: Double blind  Arm 2: Continuous ultrasound n = 30 Dose: 5 min Frequency: 5 days a week Duration: 2 weeks US / 8 weeks exercise Method of Blinding: Double blind  Arm 3: Pulsed ultrasound n = 30 Dose: 5 min Frequency: 5 days a week Duration: 2 weeks US / 8 weeks exercise Method of Blinding: Double blind | Lequesne index:  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -2.35 95% CI: (-4.11, -0.59)  Comparator: Arm 3 vs Arm 1 , MD : -2.65 95% CI: (-4.27, -1.03)  Follow-Up Time: 4 months : Comparator: Arm 2 vs Arm 1 , MD : -6.28 95% CI: (-8.31, -4.25)  Comparator: Arm 3 vs Arm 1 , MD : -5.71 95% CI: (-7.68, -3.74)  VAS pain:  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -1.33 95% CI: (-2.55, -0.11)  Comparator: Arm 3 vs Arm 1 , MD : -1.56 95% CI: (-2.82, -0.30)  Follow-Up Time: 4 months : Comparator: Arm 2 vs Arm 1 , MD : -3.30 95% CI: (-4.62, -1.98)  Comparator: Arm 3 vs Arm 1 , MD : -3.37 95% CI: (-4.70, -2.04) |
| Knoop, 2013[61](#_ENREF_61)  Study design: RCT  Trial name: None  Study Location: Netherlands  Health care setting: Physical therapy outpatient clinic  Single Site | Total n = 159  Mean Age: 62  Arm 1, Mean Age: 61.8 \_x0006\_ (6.6) BMI: 28.3(4.5) Arm 2, Mean Age: 62.1(7.6) BMI: 28.8(4.8)  Female: 66% intervention; 56% control  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 75%, unilateral 25%  Subtype: NR  Diagnosis: K-L: 35% K-L: I; 28% K-L: II; 26% K-L: III; 12% K-L: IV  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 40  Maximum Age:75  Ambulatory  Self-reported or bio-assessed knee instability  ACR: NA | Concomitant medical problems that prevent participation  Pending surgery  Other diagnosed forms of arthritis  Severe knee pain (NRS>8)  Inability to comprehend Dutch, be scheduled for therapy or provide consent | Arm 1: Land-based exercise n = 79 Dose: 60 minutes per session Frequency: 2 sessions per week plus home exercises 5 days per week Duration: 12 weeks Method of Blinding: NR  Arm 2: Agility type training n = 80 Dose: 60 minutes per session Frequency: 2 sessions per week plus home exercises 5 days per week Duration: 12 weeks Method of Blinding: NR | NRS:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.50 95% CI: (-1.16, 0.16)  Follow-Up Time: 38 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.37, 0.17)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.20 95% CI: (-0.83, 0.43)  TUG (s):  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.40 95% CI: (-0.16, 0.96)  Follow-Up Time: 38 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-0.47, 0.67)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-0.63, 0.83)  WOMAC physical function:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.90 95% CI: (-5.53, 1.73)  Follow-Up Time: 38 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-4.49, 3.89)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : 4.10 95% CI: (0.62, 7.58) |
| Koca, 2009[104](#_ENREF_104)  Study design: RCT  Trial name: None  Study Location: Turkey  Health care setting: Physical therapy outpatient clinic  Single Site | Total n = 37  Total # of knees = 37  Arm 1, Mean Age: 54.83 (9.27) BMI: 29.64 Arm 2, Mean Age: 55.36 (11.50) BMI: 31.33  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2&3, ACR  Analgesic Use: Yes, Parecetamol 1500 mg/day | Diagnosis of osteoarthritis of the knee  K-L: 2&3  ACR | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 6 month(s)  Prior acute injury to the knee  Physical Therapy or Rehab or exercise in the previous 12 month(s)  Involvement of the lateral compartment of the knee  Meniscopathy  Infective or inflammatory pathologies of knee | Arm 1: Control n = 18 Dose: Paracetamol 1500 mg; quadriceps strengthening exercises Frequency: Paracetamol once daily; Duration: 3 months Co-Intervention: Parecetamol and exercise  Arm 2: Insole n = 19 Dose: 6 mm wedge Frequency: All day long Duration: 3 months Co-Intervention: Parecetamol and exercise | VAS at rest:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -1.22 95% CI: (-2.89, 0.45)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -1.28 95% CI: (-2.84, 0.28)  VAS at standing:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -0.93 95% CI: (-2.25, 0.39)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -1.16 95% CI: (-2.55, 0.23)  VAS at walking:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -0.62 95% CI: (-2.01, 0.77)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -1.68 95% CI: (-3.16, -0.20)  WOMAC function score:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -10.06 95% CI: (-19.68, -0.44)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -11.78 95% CI: (-21.18, -2.38)  WOMAC pain score:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -3.14 95% CI: (-5.96, -0.32)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -4.02 95% CI: (-6.79, -1.25) |
| Koca, 2009[104](#_ENREF_104) -Continued |  |  |  |  | WOMAC total:  Follow-Up Time: 1 month : Comparator: Arm 2 vs Arm 1 , MD : -15.16 95% CI: (-28.42, -1.90)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -17.68 95% CI: (-30.37, -4.99) |
| Koli, 2015[41](#_ENREF_41)  Study design: RCT  Trial name: None  Study Location: Finland  Health care setting: NR  Site size: NR | Total n = 80  Age Range: 50-65  Arm 1, Mean Age: 59 (4) BMI: 69.4 (11.7) Arm 2, Mean Age: 58 (4) BMI: 73.4 (9.4)  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Patellofemora 50%, Tibiofemoral 100%  Diagnosis: K-L: I-II  Analgesic Use: Yes, Table 1: 63% T, 42% C | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: Knee pain on most days  Minimum Age: >=50  Maximum Age:64  K-L: I-II radiographic tibiofemoral joint OA | Concomitant medical problems that prevent participation  Injected corticosteroids in the prior 12 month(s)  Intensive exercise more than twice a week  Femoral neck bone and lumbar spine bone mineral density (gIcmj2) T-score lower than j2.5 (i.e., indicating osteoporosis), measured with dual-energy x-ray absorptiometry  BMI<=35  Knee instability or surgery of the knee caused by trauma  Inflammatory joint disease; contraindications to MRI (allergies to contrast agents or renal insufficiency) | Arm 1: Usual care + education / stretching n = 40 Placebo/Usual care Frequency: Every 3 months Duration: 12 months  Arm 2: Aerobic exercise n = 38 Dose: 55 min Frequency: 3 times a week Duration: 12 months | KOOS function:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -1.20 95% CI: (-3.53, 1.13)  KOOS pain:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -2.60 95% CI: (-6.82, 1.62)  KOOS quality of life:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -3.00 95% CI: (-9.40, 3.40) |
| Kulisch, 2014[73](#_ENREF_73)  Study design: RCT  Trial name: None  Study Location: Hungary  Health care setting: Academic rheumatology clinic/department, mineral spa  Single Site | Total n = 77  Mean Age: 65.6  Arm 1, Mean Age: 65.5(7.7) BMI: NR Arm 2, Mean Age: 65.6(6.4) BMI: NR  Female: 78%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 100%  Subtype: NR  Diagnosis: Mild to moderate  Analgesic Use: Yes, Any change in NSAID or chondroprotective therapy during the study was not allowed. | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: at least 3 months  Minimum Age: 45  Maximum Age:75  ACR: NA  Radiographic imaging: NR | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 months month(s)  Injected hyaluronic acid in the past or during the past 6 months month(s)  Injected corticosteroids in the prior 1 month month(s)  Prior acute injury to the knee  Physical Therapy or Rehab or exercise in the previous month(s)  Severe internal, rheumatic, urogenital, or skin diseases, radiculopathy  Conditions for which warm baths were contraindicated  Inflammatory rheumatic diseases  Effusion  Knee fracture or injury in prior 6 months or plate in knee, hip or spine surgery within previous year | Arm 1: Control n = 39 Dose: 30 minutes per session Frequency: 5 days per week Duration: 3 weeks  Arm 2: Balneotherapy n = 38 Dose: 30 minutes per session Frequency: 5 days per week Duration: 3 weeks | VAS pain at rest:  Follow-Up Time: 15 weeks : Comparator: Arm 2 vs Arm 1 , MD : -16.00 95% CI: (-26.68, -5.32)  VAS pain on exertion:  Follow-Up Time: 15 weeks : Comparator: Arm 2 vs Arm 1 , MD : -16.60 95% CI: (-25.79, -7.41)  WOMAC function:  Follow-Up Time: 15 weeks : Comparator: Arm 2 vs Arm 1 , MD : -8.10 95% CI: (-15.82, -0.38)  WOMAC pain:  Follow-Up Time: 15 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.40 95% CI: (-9.45, 4.65) |
| Laufer, 2014[82](#_ENREF_82)  Study design: RCT  Trial name: None  Study Location: Israel  Health care setting: Physical therapy outpatient clinic  Single Site | Total n = 63  Total # of knees = NR  Mean Age(SD): 68.9 (SD 7.7)  Arm 1, Mean Age: 69.4 (SD 7.7) BMI: 30.5 (SD 5.3) Arm 2, Mean Age: 68.3 (SD 7.7) BMI: 31.4 (SD 6.7)  Female: 82.5%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: >=2  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: knee pain for at least 3 months  Minimum Age: 51  Ambulatory  K-L: >=2 | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 6 month(s)  Physical Therapy or Rehab or exercise in the previous 3 month(s)  Pacemaker or medical condition that could affect functional performance  Injections to the knee joint during the previous six months  Cardiovascular, neurological problems or other orthopedic problems  Inability to follow instructions, difficulties with communication and cooperation or schedule inconvenient for them  Medical conditions with contraindications for electrical stimulation | Arm 1: Control n = 25 Placebo/Control Dose: NA Frequency: NA Duration: NA Method of Blinding: The person conducting the exercise program was blinded to treatment allocation, blindness of the assessor was not maintained in the posttreatment and follow-up assessments Co-Intervention: Group exercise program delivered biweekly  Arm 2: Neuromuscular electrical stimulation n = 25 Dose: Ten contractions were delivered at each session, at maximal tolerated intensity Frequency: Biweekly Duration: 6 weeks Method of Blinding: The person conducting the exercise program was blinded to treatment allocation, blindness of the assessor was not maintained in the posttreatment and follow-up assessments Co-Intervention: Group exercise program delivered biweekly | TUG (s):  Follow-Up Time: 18 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.20 95% CI: (-2.32, 1.92)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.20 95% CI: (-1.21, 1.61)  VAS pain:  Follow-Up Time: 18 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.90 95% CI: (-3.25, -0.55)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.70 95% CI: (-2.70, -0.70)  WOMAC total:  Follow-Up Time: 18 weeks : Comparator: Arm 2 vs Arm 1 , MD : -14.70 95% CI: (-44.05, 14.65)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -23.20 95% CI: (-43.20, -3.20) |
| Lim, 2010[63](#_ENREF_63)  Study design: RCT  Trial name: None  Study Location: Korea  Health care setting: NR  Single Site | Total n = 75  Age Range: >=50  Arm 1, Mean Age: 63.3 (5.3) BMI: 27.7 (2.0) Arm 2, Mean Age: 67.7 (7.7) BMI: 27.6 (1.7) Arm 3, Mean Age: 65.7 (8.9) BMI: 27.9 (1.5)  Female: 87%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: II+  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: >=50  Ambulatory  BMI >=25  Abdominal circumferences of more than 90 cm for men and 85 cm for women  K-L: II+ | Concomitant medical problems that prevent participation  Progressive inflammatory or ankylosing states, or had coexisting central nervous system lesions or in adequate cardiac functions  Infectious or skin diseases | Arm 1: Control n = 24 Placebo/Education Duration: 8 weeks Method of Blinding: Single-blind  Arm 2: Land-based exercise n = 25 Dose: 40 min Frequency: 3 times per week Duration: 8 weeks Method of Blinding: Single-blind  Arm 3: Aquatic exercise n = 26 Dose: 40 min Frequency: 3 times per week Duration: 8 weeks Method of Blinding: Single-blind | SF-36 MCS:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.50 95% CI: (-11.66, 2.66)  Comparator: Arm 3 vs Arm 1 , MD : -6.40 95% CI: (-13.59, 0.79)  SF-36 PCS:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-8.85, 1.85)  Comparator: Arm 3 vs Arm 1 , MD : -1.90 95% CI: (-7.11, 3.31)  WOMAC total:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.00 95% CI: (-13.64, 5.64)  Comparator: Arm 3 vs Arm 1 , MD : -6.70 95% CI: (-15.64, 2.24) |
| Mahboob, 2009[74](#_ENREF_74)  Study design: RCT  Trial name: None  Study Location: Iran  Health care setting: Hospital-outpatient  Single Site | Total n = 50  Age Range: 44-79  Arm 1, Mean Age: NR BMI: NR Arm 2, Mean Age: NR BMI: NR  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Subtype: NR  Diagnosis: ACR, severity not reported  Analgesic Use: Yes, During the therapy program, if needed, patients were allowed to take paracetamol in a dose of less than 1500 mg per day(and drug use was assessed at followup). | Diagnosis of osteoarthritis of the knee  ACR: not applicable | Prior surgery on one or both knees  Injected hyaluronic acid in the past or during the past 6 months month(s)  Injected corticosteroids in the prior 6 months month(s)  Physical Therapy or Rehab or exercise in the previous 6 months month(s)  Effusion  Severe CVD and PVD | Arm 1: Placebo n = 25 Placebo/Placebo gel (lacking only mud) Dose: 20 minutes per treatment, each knee Frequency: once per day Duration: 30 days  Arm 2: Mudpacks n = 25 Dose: 20 minutes per treatment, each knee Frequency: one treatment per day Duration: 30 days | WOMAC function:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -13.76 95% CI: (-31.63, 4.11)  WOMAC pain:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.44 95% CI: (-11.34, 0.46) |
| Makovey, 2015[129](#_ENREF_129)  Study design: Conference abstract  Trial name: Healthy weight for life  Study Location: NR  Health care setting: Remotely delivered  Site size: NR | Total n = 2175  Total # of knees = NR  Mean Age(SD): 64 (SD 8.6)  Arm 1, Mean Age: 64 (SD 8.6) BMI: 34.4 (SD 5.2)  Female: 71%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Analgesic Use: NR | Inclusion : NR | Exclusion : NR | Arm 1: Weight loss n = 2175 Dose: Phase 1 - motivational weight loss utilizing low calorie diet meal replacement, with controlled portions, and free foods for 6 weeks; phase 2 - consolidation weight loss for 6 weeks and phase 3 - short term weight maintenance Frequency: NR Duration: 18 weeks Method of Blinding: NA Co-Intervention: NR | SF-12 Mental Health Composite Score (PCS):  Follow-Up Time: 18 weeks : Comparator: <2.5% weight change (post-pre) , MD : 3.58 95% CI: (1.8, 5.4)  Comparator: 2.5-5% weight change (post-pre) , MD : 2.38 95% CI: (1.3, 3.5)  Comparator: 5.1-7.5% weight change (post-pre) , MD : 5.11 95% CI: (4.2, 6.0)  Comparator: 7.6-10% weight change (post-pre) , MD : 5.89 95% CI: (5.0, 6.8)  Comparator: >10% weight change (post-pre) , MD : 6.66 95% CI: (5.8, 7.5)  SF-12 Physical Health Composite Score (PCS):  Follow-Up Time: 18 weeks : Comparator: <2.5% weight change (post-pre) , MD : 3.16 95% CI: (1.7, 4.6)  Comparator: 2.5-5% weight change (post-pre) , MD : 4.07 95% CI: (3.2, 5.0)  Comparator: 5.1-7.5% weight change (post-pre) , MD : 6.73 95% CI: (6.0, 7.4)  Comparator: 7.6-10% weight change (post-pre) , MD : 6.65 95% CI: (5.8, 7.5)  Comparator: >10% weight change (post-pre) , MD : 8.60 95% CI: (7.9, 9.3) |
| Messier, 2013[125](#_ENREF_125)  Study design: RCT  Trial name: IDEA  Study Location: US  Health care setting:  Single Site | Total n = 454  Mean Age(SD): 66(6)  Arm 1, Mean Age: 66(6) BMI: 33.6(3.7) Arm 2, Mean Age: 66(6) BMI: 33.7(3.8) Arm 3, Mean Age: 65(6) BMI: 33.6(3.7)  Female: 72%  Racial/Ethnic Distribution: Caucasian 81%, Nonwhite 19%  Living Situation: Community Dwelling  Location of OA: bilateral, unilateral  Subtype: Patellofemora, Tibiofemoral  Diagnosis: K-L: 2&3, Mild or moderate  Analgesic Use: Yes, Patients were allowed to continue using any medications they were taking prior to the study, | Diagnosis of osteoarthritis of the knee: K-L:  Minimum Age: 55  Ambulatory  Able to sign Consent  BMI 27-41  Pain on most days  Sedentary lifestyle  K-L: 2&3 | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Knee or hip replacement  Heart problems or cancer  Injected knee medications  Difficulty with ADLs, other knee-related activities  >=21 drinks per week | Arm 1: Land-based Exercise n = 150 Placebo/Exercise Dose: 1 hour Frequency: 3 times per week Duration: 18 months Method of Blinding: NR  Arm 2: Weight loss n = 152 Dose: 800-1000 calorie deficit per day Frequency: Not applicable Duration: 18 months Method of Blinding: NR  Arm 3: Weight loss + land-based exercise n = 152 Dose: 1 hour exercise, 800-1000 calorie deficit Frequency: Exercise 3 times per week Duration: 18 months Method of Blinding: NR | 6 min walk (meter):  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 23.00 95% CI: (3.15, 42.85)  Comparator: Arm 3 vs Arm 1 , MD : -12.00 95% CI: (-33.93, 9.93)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 28.00 95% CI: (8.90, 47.10)  Comparator: Arm 3 vs Arm 1 , MD : -4.00 95% CI: (-24.52, 16.52)  SF-36 mental:  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.50 95% CI: (-1.34, 2.34)  Comparator: Arm 3 vs Arm 1 , MD : -0.70 95% CI: (-2.48, 1.08)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 1.10 95% CI: (-0.88, 3.08)  Comparator: Arm 3 vs Arm 1 , MD : -0.80 95% CI: (-2.71, 1.11)  SF-36 physical:  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.00 95% CI: (-2.33, 2.33)  Comparator: Arm 3 vs Arm 1 , MD : -2.70 95% CI: (-4.89, -0.51)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.30 95% CI: (-2.56, 1.96)  Comparator: Arm 3 vs Arm 1 , MD : -2.00 95% CI: (-4.19, 0.19)  WOMAC function:  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.10 95% CI: (-2.67, 2.87)  Comparator: Arm 3 vs Arm 1 , MD : -3.40 95% CI: (-6.02, -0.78) |
| Messier, 2013[125](#_ENREF_125) -Continued |  |  |  |  | Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 0.60 95% CI: (-1.88, 3.08)  Comparator: Arm 3 vs Arm 1 , MD : -1.20 95% CI: (-3.75, 1.35)  WOMAC pain:  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : 0.40 95% CI: (-0.31, 1.11)  Comparator: Arm 3 vs Arm 1 , MD : -0.70 95% CI: (-1.41, 0.01)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 0.40 95% CI: (-0.32, 1.12)  Comparator: Arm 3 vs Arm 1 , MD : 0.10 95% CI: (-0.68, 0.88)  Weight (kg):  Follow-Up Time: 18 months : Comparator: Arm 2 vs Arm 1 , MD : -6.00 95% CI: (-9.75, -2.25)  Comparator: Arm 3 vs Arm 1 , MD : -8.10 95% CI: (-11.92, -4.28)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -6.90 95% CI: (-10.72, -3.08)  Comparator: Arm 3 vs Arm 1 , MD : -8.10 95% CI: (-11.85, -4.35) |
| Miller, 2006[124](#_ENREF_124)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: Academic exercise science department  Single Site | Total n = 87  Mean Age: 69  Arm 1, Mean Age: 69.3(0.9) BMI: 34.3 (3.9) Arm 2, Mean Age: 69.7 (0.9) BMI: 34.9 (4.9)  Female: 62%  Racial/Ethnic Distribution: African American 11%, Asian 0%, Caucasian 84%, Hispanic 0%, Native American 2%  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: Symptomatic knee OA  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 60  BMI>=30  Self-reported difficulty in performing ADLs attributed to knee pain  symptomatic knee OA | Unstable medical condition or condition where rapid weight loss or exercise contraindicated  Unwillingness to modify diet or physical activity or inability to comply because of food allergy  Excessive alcohol consumption | Arm 1: Control n = 43 Placebo/Educational sessions Dose: NA Frequency: two sessions per month Duration: 6 months Method of Blinding: NR  Arm 2: Weight loss n = 44 Dose: 60 minutes per session Frequency: 1 session per week Duration: 6 months Method of Blinding: NR Co-Intervention: educational and behavioral sessions | 6 min walk (meter):  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -51.00 95% CI: (-96.03, -5.97)  BMI:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.40 95% CI: (-4.48, -0.32)  WOMAC function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -8.60 95% CI: (-13.50, -3.70)  WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-3.25, -0.75)  WOMAC total:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -10.70 95% CI: (-17.01, -4.39)  Weight (kg):  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -9.10 95% CI: (-16.87, -1.33) |
| Mizusaki, 2013[83](#_ENREF_83)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Academic rheumatology clinic/department  Single Site | Total n = 100  Mean Age: 61  Arm 1, Mean Age: 61.50 ± 6.94 BMI: 29.72 ± 4.11 Arm 2, Mean Age: 60.60 ± 6.72 BMI: 30.08 ± 3.80  Female: 86%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 52%, unilateral 48%, NR  Subtype: NR  Diagnosis: K-L, ACR  Analgesic Use: Yes, Patient medication was standardized and not modified during the study period. Paracetamol was prescribed for pain, and diacerein and chloroquine for OA control. | Diagnosis of osteoarthritis of the knee  Minimum Age: 50  Maximum Age:74  K-L: >=2  ACR | Physical Therapy or Rehab or exercise in the previous current month(s)  Use of a pacemaker, unstable heart conditions  Inability to exercise on a stationary bicycle ergometer, inability to walk  Diagnosis of fibromyalgia, epilepsy, and skin tumor or lesion at the NMES application site  Previous hip or knee arthroplasty | Arm 1: Exercise n = 50 Dose: 40 minutes per session Frequency: two sessions per week Duration: 8 weeks Co-Intervention: a manual including guidelines on how not to overload the knee during daily activities and instructions on the use of ice packs in case of pain and inflammation and warm compresses in case of pain without inflammation  Arm 2: NMES n = 50 Dose: 40 minutes per session Frequency: two sessions per week Duration: 8 weeks Co-Intervention: Exercise and a manual including guidelines on how not to overload the knee during daily activities and instructions on the use of ice packs in case of pain and inflammation and warm compresses in case of pain without inflammation | NRS pain score:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.03 95% CI: (-1.12, 1.18)  TUG (s):  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.65 95% CI: (-1.25, -0.05)  WOMAC function:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.92 95% CI: (-9.14, 3.30)  WOMAC pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.65 95% CI: (-2.39, 1.09) |
| Nam, 2014[51](#_ENREF_51)  Study design: RCT  Trial name: None  Study Location: NR  Health care setting: Academic orthopedic surgery clinic/department  Single Site | Total n = 30  Total # of knees = NR  Age Range: NR  Arm 1, Mean Age: 63.7 (SD 5.6) BMI: NR Arm 2, Mean Age: 64.9 (SD 6.8) BMI: NR  Female: 60%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: > 2  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 61  Able to sign Consent  Not currently exercising  Ability to understand the exercise  K-L: >2 | Prior surgery on one or both knees | Arm 1: Control n = 15 Placebo/Control Dose: 3 1-min sets, with 1-min breaks between sets for each exercise Frequency: 3 times per week Duration: 6 weeks Method of Blinding: NR Co-Intervention: NR  Arm 2: Land-based exercise: Strength/Other n = 15 Dose: 3 times per week Frequency: 3 1-min sets, with 1-min breaks between sets for each exercise Duration: 6 weeks Method of Blinding: NR Co-Intervention: NR | WOMAC total:  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.99 95% CI: (-5.48, -0.50) |
| Nelson, 2013[90](#_ENREF_90)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: NR  Single Site | Total n = 34  Mean Age(SD): 55.5 (2.5) Active; 58.4 (2  Arm 1, Mean Age: 58.4 BMI: 34.7 Arm 2, Mean Age: 55.5 BMI: 33.5  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Analgesic Use: Yes, Unrestricted use of NSAIDs | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 3 months  >= 2 h of daily standing activity in a physical occupation  Imaging study: Confirmed articular cartilage loss  VAS: >=4 | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 6 month(s)  Implanted electronic devices  On disability or with third party claims | Arm 1: Heat/ultrasound/diathermy n = 19 Placebo/Sham Dose: 15 minutes Frequency: Twice a day Duration: 6 weeks Method of Blinding: Double-blind  Arm 2: Heat/ultrasound/diathermy n = 15 Dose: 15 minutes Frequency: Twice a day Duration: 6 weeks Method of Blinding: Double-blind | VAS:  Follow-Up Time: 42 days : Comparator: Arm 2 vs Arm 1 , MD : -1.92 95% CI: (-2.35, -1.49) |
| Oliveira, 2012[47](#_ENREF_47)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Academic rheumatology clinic/department  Single Site | Total n = 100  Mean Age: 60  Arm 1, Mean Age: 58.78 (9.60) BMI: 30.00 ± 5.05 Arm 2, Mean Age: 61.50 (6.94) BMI: 29.72 ± 4.11  Female: 92%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 25%, unilateral 75%  Subtype: NR  Diagnosis: K-L: mean: 2  Analgesic Use: Yes, The patients’ medication was standardized and not modified during the study. | Diagnosis of osteoarthritis of the knee  Minimum Age: 50  Maximum Age:75  K-L: >=2  ACR: NA | Concomitant medical problems that prevent participation  Pacemaker use; unstable heart conditions  Participation in another exercise program  Inability to pedal a stationary bike; inability to walk  Previous knee or hip arthroplasty  Diagnosis of fibromyalgia; epilepsy; and presence of a tumor or cutaneous lesion that could interfere with the procedure | Arm 1: Control n = 50 Duration: 8 weeks  Arm 2: Land-based exercise n = 50 Dose: NR Frequency: two sessions per week Duration: 8 weeks | Lequesne Index:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.98 95% CI: (-3.75, -0.21)  TUG:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.80 95% CI: (-2.83, -0.77)  WOMAC function:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.61 95% CI: (-11.67, 0.45)  WOMAC pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.77 95% CI: (-2.38, 0.84) |
| Palmer, 2014[88](#_ENREF_88)  Study design: RCT  Trial name: None  Study Location: UK  Health care setting: NR  Site size: NR | Total n = 224  Age Range: >=18  Arm 1, Mean Age: 60.9 (10.8) BMI: 29.1 (9.0) Arm 2, Mean Age: 61.2 (11.4) BMI: 29.7 (11.1) Arm 3, Mean Age: 62 (9.4) BMI: 29.8 (7.4)  Female: 37%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: >=18  ACR: 3 of 6 signs and symptoms | Concomitant medical problems that prevent participation  Prior experience with the intervention of interest  Contraindications to TENS | Arm 1: Sham TENS n = 74 Placebo/Sham Dose: As needed; 30 minutes instructional program Frequency: As needed Duration: 6 weeks Method of Blinding: Single-blinded  Arm 2: TENS n = 73 Dose: As needed; 30 minutes instructional program Frequency: As needed Duration: 6 weeks Method of Blinding: Single-blinded Co-Intervention: Exercise program  Arm 3: Exercise program n = 77 Dose: 1 hour Frequency: Weekly Duration: 6 weeks Method of Blinding: Single-blinded Co-Intervention: | WOMAC function:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 3 , MD : 0.50 95% CI: (-4.16, 5.16)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 3 , MD : 1.30 95% CI: (-3.38, 5.98)  WOMAC pain:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 3 , MD : 1.00 95% CI: (-0.92, 2.92)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 3 , MD : -2.00 95% CI: (-3.46, -0.54)  WOMAC total:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 3 , MD : 1.00 95% CI: (-5.48, 7.48)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 3 , MD : 1.60 95% CI: (-4.76, 7.96)  Clinically significant on WOMAC function:  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 3 , RR : 1.08 95% CI: (0.69, 1.69) |
| Park, 2013[98](#_ENREF_98)  Study design: RCT  Trial name: None  Study Location: Korea  Health care setting: NR  Single Site | Total n = 44  Arm 1, Mean Age: 60 (6.22) BMI: 24.8 (1.76) Arm 2, Mean Age: 62.5 (5.66) BMI: 25.3 (2.92)  Female: 100  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Subtype: NR  Diagnosis: K-L: 2&3, ACR  Analgesic Use: Yes, One control group patient took NSAIDs for a heart condition. | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >= 6 months  Minimum Age: >=40  ACR  K-L: 2&3 | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 6 month(s)  No serious knee trauma in last six months  No acute symptomatic OA, comorbidities such as any peripheral or central neuro logic disorders in last 6 months  K-L IV | Arm 1: Home-based exercise (HBE) n = 19 Placebo/Control Dose: 10 repetitions of each exercise Frequency: Daily; 3 instructional sessions/week for 8 weeks Duration: 8 weeks  Arm 2: Whole body vibration (WBV) n = 17 Dose: 20 minutes Frequency: 3 times a week Duration: 8 weeks | NRS:  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-3.77, -0.23)  WOMAC total:  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -3.36 95% CI: (-10.01, 3.29) |
| Patel, 2013[23](#_ENREF_23)  Study design: RCT  Trial name: None  Study Location: India  Health care setting: Academic orthopedic surgery clinic/department  Single Site | Total n = 78  Total # of knees = 156  Age Range: 33-80  Arm 1, Mean Age: 53.65 (8.17) BMI: 26.21 (2.93) Arm 2, Mean Age: 53.11 (11.55) BMI: 26.28 (3.23) Arm 3, Mean Age: 51.64 (9.22) BMI: 25.81 (3.31)  Female: 70.7%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: bilateral 100%  Subtype: NR  Diagnosis: Ahlback grade 1-2, ACR  Analgesic Use: Yes, Paracetamol 500mg if discomfort | Diagnosis of osteoarthritis of the knee: ACR  Ahlback grade: 1-2 | Surgery knee limb in prior 12 month(s)  Injected hyaluronic acid in the past or during the past 3 month(s)  Injected corticosteroids in the prior 3 month(s)  Secondary OA due to joint inflammatory diseases, Generalized OA, Advanced stages of OA  Metabolic diseases of the bone  Coexisting backache  Receiving anticoagulant therapy  Hemoglobin level less than 10 gm% or associated comorbidities, infection, tumor, crystal arthropathies, or tense joint effusion | Arm 1: Control n = 23 Placebo/Normal saline injection Dose: 8 mL Frequency: Single injection  Arm 2: Single PRP Injection n = 27 Dose: 8 mL Frequency: Single injection Co-Intervention: 1 mL of CaCl2 (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP  Arm 3: 2 PRP Injections n = 25 Dose: 8 mL Frequency: 2 injections 3 weeks apart Co-Intervention: 1 mL of CaCl2 (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP | VAS:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.45 95% CI: (-2.92, -1.98)  Comparator: Arm 3 vs Arm 1 , MD : -2.07 95% CI: (-2.59, -1.55)  WOMAC function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -19.38 95% CI: (NC, NC)  Comparator: Arm 3 vs Arm 1 , MD : -17.06 95% CI: (NC, NC)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -15.56 95% CI: (NC, NC)  Comparator: Arm 3 vs Arm 1 , MD : -16.24 95% CI: (NC, NC)  WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -5.87 95% CI: (NC, NC)  Comparator: Arm 3 vs Arm 1 , MD : -4.69 95% CI: (NC, NC)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.22 95% CI: (NC, NC)  Comparator: Arm 3 vs Arm 1 , MD : -5.10 95% CI: (NC, NC)  WOMAC total:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -25.91 95% CI: (NC, NC)  Comparator: Arm 3 vs Arm 1 , MD : -22.61 95% CI: (NC, NC)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -21.42 95% CI: (NC, NC)  Comparator: Arm 3 vs Arm 1 , MD : -21.82 95% CI: (NC, NC) |
| Perlman, 2012[121](#_ENREF_121)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: Hospital-outpatient  Multiple Sites: 2 | Total n = 125  Total # of knees = NR  Age Range: NR  Arm 1, Mean Age: 63.6 (SD 10.2) BMI: 31.7 (SD 6.5) Arm 2, Mean Age: 69.9 (SD 8.6) BMI: 31.0 (SD 7.5) Arm 3, Mean Age: 61.9 (SD 9.5) BMI: 32.1 (SD 6.8) Arm 4, Mean Age: 62.6 (SD 10.6) BMI: 31.8 (SD 6.7) Arm 5, Mean Age: 63.6 (SD 13.0) BMI: 31.3 (SD 7.1)  Female: 70.4%  Racial/Ethnic Distribution: African American 11.2%, Asian 0.8%, Caucasian 84.8%, Hispanic 0.8%, 0.8% White/Asian, 1.6% Unknown  Location of OA: NR  Subtype: NR  Diagnosis: Met the ACR criteria for knee OA  Analgesic Use: Yes, Subjects using NSAIDS or other medications to control pain were included if their doses remained stable 3 months prior to starting the intervention | Minimum Age: 35  Pre-randomization score of 40-90 on the visual analog pain scale  Subjects using NSAIDS or other medications to control pain were included if their doses remained stable 3 months prior to starting the intervention | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Concomitant or prior use of other meds  Injected hyaluronic acid in the past or during the past 1-12 months prior to enrollment month(s)  Injected corticosteroids in the prior 1-12 months prior to enrollment month(s)  Rheumatoid arthritis, fibromyalgia, recurrent or active pseudogout, cancer, or other serious medical conditions  A rash or open wound over the knee and regular use of massage therapy (greater than once a month)  Signs or history of kidney or liver failure; unstable asthma; knee replacement of both knees; reported recent use (4 weeks–1 year prior to enrollment) of oral or intra-articular corticosteroids or intra-articular hyaluronate; or knee arthroscopy or significant knee injury one year prior to enrollment | Arm 1: Control (usual care) n = 25, Dose: NR, Frequency: NR, Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR  Arm 2: Massage n = 25, Dose: 30 minutes, Frequency: Once per week, Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR  Arm 3: Massage n = 25, Dose: 30 minutes, Frequency: 2 times per week for 4 weeks, followed by once per week for 4 weeks, Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR  Arm 4: Massage n = 25, Dose: 60 minutes, Frequency: Once per week, Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR  Arm 5: Massage n = 25, Dose: 60 minutes, Frequency: 2 times per week for 4 weeks, followed by once per week for 4 weeks | VAS pain:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.90 95% CI: (-17.89, 12.09)  Comparator: Arm 3 vs Arm 1 , MD : -2.50 95% CI: (-16.81, 11.81)  Comparator: Arm 4 vs Arm 1 , MD : -7.00 95% CI: (-21.09, 7.09)  Comparator: Arm 5 vs Arm 1 , MD : -11.30 95% CI: (-27.16, 4.56)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.40 95% CI: (-18.27, 9.47)  Comparator: Arm 3 vs Arm 1 , MD : -16.30 95% CI: (-30.17, -2.43)  Comparator: Arm 4 vs Arm 1 , MD : -30.00 95% CI: (-42.09, -17.91)  Comparator: Arm 5 vs Arm 1 , MD : -21.40 95% CI: (-33.42, -9.38)  WOMAC function:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -11.10 95% CI: (-22.60, 0.40)  Comparator: Arm 3 vs Arm 1 , MD : -3.20 95% CI: (-13.32, 6.92)  Comparator: Arm 4 vs Arm 1 , MD : -7.90 95% CI: (-20.05, 4.25)  Comparator: Arm 5 vs Arm 1 , MD : -10.20 95% CI: (-21.54, 1.14)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -11.40 95% CI: (-20.90, -1.90)  Comparator: Arm 3 vs Arm 1 , MD : -10.60 95% CI: (-21.76, 0.56)  Comparator: Arm 4 vs Arm 1 , MD : -14.60 95% CI: (-24.50, -4.70)  Comparator: Arm 5 vs Arm 1 , MD : -15.40 95% CI: (-26.48, -4.32) |
| Perlman, 2012[121](#_ENREF_121) -Continued |  |  |  | Duration: 8 weeks Method of Blinding: Single-blind, measurements were assessed by separate personnel blinded to treatment assignments Co-Intervention: NR | WOMAC global:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -8.30 95% CI: (-19.08, 2.48)  Comparator: Arm 3 vs Arm 1 , MD : -1.00 95% CI: (-11.78, 9.78)  Comparator: Arm 4 vs Arm 1 , MD : -8.20 95% CI: (-19.46, 3.06)  Comparator: Arm 5 vs Arm 1 , MD : -9.10 95% CI: (-21.03, 2.83)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -11.10 95% CI: (-21.34, -0.86)  Comparator: Arm 3 vs Arm 1 , MD : -12.10 95% CI: (-23.31, -0.89)  Comparator: Arm 4 vs Arm 1 , MD : -17.70 95% CI: (-28.02, -7.38)  Comparator: Arm 5 vs Arm 1 , MD : -17.70 95% CI: (-28.50, -6.90)  WOMAC pain:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.70 95% CI: (-18.04, 8.64)  Comparator: Arm 3 vs Arm 1 , MD : 3.60 95% CI: (-8.70, 15.90)  Comparator: Arm 4 vs Arm 1 , MD : -6.20 95% CI: (-19.16, 6.76)  Comparator: Arm 5 vs Arm 1 , MD : -6.70 95% CI: (-20.19, 6.79)  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -9.50 95% CI: (-20.69, 1.69)  Comparator: Arm 3 vs Arm 1 , MD : -8.80 95% CI: (-20.75, 3.15)  Comparator: Arm 4 vs Arm 1 , MD : -21.60 95% CI: (-33.47, -9.73)  Comparator: Arm 5 vs Arm 1 , MD : -22.10 95% CI: (-33.89, -10.31) |
| Rabini, 2015[94](#_ENREF_94)  Study design: RCT  Trial name: None  Study Location: Italy  Health care setting: Hospital-outpatient  Single Site | Total n = 50  Total # of knees = NR  Mean Age(SD): 73.72 (SD 5.24) 75.08 (SD  Arm 1, Mean Age: 75.08 (SD 5.74) BMI: NR Arm 2, Mean Age: 73.72 (SD 5.24) BMI: NR  Female: 78%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2&3  Analgesic Use: Yes, Allowed rescue dose the use of 3 g of paracetamol for a maximum of 2 consecutive days. | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: chronic knee pain, for at least 3 months  Minimum Age: 60  Able to sign Consent  K-L: 2&3 | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Surgery knee limb in prior 24 month(s)  BMI > 30 kg/m2  Neurological diseases involving the lower limbs or causing balance problems, systemic inflammatory diseases; severe heart disease; acute infections or bone tuberculosis  Arthroprosthesis of lower limbs  History of surgery on the affected knee in the last two years  Active cancer or anticancer treatment | Arm 1: Sham procedure n = 25 Placebo/Sham procedure Dose: NR Frequency: 10 minutes Duration: NR Method of Blinding: Patients and the researcher responsible of the outcome assessments were unaware of patients’ allocation Co-Intervention: Allowed rescue dose of 3g of paracetamol for a maximum of 2 consecutive days and the application of ice package  Arm 2: Vibrating platform (whole body vibration) n = 25 Dose: Frequency of 100 Hz and an amplitude of approximately 0.2-0.5 mm for 10 minutes Frequency: 3 doses per day, for 3 consecutive days Duration: NR Method of Blinding: patients and the researcher responsible of the outcome assessments were unaware of patients’ allocation Co-Intervention: Allowed rescue dose of 3g of paracetamol for a maximum of 2 consecutive days and the application of ice package | WOMAC total:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -19.04 95% CI: (-27.43, -10.65) |
| Rayegani, 2014[25](#_ENREF_25)  Study design: RCT  Trial name: None  Study Location: Iran  Health care setting: Hospital-outpatient  Single Site | Total n = 62  Mean Age(SD): 56.19 (10)  Arm 1, Mean Age: 54.68 (10.83) BMI: 27.30 (3.27) Arm 2, Mean Age: 58.07 (8.95) BMI: 28.23 (4.1) Arm 3, Mean Age: BMI:  Female: 93.5%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 1-4, ACR  Analgesic Use: Yes, Acetaminophen 500 mg without codeine (up to 2g/day); a single dose of acetaminophen-codeine2 hours before injection | Diagnosis of osteoarthritis of the knee: ACR  Duration of Symptoms: 3 months  K-L: 1-4 | Concomitant or prior use of other meds  Analgesics use in the previous3 days month(s)  Injected corticosteroids in the prior 3 weeks (systemic in prior 2 weeks) month(s)  Prior acute injury to the knee  Age > 75  Diabetes mellitus, immunosuppressive and collagen vascular disorders, history of vasovagal shock, history or presence of cancer or malignant disorders, infection or active wound of the knee, Autoimmune and platelet disorders, treatment with anticoagulant and anti-platelet medications 10 days before injection, Hb < 12 g/dL platelet counts < 150,000/mL  Pregnancy or breastfeeding  Genu valgum/varum greater than 20 degrees | Arm 1: Control n = 31 Method of Blinding: No blinding Co-Intervention: Exercise and acetaminophen 500 mg without codeine  Arm 2: Platelet Rich Plasma n = 31 Dose: 4-6 mL Frequency: 2 doses 4 weeks apart Duration: 4 weeks Method of Blinding: No blinding Co-Intervention: Exercise and acetaminophen 500 mg without codeine  Arm 3: n = Dose: Frequency: Duration: Method of Blinding: Co-Intervention: | SF-36 mental health:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 1.00 95% CI: (NC, NC)  SF-36 physical health:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 1.00 95% CI: (NC, NC)  WOMAC function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 0.17 95% CI: (-5.54, 5.88)  WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.96 95% CI: (-2.88, 0.96) |
| Richette, 2011[131](#_ENREF_131)  Study design: Single arm trial  Trial name: None  Study Location: France  Health care setting: Department of Nutrition, Center of Reference for Medical and Surgical Care of Obesity  Single Site | Total n = 44  Mean Age(SD): 44 (10.3)  Arm 1, Mean Age: 44 (10.3) BMI: 50.7 (7.2)  Female: 82%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2-4  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 1 month  K-L: 2-4  VAS: >= 30 mm | Concomitant medical problems that prevent participation  Concomitant or prior use of other meds  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 1 month(s)  K-L: stage 1  Inflammatory joint disease, chondrocalcinosis of the knee  Current use of symptomatic slow-acting drugs, viscosupplementation within the past 6 month | Arm 1: Bariatric surgery n = 44 Duration: 6 months | BMI:  Follow-Up Time: 6 months : Comparator: pre-post , MD : 10.30 95% CI: (7.4, 13.2)  VAS pain:  Follow-Up Time: 6 months : Comparator: pre-post , MD : 25.50 95% CI: (15.5, 35.5)  WOMAC function:  Follow-Up Time: 6 months : Comparator: pre-post , MD : 371.30 95% CI: (219.6, 523.0)  WOMAC pain:  Follow-Up Time: 6 months : Comparator: pre-post , MD : 93.20 95% CI: (47.1, 139.3)  WOMAC stiffness:  Follow-Up Time: 6 months : Comparator: pre-post , MD : 31.80 95% CI: (11.7, 51.9)  Weight (kg):  Follow-Up Time: 6 months : Comparator: pre-post , MD : 28.60 95% CI: (19.4, 37.8) |
| Rodrigues, 2008[103](#_ENREF_103)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Academic rheumatology clinic/department  Single Site | Total n = 30  Age Range: 45-86  Arm 1, Mean Age: 61.9 (11.3) BMI: 30.6 (3.1) Arm 2, Mean Age: 61.6 (11.4) BMI: 28.9 (3.5)  Female: 100%  Racial/Ethnic Distribution: Caucasian 50%  Living Situation: NR  Location of OA: bilateral 100%  Subtype: Lateral 100%  Diagnosis: K-L: 2-4  Analgesic Use: Yes, If prescribed at least 4 weeks and 8 weeks, respectively, before entry and remained unchanged throughout the study. | Diagnosis of osteoarthritis of the knee  K-L: >=2 at lateral compartment  K-L: 0&1 at medial compartment  VAS on movement: >=2 | Prior surgery on one or both knees  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 3 month(s)  BMI>=40  Difference in lower limb length > \_x0001\_1 cm  Hallux rigidus  History of rheumatologic disease (rheumatoid arthritis, connective tissue disease, microcrystalline arthropathy, and seronegative arthropathy)  Soft tissue involvement (anserine, patellar, and calcaneal tendinopathy); foot/lower leg symptoms | Arm 1: Control n = 14 Dose: 3– 6 hours daily Duration: 8 weeks Method of Blinding: Received new shoes with insoles  Arm 2: Medial insole n = 16 Dose: 3– 6 hours daily Duration: 8 weeks Method of Blinding: Received new shoes with insoles | Lequesne index:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.40 95% CI: (-5.28, 0.48)  VAS movement:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.20 95% CI: (-4.04, -0.36)  VAS night:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-3.12, 0.12)  VAS rest:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.40 95% CI: (-2.16, 1.36)  WOMAC total:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -6.70 95% CI: (-17.09, 3.69)  Clinically significant on Lequesne index:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , RR : 0.79 95% CI: (0.59, 1.06) |
| Rogers, 2012[46](#_ENREF_46)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: Home  Single Site | Total n = 33  Mean Age: 70  Arm 1, Mean Age: 71.2(10.9) BMI: 30.8 Arm 2, Mean Age: 70.7(10.7) BMI: 28.9 Arm 3, Mean Age: 70.8(6.5) BMI: 28.2 Arm 4, Mean Age: 68.8(10.1) BMI: 29.2  Female: 60%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: bilateral 70%, unilateral 30%  Subtype: NR  Diagnosis: ACR  Analgesic Use: Yes, All participants were advised to continue usual care as prescribed by their physicians, including any use of pain medication, but not to take up any lower extremity exercise program other than the prescribed intervention | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >=1 month  Minimum Age: 50  Ambulatory  ACR: NA  WOMAC function: >=17 | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Injected hyaluronic acid in the past or during the past prior 4 weeks month(s)  Injected corticosteroids in the prior 4 weeks month(s)  Physical Therapy or Rehab or exercise in the previous 6 months month(s)  Rheumatic disease other than OA  Unresolved balance or neurological disorder  Major knee trauma, hip or knee arthroplasty, hip or ankly instability or excessive weakness | Arm 1: Control n = 8 Duration: 8 weeks Co-Intervention: Application of intert skin lotion to knees once daily  Arm 2: Agility-type exercise n = 8 Dose: 30-40 minutes Frequency: 3 times per week Duration: 8 weeks Co-Intervention: 30-second stic stretches per session  Arm 3: Strength/resistance n = 8 Dose: 15 repetitions Frequency: 3 times per week Duration: 8 weeks Co-Intervention: 30-second stic stretches per session  Arm 4: Agility- type plus strength/resistance n = 9 Dose: Comparable to individual intervention groups Frequency: 3 times per week Duration: 8 weeks | WOMAC function:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.87 95% CI: (-13.22, 1.48)  Comparator: Arm 3 vs Arm 1 , MD : -9.62 95% CI: (-19.04, -0.20)  Comparator: Arm 4 vs Arm 1 , MD : -11.98 95% CI: (-19.15, -4.81)  WOMAC pain:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.13 95% CI: (-5.86, -0.40)  Comparator: Arm 3 vs Arm 1 , MD : -3.75 95% CI: (-6.39, -1.11)  Comparator: Arm 4 vs Arm 1 , MD : -3.00 95% CI: (-5.45, -0.55)  WOMAC total:  Follow-Up Time: 8 weeks : Comparator: Arm 2 vs Arm 1 , MD : -9.00 95% CI: (-19.79, 1.79)  Comparator: Arm 3 vs Arm 1 , MD : -13.62 95% CI: (-26.37, -0.87)  Comparator: Arm 4 vs Arm 1 , MD : -15.26 95% CI: (-25.16, -5.36) |
| Rosedale, 2014[64](#_ENREF_64)  Study design: RCT  Trial name: None  Health care setting: Academic physical therapy clinic/department  Single Site | Total n = 158  Mean Age: 65  Arm 1, Mean Age: 64(11) BMI: 30.7(5.3) Arm 2, Mean Age: 64(9) BMI: 32(8.9) Arm 3, Mean Age: 68(10) BMI: 30.6(5.4)  Female: 56%  Living Situation: Community Dwelling  Subtype: NR  Diagnosis: Radiological confirmation, not otherwise described  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: > 4 months  On knee replacement waiting lists  radiologic: NR | Inability to attend exercise-based physiotherapy 2&3 times/week  Neurological conditions affecting lower extremities  Unable to understand English or provide informed consent | Arm 1: Control n = 59 Duration: NA  Arm 2: Land-based exercise, generic n = 59 Dose: 20 minutes Frequency: 4-6 sessions per 2 weeks Duration: 2 weeks  Arm 3: Land-based exercise, patient-tailored n = 40 Dose: 20 minutes Frequency: 4-6 sessions per 2 weeks Duration: 2 weeks | KOOS function:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -9.00 95% CI: (-14.28, -3.72)  KOOS pain:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -10.00 95% CI: (-15.28, -4.72)  P4 pain scale:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -3.00 95% CI: (-5.84, -0.16)  Number with improvements in KOOS function score greater than MDC:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , RR : 0.71 95% CI: (0.39, 1.30)  Number with improvements in KOOS pain score greater than MDC:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , RR : 0.77 95% CI: (0.45, 1.33) |
| Salacinski, 2012[43](#_ENREF_43)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: NR  Site size: NR | Total n = 41  Age Range: 37-74  Arm 1, Mean Age: 60.6 (8.4) BMI: 25.7 (6.3) Arm 2, Mean Age: 55.1 (10.5) BMI: 22.4 (3.3)  Female: 73%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 1-3, Mild to moderate  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 1 month+  >= 90d degree knee range of motion  Stable baseline BP  K-L: 1-3  radiographic evidence: of OAK | Concomitant medical problems that prevent participation  Personal physician sign off to participate  Knee swelling | Arm 1: Usual exercise n = 18 Placebo/Usual care Duration: 12 weeks  Arm 2: Cycling n = 19 Dose: 40-60 min Frequency: Twice a week (at least) Duration: 12 weeks | WOMAC function:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 13.10 95% CI: (3.35, 22.85)  WOMAC pain:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 15.70 95% CI: (6.20, 25.20)  WOMAC total:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 13.20 95% CI: (3.64, 22.76)  Knee related qol:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -12.50 95% CI: (-25.60, 0.60) |
| Samut, 2015[40](#_ENREF_40)  Study design: RCT  Trial name: None  Study Location: Turkey  Health care setting: Academic physical medicine/rehab department  Single Site | Total n = 42  Age Range: >=50  Arm 1, Mean Age: 60.92 (8.85) BMI: 30.36 (5.67) Arm 2, Mean Age: 62.46 (7.71) BMI: 30.54 (4.45) Arm 3, Mean Age: 57.57 (5.79) BMI: 33.94 (7.33)  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2&3, ACR  Analgesic Use: Yes, All three groups were allowed to take acetaminophen whenever needed. | Diagnosis of osteoarthritis of the knee  Sedentary lifestyle (less than 60 min of moderate to high-intensity activity per week)  ACR: diagnosis of knee OA  K-L: 2&3 | Concomitant medical problems that prevent participation  Injected hyaluronic acid in the past or during the past 3 month(s)  Injected corticosteroids in the prior 3 month(s)  Physical Therapy or Rehab or exercise in the previous 3 month(s)  Cooperation problems, depression, cognitive impairment, neurologic impairment/disease, orthopedic problems, inflammatory arthritis, cardiovascular problems, end-stage disease, immunosuppressive drug usage, and having an infection or inflammatory condition, pregnancy, and malignant disease.  Regular exercise habits | Arm 1: Control n = 13 Placebo/Control Duration: 6 weeks  Arm 2: Isokinetic exercise n = 15 Frequency: 3 days week Duration: 6 weeks  Arm 3: Aerobic exercise n = 14 Frequency: 3 days a week Duration: 6 weeks | 6-min walking test:  Follow-Up Time: 6 weeks : Comparator: Arm 3 vs Arm 1 , MD : -45.83 95% CI: (-115.76, 24.10)  WOMAC function:  Follow-Up Time: 6 weeks : Comparator: Arm 3 vs Arm 1 , MD : -15.35 95% CI: (-24.02, -6.68)  WOMAC pain:  Follow-Up Time: 6 weeks : Comparator: Arm 3 vs Arm 1 , MD : -4.02 95% CI: (-6.01, -2.03)  WOMAC total:  Follow-Up Time: 6 weeks : Comparator: Arm 3 vs Arm 1 , MD : -18.58 95% CI: (-29.65, -7.51) |
| Sattari, 2011[102](#_ENREF_102)  Study design: RCT  Trial name: None  Study Location: Iran  Health care setting: Hospital-outpatient  Multiple Sites: 3 | Total n = 60  Total # of knees = NR  Mean Age: 48 years  Arm 1, Mean Age: NR BMI: NR Arm 2, Mean Age: NR BMI: NR Arm 3, Mean Age: NR BMI: NR  Female: 63%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: Medial 100%  Diagnosis: K-L: 3&4  Analgesic Use: Yes, When needed | Diagnosis of osteoarthritis of the knee  Minimum Age: 35  Maximum Age:65  Genu varum based on radiographic evidence  Complaint of knee pain  K-L: 3&4 | Prior surgery on one or both knees  Surgery knee limb in prior NR month(s)  Whole knee degenerative joint disease  Symptomatic patellofemoral pain syndrome  Rheumatoid arthritis  BMI greater than 30  Any superimposed hip or ankle problems | Arm 1: Control group n = 20 Placebo/Control with co-intervention (see below) Dose: NA Frequency: NA Duration: 9 months Method of Blinding: Evaluated by a blind examiner Co-Intervention: Conservative management included activity modification, heating agents at home, straight leg rising and isometric quadriceps home exercises and analgesics when needed  Arm 2: Orthotics/orthoses/shoe inserts n = 20 Dose: all the time Frequency: all the time Duration: 9 months Method of Blinding: Evaluated by a blind examiner Co-Intervention: Conservative management included activity modification, heating agents at home, straight leg rising and isometric quadriceps home exercises and analgesics when needed  Arm 3: Knee brace n = 20 Dose: Wear it on and off every 2&3 hours for the first week and then put it on as long as possible during the day and take it off at nights Frequency: Daily Duration: 9 months Method of Blinding: Evaluated by a blind examiner Co-Intervention: Conservative management included activity modification, heating agents at home, straight leg rising and isometric quadriceps home exercises and analgesics when needed | VAS pain:  Follow-Up Time: 9 months : Comparator: Arm 2 vs Arm 1 , MD : -1.60 95% CI: (-2.31, -0.89)  Comparator: Arm 3 vs Arm 1 , MD : -2.80 95% CI: (-3.58, -2.02) |
| Sawitzke, 2010[28](#_ENREF_28)  Study design: RCT  Trial name: GAIT  Study Location: US  Health care setting: NR  Multiple Sites: 9 | Total n = 662  Age Range: >=40  Arm 1, Mean Age: 56.9 (9.8) BMI: 25.5 Arm 2, Mean Age: 56.7 (10.5) BMI: 27.6 Arm 3, Mean Age: 56.3 (8.8) BMI: 30.2 Arm 4, Mean Age: 56.7 (10.7) BMI: 27.1 Arm 5, Mean Age: 57.6 (10.6) BMI: 25.4  Female: 67.5%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: Tibiofemoral 100%  Diagnosis: K-L: 2&3  Analgesic Use: Yes, <= 4000 mg of acetaminophen (Tylenol, McNeil) daily | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 6 months  Minimum Age: 40  K-L: 2&3  WOMAC: 125 to 400 mm  American Rheumatism Association functional class: 1-3 | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Prior acute injury to the knee  Predominant patellofemoral disease | Arm 1: Placebo n = 131 Placebo/Capsules Frequency: Once daily Duration: 24 months Method of Blinding: Double placebo  Arm 2: Glucosamine n = 134 Dose: 500 mg Frequency: 3 times daily Duration: 24 months Method of Blinding: Double dummy  Arm 3: Chondroitin n = 126 Dose: 400 mg Frequency: 3 times daily Duration: 24 months Method of Blinding: Double dummy  Arm 4: Glucosamine and Chondroitin n = 129 Dose: 500mg and 400 mg Frequency: 3 times daily Duration: 24 months Method of Blinding: Double dummy  Arm 5: Celecoxib n = 142 Dose: 200 mg Frequency: Once daily Duration: 24 months Method of Blinding: Double dummy | WOMAC function:  Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : 9.56 95% CI: (-79.79, 98.91)  Comparator: Arm 3 vs Arm 1 , MD : 36.64 95% CI: (-64.57, 137.86)  Comparator: Arm 4 vs Arm 1 , MD : 54.41 95% CI: (-37.59, 146.41)  Comparator: Arm 5 vs Arm 1 , MD : -15.82 95% CI: (-102.31, 70.67)  WOMAC pain:  Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : -4.84 95% CI: (-28.29, 18.61)  Comparator: Arm 3 vs Arm 1 , MD : 11.50 95% CI: (-15.40, 38.40)  Comparator: Arm 4 vs Arm 1 , MD : 1.04 95% CI: (-21.44, 23.51)  Comparator: Arm 5 vs Arm 1 , MD : -13.54 95% CI: (-35.92, 8.84) |
| Schlenk, 2011[42](#_ENREF_42)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: Hospital-outpatient  Single Site | Total n = 26  Arm 1, Mean Age: 63.2 (9.8) BMI: 33.3(6) Arm 2, Mean Age: 63.2 (9.8) BMI: 33.3(6)  Female: 96  Racial/Ethnic Distribution: Caucasian 83%, NR 16%  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: Physician reported  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 50  Overweight  physician confirmation | Concomitant medical problems that prevent participation  Pending surgery  Prior acute injury to the knee  Physical Therapy or Rehab or exercise in the previous currently month(s)  Self report of current regular lower extremity exercise program or fitness walking  OA of the hip  Current participation in a drug trial  Contraindications to exercise  Inability to use phone, lack of English proficiency, inabiolity to manage own treatment | Arm 1: Control n = 13 Placebo/Usual care Dose: NA Frequency: NA Duration: 6 months Method of Blinding: NR  Arm 2: Staying Active with Arthritis (STAR) n = 13 Dose: Initial 1 hour per week sessions of strengthening and flexibility exercise followed by fitness walking Frequency: 150 minutes per week Duration: 6 months Method of Blinding: NR | 6-minute walk:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : 22.30 95% CI: (-63.28, 107.88)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 38.30 95% CI: (-50.86, 127.46)  WOMAC function:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -2.70 95% CI: (-12.78, 7.38)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -5.60 95% CI: (-17.65, 6.45) |
| Segal, 2015[60](#_ENREF_60)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: NR  Site size: NR | Total n = 58  Age Range: >=60  Arm 1, Mean Age: 69.1 (7.3) Arm 2, Mean Age: 69.6 (6.4)  Female: 66%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: I1-4  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >=30 days  Minimum Age: 60  Ambulatory  Mobility disability (LLFDI advanced lower limb function score below 32 points  defined using a definite osteophyte or joint space narrowing in either tibiofemoral compartment on posteroanterior knee radiographs16 and an affirmative response to BHave you had pain or stiffness in one or both knees on most of the past 30 days?[ on both the telephone screen and screening visit | Concomitant medical problems that prevent participation  Injected corticosteroids in the prior 3 month(s)  Conditions other than knee OA, which could affect walking, were exclusionary (e.g., amputation, severe back pain, severe peripheral vascular or heart disease and neurological or develop mental disease including multiple sclerosis, Parkinson disease, myositis, rickets, or lower limb musculoskeletal surgery in the past 6 mos).  Other prospective exclusion criteria that no volunteers met were as follows: medical conditions that may preclude safe participation in the study protocol, including but not limited to acute or terminal illness or unstable cardiovascular condition (e.g., New York Heart Association class 3&4 congestive heart failure, clinically significant aortic stenosis, history of cardiac arrest, use of a cardiac defibrillator, uncontrolled angina); report of medical conditions that may impair ability to participate including but not limited to pulm  Inability or unwillingness to comply with the study protocol or be randomized | Arm 1: Physical therapist directed gait training n = 36 Placebo/Usual care Dose: 45 min Frequency: Twice a week Duration: 3 months  Arm 2: Usual care / symptom diary n = 22 Frequency: 1-2 times a week Duration: 3-12 months: To provide a similar frequency of study contact as was provided to the gait-training participants, the control participants were given an Arthritis Foundation symptom diary and instructed to record twice each week for the first 3 mos (Sunday and Wednesday) and once a week Sunday) for the following 9 months: their knee symptoms, healthcare appointments related to their knee OA, or any changes in the way in which they treated their knee OA. The researchers contacted the control participants by telephone at 1, 2, 4, 5, 8, and 10 mos in addition to meeting with them at 3, 6, | KOOS pain:  Follow-Up Time: 12 months : Comparator: Arm 2 vs Arm 1 , MD : -7.30 95% CI: (-16.56, 1.96)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.70 95% CI: (-12.09, 4.69) |
| Segal, 2015[60](#_ENREF_60) -Continued |  |  | Inability to obtain written clearance for participation in the study by a physician  Concurrent participation in another observational or interventional research study; current consumption of more than 14 alcoholic drinks per week; and/or judgment of the principal investigator that participation would endanger the safety of an individual. |  |  |
| Simao, 2012[97](#_ENREF_97)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Academic exercise physiology lab  Single Site | Total n = 31  Mean Age: 72  Arm 1, Mean Age: 71(5.3) BMI: 26.7(2.4) Arm 2, Mean Age: 75(7.4) BMI: 27.4(9.7) Arm 3, Mean Age: 69(3.7) BMI: 29.8(2.53)  Female: 86%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: ACR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: most days of previous month  Minimum Age: 60  Osteophytes  Synovial fluid typical of OA  Crepitus  Morning stiffness 30 minutes or less  ACR: NA  K-L: 2 | Injected corticosteroids in the prior at least 2 months month(s)  Prior acute injury to the knee  Physical Therapy or Rehab or exercise in the previous 3 months month(s)  Use of any assistive walking device  The absence of the minimum clinical and cognitive conditions for performing physical activities  Orthopedic disease; neurologic, respiratory, or acute cardiac issues that prevented the performance of the required exercises; vestibular disorders; immunosuppression or immunodeficiency; lack of sphincter control (anal and bladder); or cognitive deficits | Arm 1: Control n = 11 Dose: NA Frequency: NA Duration: NA  Arm 2: Vibrating platform n = 10 Dose: NR Frequency: 3 sessions per week Duration: 12 weeks  Arm 3: Strength training n = 10 Dose: NR Frequency: 3 sessions per week Duration: 12 weeks | 6 min walk:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 3 , MD : -27.40 95% CI: (-84.05, 29.25)  WOMAC function:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 3 , MD : -122.50 95% CI: (-551.90, 306.90)  WOMAC pain:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 3 , MD : 25.00 95% CI: (-93.83, 143.83) |
| Simental-Mendia, 2016[27](#_ENREF_27)  Study design: RCT  Trial name: None  Study Location: Mexico  Health care setting:  Site size: NR | Total n = 75  Age Range: >=18  Arm 1, Mean Age: 55.6 (11.4) BMI: 29.5 (3.8) Arm 2, Mean Age: 57.2 (8.1) BMI: 32.2 (6.2)  Female: 65%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >=3 months  Minimum Age: >=18  Multiple: degenerative OA based on a detailed clinical history of knee pain, a complete physical examination and radiologic findings  K-L: I-II | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Analgesics use in the previouscurrent month(s)  Any surgical intervention of the knee, pregnancy, rheumatic disease, hepatological disease, liver disease, severe cardiovascular disease, diabetes, coagulopathy, infection, immunodepression, anticoagulant therapy, and an Hb value \11 g/dL and platelet value \150,000/lL  No use of NSAIDs | Arm 1: Acetaminophen n = 32 Placebo/Usual care Dose: 500mg Frequency: Every 8 hrs Duration: 6 weeks  Arm 2: Autologous leukocyte-poor platelet-rich plasma n = 33 Frequency: Every 2 weeks Duration: 6 weeks | SF-12 mental component:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.30 95% CI: (-6.10, 1.50)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.40 95% CI: (-11.96, -2.84)  SF-12 physical component:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -9.90 95% CI: (-14.07, -5.73)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -7.60 95% CI: (-11.72, -3.48)  VAS pain:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.20 95% CI: (-3.25, -1.15)  WOMAC total:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -12.30 95% CI: (-19.59, -5.01)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -13.40 95% CI: (-20.09, -6.71) |
| Singh, 2016[50](#_ENREF_50)  Study design: RCT  Trial name: None  Study Location: India  Health care setting: NR  Site size: NR | Total n = 30  Age Range: >=50  Arm 1, Mean Age: 54.86 (4.35) Arm 2, Mean Age: 55.33 (3.99)  Female: 53%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: Medial 100%  Diagnosis: K-L: 2&3, ACR, 30mm+ of pain on WOMAC  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >=6 months  Minimum Age: >=50  Ambulatory  Medial knee OAK  ACR: symptomatic OAK  WOMAC: >=30mm of pain while walking  K-L: 2&3 | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Injected corticosteroids in the prior 6 month(s)  Lateral tibiofemoral joint space width less than medial  Hip OA / hip trauma  Systemic arthritic conditions  Other lower limb muscular/joint/neurological conditions | Arm 1: Conventional strength training n = 15 Placebo/Usual care Frequency: 5 times a week Duration: 6 weeks  Arm 2: Hip adductor exercise n = 15 Frequency: 5 times a week Duration: 6 weeks | 6MWT:  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -58.30 95% CI: (-85.68, -30.92)  WOMAC function:  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -23.27 95% CI: (-32.73, -13.81) |
| Somers, 2012[127](#_ENREF_127)  Study design: RCT  Trial name: OA Life  Study Location: US  Health care setting: NR  Single Site | Total n = 232  Age Range: >=18  Arm 1, Mean Age: 57.94 (10.09) BMI: 34.1 (32.8–35.4) Arm 2, Mean Age: 58.13 (11.25) BMI: 34.4 (33.3–35.5) Arm 3, Mean Age: 58.27 (11.02) BMI: 33.5 (32.4–34.7) Arm 4, Mean Age: 57.47 (9.43) BMI: 34.1 (33.0–35.2)  Female: 79  Racial/Ethnic Distribution: 38% Nonwhite, 62% White  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 1-4, ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: >=6 months  Minimum Age: 18  No other joints affected by OA  BMI>=25, =<42  Provider considers OAK a condition that most contributes to limitations  Ability to read/speak English  ACR  K-L: 1-4 | Concomitant medical problems that prevent participation  Concomitant or prior use of other meds  Current use of exercise/weight loss program  Other arthritic disorder | Arm 1: Standard care n = 51 Placebo/Standard care Duration: 6 months Method of Blinding: Unblinded  Arm 2: Pain coping skills training (PCST) n = 60 Dose: 60 minutes per session Frequency: Weekly / biweekly (first/last 12 weeks) Duration: 6 months Method of Blinding: Unblinded  Arm 3: Behavioral weight management (BWM) n = 59 Dose: 60 minutes per session + 3 90 minute exercise sessions per week for first 12 weeks Frequency: Weekly / biweekly (first/last 12 weeks) Duration: 6 months Method of Blinding: Unblinded  Arm 4: PCST + BWM n = 62 Dose: 120 minutes per session + 3 90 minutes exercise sessions per week Frequency: Weekly / biweekly (first/last 12 weeks) Duration: 6 months Method of Blinding: Unblinded Co-Intervention: PCST or BWM | BMI:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -0.20 95% CI: (-0.91, 0.51)  Comparator: Arm 3 vs Arm 1 , MD : -0.60 95% CI: (-1.24, 0.04)  Comparator: Arm 4 vs Arm 1 , MD : -1.80 95% CI: (-2.44, -1.16)  WOMAC activity:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -2.30 95% CI: (-7.32, 2.72)  Comparator: Arm 3 vs Arm 1 , MD : -1.50 95% CI: (-6.46, 3.46)  Comparator: Arm 4 vs Arm 1 , MD : -12.40 95% CI: (-17.29, -7.51)  WOMAC pain:  Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : -9.00 95% CI: (-20.25, 2.25)  Comparator: Arm 3 vs Arm 1 , MD : -2.00 95% CI: (-13.18, 9.18)  Comparator: Arm 4 vs Arm 1 , MD : -14.00 95% CI: (-24.77, -3.23)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -3.50 95% CI: (-8.80, 1.80)  Comparator: Arm 3 vs Arm 1 , MD : -2.50 95% CI: (-7.67, 2.67)  Comparator: Arm 4 vs Arm 1 , MD : -10.80 95% CI: (-15.77, -5.83)  Weight (lbs):  Follow-Up Time: 24 months : Comparator: Arm 2 vs Arm 1 , MD : -1.00 95% CI: (NC, NC)  Comparator: Arm 3 vs Arm 1 , MD : -5.00 95% CI: (NC, NC)  Comparator: Arm 4 vs Arm 1 , MD : -8.00 95% CI: (NC, NC) |
| Somers, 2012[127](#_ENREF_127) -Continued |  |  |  |  | Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : 0.30 95% CI: (-3.59, 4.19)  Comparator: Arm 3 vs Arm 1 , MD : -4.20 95% CI: (-7.95, -0.45)  Comparator: Arm 4 vs Arm 1 , MD : -10.30 95% CI: (-13.92, -6.68) |
| Stambolova, 2015[34](#_ENREF_34)  Study design: RCT  Trial name: None  Study Location: Bulgaria  Health care setting: NR  Site size: NR | Total n = 191  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Analgesic Use: NR | Inclusion : NR | Exclusion : NR | Arm 1: Placebo n = 98 Placebo/Not otherwise described Frequency: Placebo once daily + physiotherapy 30 days a year Duration: 3 years Co-Intervention: Physiotherapy  Arm 2: Glucosamine n = 93 Dose: 1500 mg Frequency: GS once daily, 4 months a year; Physiotherapy 30 days a year Duration: 3 years Co-Intervention: Physiotherapy | Change in VAS pain:  Follow-Up Time: 3 years : Comparator: Arm 2 vs Arm 1 , MD : -4.60 95% CI: (NC, NC) |
| Stefanik, 2015[132](#_ENREF_132)  Study design: Single arm trial  Trial name: None  Study Location: US  Health care setting: NR  Site size: NR | Total n = 23  Age Range: 25-60  Arm 1, Mean Age: 45.7 (8.2) BMI: 41.6 (3.4)  Female: 86%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Analgesic Use: NR | Duration of Symptoms: Most days of the month  Minimum Age: 25  Maximum Age:59  BMI >=35  Approved for bariatric surgery | Exclusion : NR | Arm 1: Weight loss n = 23 | VAS Pain:  Follow-Up Time: post surgery : Comparator: pre-post , MD : 5.10 95% CI: (NC, NC)  WOMAC Pain:  Follow-Up Time: post surgery : Comparator: pre-post , MD : 27.80 95% CI: (NC, NC) |
| Toda, 2006[108](#_ENREF_108)  Study design: RCT  Trial name: None  Study Location: Japan  Health care setting: Orthopedic Rheumatology Clinic  Single Site | Total n = 61  Age Range: 63.1-66.4  Arm 1, Mean Age: 66.4 BMI: 25.00 Arm 2, Mean Age: 63.1 BMI: 24.58  Female: 100%  Racial/Ethnic Distribution: Asian 100%  Living Situation: NR  Location of OA: NR  Subtype: Medial 100%  Diagnosis: ACR  Analgesic Use: Yes, Lornoxicam (NSAID) 4mg twice daily | Diagnosis of osteoarthritis of the knee  ACR  Standing FTA: >176 degrees | Surgery knee limb in prior month(s)  Injected corticosteroids in the prior 1 month(s)  Prior acute injury to the knee  Prior experience with the intervention of interest  Steinbrocker 4  Greater or similar reduction in the lateral than the medial femorotibial joint space width  Bilateral OA, hip OA, ankle OA  Hallux rigidus, valgus deformity of the midfoot, other symptomatic deformities of the foot, advanced arthroplasty of the hindfoot | Arm 1: Traditional shoe insert n = 32 Placebo/Traditional shoe inserts Duration: 6 months  Arm 2: Wedge strapped insole n = 29 Duration: 6 months | Lequesne index:  Follow-Up Time: 2 years : Comparator: Arm 2 vs Arm 1 , MD : -2.30 95% CI: (-5.45, 0.85)  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-4.23, 1.23) |
| Trombini-Souza, 2013[111](#_ENREF_111)  Study design: Conference abstract  Trial name: None  Study Location: NR  Health care setting: NR  Site size: NR | Total n = 28  Total # of knees = NR  Age Range: NR  Arm 1, Mean Age: NR BMI: NR Arm 2, Mean Age: NR BMI: NR  Female: 100%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: K-L: 2&3  Analgesic Use: Yes, Paracetamol was permitted, dose unclear | Diagnosis of osteoarthritis of the knee: K-L: 2&3 | Physical therapy during the study duration | Arm 1: Control n = 12 Placebo/Control, did not wear similar shoes Dose: NR Frequency: NR Duration: 6 months Method of Blinding: NR Co-Intervention: NR  Arm 2: Orthotics/orthoses/shoe inserts n = 16 Dose: NA Frequency: At least 6 hours daily Duration: 6 months Method of Blinding: NR Co-Intervention: NR | WOMAC function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -37.00 95% CI: (NC, NC)  WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -44.00 95% CI: (NC, NC)  WOMAC total:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -37.00 95% CI: (NC, NC) |
| Trombini-Souza, 2015[112](#_ENREF_112)  Study design: RCT  Trial name: None  Study Location: Brazil  Health care setting: Academic rheumatology clinic/department, Physical Therapy Department  Single Site | Total n = 56  Age Range: 60-80  Arm 1, Mean Age: 66 (4) Arm 2, Mean Age: 66 (5)  Female: 100  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Medial 100%  Diagnosis: K-L: 2&3, ACR  Analgesic Use: Yes | Diagnosis of osteoarthritis of the knee  Minimum Age: 60  Maximum Age:79  Ambulatory  Able to sign Consent  ACR  K-L: 2&3  VAS: 3-8 | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Concomitant or prior use of other meds  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 3 month(s)  No leg length discrepancy greater than 1 cm  Currently not using the Moleca® or similar shoes for more than 25 hours/week | Arm 1: Waitlist control n = 28 Placebo/Waitlist Duration: 6 months Method of Blinding: Unblinded  Arm 2: Orthotic shoe n = 28 Dose: 6 hr/day Frequency: Daily Duration: 6 months Method of Blinding: Unblinded | 6 min walk (meter):  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -11.00 95% CI: (-31.81, 9.81)  Lequesne index:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -4.20 95% CI: (-6.29, -2.11)  WOMAC function:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -43.80 95% CI: (-52.70, -34.90)  WOMAC pain:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -38.60 95% CI: (-41.22, -35.98)  WOMAC total:  Follow-Up Time: 6 months : Comparator: Arm 2 vs Arm 1 , MD : -43.20 95% CI: (-55.77, -30.63) |
| Tsai, 2013[69](#_ENREF_69)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: NR  Multiple Sites: 8 | Total n = 55  Age Range: >=60  Arm 1, Mean Age: 78.93 (8.30) Arm 2, Mean Age: 78.89 (6.91)  Female: 72.7%  Racial/Ethnic Distribution: Caucasian 92.7%, 7.3% Other  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: A diagnosis of knee OA based on medical history reviewed with elders or family members/staff and confirmed by a health care provider  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 60  Ambulatory  Able to sign Consent  Mild, moderate or subtle cognitive impairment  Ability to speak English  MD's/NP's permission to participate  Verbal Descriptive Scale (VDS): >=2  estern Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Score: 3+ | Concomitant medical problems that prevent participation  Surgery knee limb in prior 6 month(s)  Physical Therapy or Rehab or exercise in the previous 1 month(s)  Fractures in last 6 months  Falls in last 3 months  Vertigo in last month | Arm 1: Attention Control n = 27 Placebo/Attention control Dose: 20-40 minutes (increasing over treatment period) Frequency: 3 sessions/week Duration: 20 weeks Method of Blinding: Unblinded  Arm 2: Tai Chi n = 28 Dose: 20-40 minutes (increasing over treatment period) Frequency: 3 sessions/week Duration: 20 weeks Method of Blinding: Unblinded | GUG:  Follow-Up Time: 21 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.15 95% CI: (-0.07, 2.37)  Follow-Up Time: 9 weeks : Comparator: Arm 2 vs Arm 1 , MD : 1.54 95% CI: (0.32, 2.76)  WOMAC pain:  Follow-Up Time: 21 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.58 95% CI: (-2.76, -0.40)  Follow-Up Time: 9 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.14 95% CI: (-2.34, 0.06)  WOMAC physical:  Follow-Up Time: 21 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.52 95% CI: (-9.70, -1.34)  Follow-Up Time: 9 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.54 95% CI: (-9.72, -1.36) |
| Wallace, 2006[107](#_ENREF_107)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: Academic sport science department  Single Site | Total n = 39  Arm 1, Mean Age: 61.0 ± 9.2 BMI: 27.9 ± 4.2 Arm 2, Mean Age: 60.8 ± 9.8 BMI: 28.7 ± 3.7  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Medial tibiofemoral 100%  Diagnosis: K-L: mean 3.2  Analgesic Use: Yes, Subjects were allowed to continue all medications and other treatments as prescribed by their physicians including over-the-counter or prescription nonsteroidal anti-inflammatory drugs (NSAIDs) | Diagnosis of osteoarthritis of the knee: physician diagnosis of medial tibiofemoral OA  Minimum Age: 39  Radiographic medial knee narrowing  Mild to moderate pain during walking  Pain more than half the days of the month  K-L: >=2 | Prior experience with the intervention of interest  Prior tibial osteotomy or total knee replacement  Significant peripheral or central nervous system disease  Clinically serious OA of the hip or ankle  Requirement for an assistive device to walk | Arm 1: Orthotics n = 18 Dose: NA Frequency: NA Duration: 12 weeks  Arm 2: Orthotics n = 18 Dose: NA Frequency: NA Duration: 12 weeks | VAS pain during stair descent:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -19.60 95% CI: (-22.70, -16.50)  VAS pain while walking:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -15.10 95% CI: (-25.69, -4.51)  WOMAC function:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.39 95% CI: (-7.95, 3.17)  WOMAC pain:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.00 95% CI: (-10.56, 0.56) |
| Wang, 2015[95](#_ENREF_95)  Study design: RCT  Trial name: None  Study Location: China  Health care setting: Academic rehabilitative medicine clinic/department  Single Site | Total n = 99  Arm 1, Mean Age: 61.5±9.1 BMI: 26.7± 1.5 Arm 2, Mean Age: 61.2±9.6 BMI: 26.1 ± 1.2  Female: 72%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: at least 3 months  Minimum Age: 40  Maximum Age:65  BMI<=30  No previous knee surgeries  ACR criteria: NA  K-L: 2&3 | Surgery knee limb in prior month(s)  Any surgery in the preceding year  Central nervous system disease, especially epilepsy and serious psychotic disorders  History of arthritis (inflammatory or metabolic disease)  Deep venous thrombosis in prior 24 weeks  Severe heart or lung disease or advanced cancer | Arm 1: Strength/resistance training n = 50 Dose: 3 sets of 10 reps, 40 minutes per day Frequency: 5 days per week Duration: 24 weeks  Arm 2: Whole body vibration n = 49 Dose: 30 minutes per day Frequency: 5 days per week Duration: 24 weeks Co-Intervention: quadriceps resistance exercise | 6 min walk (meter):  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -77.07 95% CI: (-119.18, -34.96)  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.14 95% CI: (-47.01, 40.73)  Lequesne index:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.19 95% CI: (-2.30, -0.08)  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.47 95% CI: (-1.59, 0.65)  SF-36:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -8.88 95% CI: (-12.03, -5.73)  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.89 95% CI: (-5.03, 1.25)  TUG (s):  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.01 95% CI: (-3.92, -2.10)  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.26 95% CI: (-1.22, 0.70)  VAS pain walking:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.71 95% CI: (-1.21, -0.21)  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.50 95% CI: (-1.10, 0.10)  WOMAC function:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.63 95% CI: (-5.63, 0.37) |
| Wang, 2015[95](#_ENREF_95) -Continued |  |  |  |  | Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.21 95% CI: (-2.63, 3.05)  WOMAC pain:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.49 95% CI: (-3.53, -1.45)  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.45 95% CI: (-1.40, 0.50) |
| Wang, 2015[96](#_ENREF_96)  Study design: RCT  Trial name: None  Study Location: China  Health care setting: Rehab medicine clinic  Single Site | Total n = 39  Age Range: NR  Arm 1, Mean Age: 61.5 (7.3) BMI: 26.2(2.7)  Female: 59%  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: Medial 100%  Diagnosis: K-L: NR, ACR  Analgesic Use: NR | Diagnosis of osteoarthritis of the knee  Minimum Age: 40  Maximum Age:80  Pain predominantly over medial knee  Radial evidence of medial compartment KOA  Medial joint space narrowing>lateral joint space narrowing  Medial compartment osteophyte grade>+lateral osteophyte grade  K-L: >=2  ACR | Concomitant medical problems that prevent participation  Secondary or inflammatory KOA  Ankle, hip, or foot disorders  Chronic back pain  Alzheimers, Parkinson's, motor neuron disorders, inability to understand procedure  Diabetes mellitus, cardiac or respiratory insufficiency | Arm 1: Strength/resistance training n = 20 Dose: NR Frequency: 5 days per week Duration: 12 weeks  Arm 2: Vibrating platform | 6 min walk (meter):  Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.40 95% CI: (-11.12, 4.32)  TUG (s):  Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.30 95% CI: (-3.25, 0.65)  VAS pain:  Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-1.39, 0.19)  WOMAC function:  Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.60 95% CI: (-4.78, 3.58)  WOMAC pain:  Follow-Up Time: 16 weeks : Comparator: Arm 2 vs Arm 1 , MD : -0.10 95% CI: (-2.17, 1.97) |
| Wang, 2016[70](#_ENREF_70)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: Medical center (inpatient?)  Single Site | Total n = 204  Age Range: >=40  Arm 1, Mean Age: 60.1 (10.5) BMI: 32.6 (7.3) Arm 2, Mean Age: 60.3 (10.5) BMI: 33.0 (7.1)  Female: 70% (71% T, 69% C)  Racial/Ethnic Distribution: African American 39% T, 32% C, Asian 4% T, 2% C, Caucasian 53% (51% T, 55% C), 7% T, 11% C, NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: ACR; radiographic evidence of tibiofemoral or patellofemoral osteoarthritis  Analgesic Use: Yes, Participants were permitted to continue using routine medications, such as NSAIDs and acetaminophen, and maintain their usual physician visits throughout the study. Participants were not required to discontinue use of their pain medications before formal assessment visits. We kept a written record of changes in use of analgesics and NSAIDs throughout the entire intervention and evaluation period. We did not change or recommend changes in medical therapy. | Diagnosis of osteoarthritis of the knee  Minimum Age: >=40  Required to have a score of 40 or greater on at least 1 of the 5 questions in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale (range of 0 to 100, with higher scores indicating greater pain) at baseline.  ACR: criteria for symptomatic knee osteoarthritis  radiographic evidence: d radiographic evidence of tibiofemoral or patellofemoral osteoarthritis (defined as the presence of a definite osteophyte in the tibiofemoral compartment and/or the patellofemoral compartment, as assessed on standing anterior– posterior and lateral or sunrise views) | Concomitant medical problems that prevent participation  Prior surgery on one or both knees  Injected hyaluronic acid in the past or during the past 6 month(s)  Injected corticosteroids in the prior 3 month(s)  Prior experience with the intervention of interest  Erious medical conditions, such as dementia, symptomatic heart or vascular disease, or recent stroke, that would limit full participation  Score less than 24 on the Mini-Mental State Examination | Arm 1: Physical therapy n = 98 Placebo/Usual care Dose: 30 minutes Frequency: Twice a week with physical therapist for 6 weeks; Four times a week with phone followup for last 6 weeks Duration: 12 weeks Method of Blinding: Single-blind  Arm 2: Tai chi n = 106 Dose: 60 min Frequency: Twice a week Duration: 12 weeks Method of Blinding: Single-blind | 6MWT:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.40 95% CI: (-22.30, 13.50)  Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -4.30 95% CI: (-26.02, 17.42)  SF-36 mental health:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.10 95% CI: (-3.87, 1.67)  Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.40 95% CI: (-4.09, 1.29)  SF-36 physical health:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.70 95% CI: (-6.53, -0.87)  Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -2.00 95% CI: (-4.90, 0.90)  WOMAC function:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -131.10 95% CI: (-251.35, -10.85)  Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -88.30 95% CI: (-223.31, 46.71)  WOMAC pain:  Follow-Up Time: 24 weeks : Comparator: Arm 2 vs Arm 1 , MD : -34.30 95% CI: (-69.74, 1.14)  Follow-Up Time: 52 weeks : Comparator: Arm 2 vs Arm 1 , MD : -17.80 95% CI: (-58.18, 22.58) |
| Wortley, 2013[45](#_ENREF_45)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: NR  Single Site | Total n = 31  Arm 1, Mean Age: 70.5 (5.0) BMI: 30.0(6.2) Arm 2, Mean Age: 69.5(6.7) BMI: 30.5(6.0) Arm 3, Mean Age: 68.1(5.3) BMI: 35.1(5.9)  Female: 22/31  Racial/Ethnic Distribution: NR  Living Situation: Community Dwelling  Location of OA: NR  Subtype: NR  Diagnosis: ACR  Analgesic Use: Yes, Groups were asked not to alter their regular physical activity or pain medications during the intervention programs | Diagnosis of osteoarthritis of the knee  Minimum Age: 60  Maximum Age:85  ACR: NR  K-L: 1-4 | Injected hyaluronic acid in the past or during the past 3 month(s)  Injected corticosteroids in the prior 3 month(s)  Arthroscopic surgery within prior 3 months  Participated in a resistance training or Tai Ji in the past 6 months  Neurological disorders | Arm 1: Control n = 6 Placebo/No activity Dose: NA Frequency: NA Duration: 10 weeks  Arm 2: Land-based exercise: strength/resistance n = 13 Dose: 5 or 10 lb. weight, 1 hour per session, two sets of eight repetitions to three sets of 12 repetitions during the first 6 weeks Frequency: 2 sessions per week Duration: 10 weeks  Arm 3: Tai Chi n = 12 Dose: 1 hour per session Frequency: 2 sessions per week Duration: 10 weeks | 6 min walk:  Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : 33.40 95% CI: (-66.24, 133.04)  Comparator: Arm 3 vs Arm 1 , MD : 75.60 95% CI: (-26.73, 177.93)  TUG (s):  Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.50 95% CI: (-0.85, 1.85)  Comparator: Arm 3 vs Arm 1 , MD : 0.60 95% CI: (-0.91, 2.11)  WOMAC function:  Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : -235.00 95% CI: (-498.13, 28.13)  Comparator: Arm 3 vs Arm 1 , MD : 77.00 95% CI: (-239.40, 393.40)  WOMAC pain:  Follow-Up Time: 10 weeks : Comparator: Arm 2 vs Arm 1 , MD : -86.00 95% CI: (-180.10, 8.10)  Comparator: Arm 3 vs Arm 1 , MD : -16.00 95% CI: (-113.80, 81.80) |
| Yildirim, 2010[77](#_ENREF_77)  Study design: RCT  Trial name: None  Study Location: Turkey  Health care setting: Home, Physical therapy outpatient clinic  Site size: NR | Total n = 46  Total # of knees = 80  Age Range: 58.78  Arm 1, Mean Age: 58.78 (SD 9.55) BMI: 29.24 (SD 3.33) Arm 2, Mean Age: 58.78 (SD 10.56) BMI: 30.67 (SD 5.37)  Female: 84.8%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: Diagnosed with knee OA according to ACR criteria  Analgesic Use: Yes, When recruited, patients underwent an outpatient pharmacological treatment such as NSAID and paracetamol. Patients were allowed to continue routine medication. | Diagnosis of osteoarthritis of the knee  Able to sign Consent  Literate  ACR: Diagnosis of knee OA | Concomitant medical problems that prevent participation  Prior acute injury to the knee  Acute trauma or inflammation around the leg  Cardiac pacemaker  Sensitivity or allergy for heat  Communication disorder or psychological problems  Sensory complications, peripheral vascular diseases, tendency to haemorrhage, oedema on the knee, large scar tissue, malignancy, or deformity to attract the attention during examination or thigh OA | Arm 1: Control n = 23 Placebo/Control, received home visit 2 times Dose: NA Frequency: Visited 2 times Duration: 4 weeks Method of Blinding: NR Co-Intervention: Training guideline with equal information on OA, its effects and treatment based on the available literature  Arm 2: Heat n = 23 Dose: 20 minutes Frequency: Visited 15 times Duration: 4 weeks Method of Blinding: NR Co-Intervention: Training guideline with equal information on OA, its effects and treatment based on the available literature | SF-36 pain:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -10.95 95% CI: (-20.79, -1.11)  SF-36 physical function:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -12.61 95% CI: (-21.49, -3.73)  WOMAC function:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -6.05 95% CI: (-9.65, -2.45)  WOMAC pain:  Follow-Up Time: 4 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.85 95% CI: (-3.15, -0.55) |
| Zegels, 2013[37](#_ENREF_37)  Study design: RCT  Trial name: None  Study Location: Belgium, France, Switzerland  Health care setting: Hospital-outpatient  Multiple Sites: 10 | Total n = 352  Age Range: >=45  Arm 1, Mean Age: 64.9 (10.6) BMI: 28.6 (5.3) Arm 2, Mean Age: 65.4 (10.4) BMI: 28.8 (5.2) Arm 3, Mean Age: 65.3 (8.8) BMI: 28.4 (4.4)  Female: 64.6%  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Diagnosis: ACR  Analgesic Use: Yes, Paracetamol 500 mg up to 4g | Diagnosis of osteoarthritis of the knee: ACR  Minimum Age: 45  VAS: >=40mm  Lequesne index: >=7 | Concomitant medical problems that prevent participation  Surgery knee limb in prior 3 month(s)  Pending surgery  Concomitant or prior use of other meds  Injected hyaluronic acid in the past or during the past 6 month(s)  Prior experience with the intervention of interest  Genu varum or valgum >8 degrees  Arthritis and metabolic arthropathies, Paget’s illness  Pregnancy | Arm 1: Placebo n = 117 Placebo/Matching sachets and capsules Frequency: Sachet once daily, capsule three times daily Duration: 3 months Method of Blinding: Double dummy  Arm 2: Chondroitin n = 117 Dose: 1200 mg Frequency: Once daily Duration: 3 months Method of Blinding: Double dummy  Arm 3: Chondroitin n = 119 Dose: 400 mg Frequency: 3 times daily Duration: 3 months Method of Blinding: Double dummy | Lequesne function:  Follow-Up Time: 2 months : Comparator: Arm 2 vs Arm 1 , MD : -1.50 95% CI: (-2.62, -0.38)  Comparator: Arm 3 vs Arm 1 , MD : -1.50 95% CI: (-2.59, -0.41)  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -1.90 95% CI: (-3.11, -0.69)  Comparator: Arm 3 vs Arm 1 , MD : -2.20 95% CI: (-3.37, -1.03)  VAS pain:  Follow-Up Time: 3 months : Comparator: Arm 2 vs Arm 1 , MD : -7.70 95% CI: (-14.43, -0.97)  Comparator: Arm 3 vs Arm 1 , MD : -8.30 95% CI: (-15.20, -1.40) |
| Zhang, 2012[119](#_ENREF_119)  Study design: RCT  Trial name: None  Study Location: US  Health care setting: NR  Site size: NR | Total n = 36  Age Range: 50-70  Arm 1, Mean Age: 59.86 (4.91) BMI: 28.46 (4.05) Arm 2, Mean Age: 63.47 (2.64) BMI: 28.89 (4.16)  Female: 100  Racial/Ethnic Distribution: NR  Living Situation: NR  Location of OA: NR  Subtype: NR  Analgesic Use: Yes, Stable use in previous month | Diagnosis of osteoarthritis of the knee  Duration of Symptoms: 6 months  Minimum Age: 50  Maximum Age:69  Otherwise Healthy  Able to sign Consent  Female  BMI<=35  Health good to satisfactory  Pain in the knee in the preceding 2 weeks \_3/10 on a Likert pain scale from 1–10,  Stable treatment with nonsteroidal anti inflammatory drugs and analgesics in the previous month, (9) if receiving glucosamine, a stable dose for the past 2 months,  Unspecified diagnosis of OAK  Mild/moderate symptoms of OAK: Most days last month | Concomitant medical problems that prevent participation  Injected corticosteroids in the prior 2 month(s)  Prior experience with the intervention of interest  Knee or hip replacement  Current treatment of acupuncture for knee pain  Autoimmune dis ease that caused joint pain such as rheumatoid arthritis and lupus  Severe unstable chronic illness or terminal dis ease | Arm 1: Usual care n = 21 Placebo/Usual care Duration: 12 weeks Method of Blinding: Unblinded  Arm 2: Acupressure n = 15 Dose: 30 minutes Frequency: 5 times a week; 2 training session and 1 conclusion session Duration: 12 weeks Method of Blinding: Unblinded | WOMAC function:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.88 95% CI: (-10.58, 6.82)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.40 95% CI: (-12.56, 5.76)  WOMAC pain:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : 0.08 95% CI: (-2.36, 2.52)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -1.15 95% CI: (-3.45, 1.15)  WOMAC total:  Follow-Up Time: 12 weeks : Comparator: Arm 2 vs Arm 1 , MD : -3.74 95% CI: (-15.65, 8.17)  Follow-Up Time: 6 weeks : Comparator: Arm 2 vs Arm 1 , MD : -5.51 95% CI: (-16.97, 5.95) |