PHYSIOTHERAPY THEORY AND PRACTICE
https://doi.org/10.1080/09593985.2025.2575837

Taylor & Francis
Taylor & Francis Group

RESEARCH REPORT

Effect of dose interval of periosteal and intraarticular electrical dry needling boosters on pain and disability in patients with knee osteoarthritis: a multi-center randomized clinical trial

James Dunning PhD, DPT, MSc[a,b,c], Ian Young DSc, PT[b,d], Norman Taylor MD, PhD[e], Firas Mourad PhD, PT[f,g], Paul Bliton DPT, FAAOMPT[b,h], Raymond Butts PhD, DPT[b,i], James Escaloni DPT, FAAOMPT[b], Patrick Gorby DPT, MPH[b,j], Rejoy Varghese DPT, MSc[k], Filippo Maselli PhD, PT[l], and César Fernández-de-Las-Peñas PhD, PT[a,m]

[a]Department of Physical Therapy, Occupational Therapy, Rehabilitation and Physical Medicine, Universidad Rey Juan Carlos, Alcorcón, Spain; [b]American Academy of Manipulative Therapy Fellowship in Orthopaedic Manual Physical Therapy, Montgomery, Alabama, USA; [c]Montgomery Osteopractic Physical Therapy & Acupuncture, Montgomery, Alabama, USA; [d]Tybee Wellness & Osteopractic, Tybee Island, Georgia, USA; [e]Department of Anesthesiology, University of Utah School of Medicine, Salt Lake City, Utah, USA; [f]Department of Physiotherapy, LUNEX International University of Health, Exercise and Sports, Differdange, Luxembourg; [g]Luxembourg Health & Sport Sciences Research Institute, Differdange, Luxembourg; [h]William Middleton VA Hospital, Madison, Wisconsin, USA; [i]Symmetry Physical Therapy, Miami, Florida, USA; [j]Gorby Physiotherapy, Colorado Springs, Colorado, USA; [k]Carrollton Regional Medical Center, Carrollton, Texas, USA; [l]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy; [m]Cátedra de Clínica, Investigación Y Docencia En Fisioterapia: Terapia Manual, Punción Seca Y, Ejercicio, Universidad Rey Juan Carlos, Alcorcón, Spain

ABSTRACT

Background: Periosteal and intraarticular electrical dry needling (PIEDN) has been found to reduce pain, stiffness, and disability in individuals with knee osteoarthritis (OA) in the short-term. Optimum dosing interval of PIEDN to maintain these improvements in the longer-term has yet to be determined.

Objective: Compare the longer-term effects (30 weeks) of three different dosing intervals of PIEDN boosters on pain, stiffness, and disability in individuals with knee OA, and to quantify the effect size of PIEDN as a stand-alone treatment.

Methods: Patients with knee OA ($n = 586$) received PIEDN (1–2 times per week) over 6 weeks. Patients were then randomized to receive a PIEDN booster session once every 4 weeks ($n = 195$), once every 8 weeks ($n = 197$), or no further treatment ($n = 194$) for the next 6 months. The primary outcome was the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index.

Results: Patients receiving PIEDN every 4 weeks experienced significantly greater improvements in disability (WOMAC: $F = 33.060$; $p < .001$) than those receiving PIEDN every 8 weeks, or those receiving no further treatment. Patients receiving PIEDN boosters every 4 weeks experienced significantly greater improvements in pain (NPRS: $F = 25.678$, $p < .001$; WOMAC-Pain: $F = 22.816$, $p < .001$), stiffness (WOMAC-Stiffness: $F = 27.416$, $p < .001$) and function (WOMAC-Physical Function: $F = 32.856$; $p < .001$). The between-group effect size was large (WOMAC: SMD = 1.32; 95% CI: 1.10, 1.54) at 30 weeks in favor of the group that received PIEDN every 4 weeks. The between-group effect size was large for the NPRS (SMD = 1.14; 95% CI: 0.93, 1.36) at 30 weeks for the PIEDN-4 group. At 30 weeks, significantly more patients in the PIEDN-4 group ($n = 123$, 63.1%) had completely stopped taking medication compared to the control group ($X^2 = 70.158$; $p < .001$; $n = 41$, 21.1%).

Conclusion: PIEDN boosters every 4 weeks were a more effective dosage regimen for maintaining improvements in pain, stiffness, function, and disability than once every 8 weeks or no further treatment sessions.

Trial Registration: www.clinicaltrials.gov NCT05365061 May 4, 2022.

ARTICLE HISTORY
Received 17 July 2025
Revised 11 October 2025
Accepted 11 October 2025

KEYWORDS
Knee osteoarthritis; dry needling; periosteal; Intraarticular; dosage; frequency; interval; treatment

Introduction

The pooled global prevalence of knee osteoarthritis (OA) has been estimated to be 23% in individuals aged 40 and above (Cui et al., 2020). Knee OA is considered the most common joint disease in middle-aged and older adults (Cross et al., 2014). The pathogenesis of knee OA may include degeneration of articular cartilage with osteophyte formation, microfractures, subchondral

CONTACT James Dunning drjamesdunning@gmail.com The Study was Approved by the Ethics Committee at Universidad Rey Juan Carlos, Madrid, Spain

sclerosis and plate thickening, synovial hyperplasia, and exposure of the articular end of the bone (Yunus, Nordin, and Kamal, 2020).

Several meta-analyses and international clinical guidelines recommend exercise (Fransen et al., 2015; Jansen et al., 2011) and acupuncture (Corbett et al., 2013; Lin et al., 2016; Zhang et al., 2010) as two non-pharmacological interventions for individuals suffering from knee OA. Although statistically significant benefits for various forms of exercise in individuals with moderate knee OA have been found, small effect sizes for pain (SMD: 0.24) and physical function (SMD: 0.15) are to be expected at 2–6 months follow-up (Fransen et al., 2015). In comparision, Zhang et al. (2010) concluded that acupuncture was superior to usual care and wait-list controls with a pooled effect size of 0.58 for pain relief in patients with knee OA. This effect size is higher than most other conservative treatments applied to patients with knee OA, including NSAIDs (0.32), muscle strengthening exercises (0.32) and aerobic exercises (0.52) (Zhang et al., 2010).

Pain may be a potential barrier leading to underdosage of strength training and aerobic exercise stimulus in individuals with painful knee OA; therefore, needling therapies may be a reasonable non-pharmacologic alternative for the reduction of persistent pain in individuals participating in exercise programs for knee OA (Corbett et al., 2013; Lin et al., 2016). Needling therapy refers to the insertion of thin monofilament needles for therapeutic purposes without the use of injectate (Dunning et al., 2014). However, unlike traditional Chinese acupuncture, Western medical acupuncture or dry needling neither attempts to move *qi* along meridians, nor does it rely on diagnoses from Oriental medicine (Deadman, Al-Khafaji, and Baker, 2011; Dunning et al., 2014; Zhou, Ma, and Brogan, 2015).

Targeting the periosteum with acupuncture needles is not a new approach in the treatment of knee OA (Dunning et al., 2018; Elbadawy, 2017; Weiner et al., 2007, 2013; Zhang, Bao, Wang, and Wu, 2016). Following 4 weeks of 7-point low-frequency electroacupuncture in 100 knees, Zhang, Bao, Wang, and Wu, (2016) reported significantly lower T2 values in cartilage on MRI at the anteromedial and anterolateral tibial subregions, suggesting electroacupuncture may play a role in cartilage repair in individuals with knee OA. In 2018, a multi-center clinical trial ($n = 242$) found that the addition of a 9-point periosteal electrical dry needling (PEDN) protocol to a program of manual therapy and exercise resulted in significant reductions in pain, stiffness, and disability compared to manual therapy and exercise alone (SMD = 0.94) in patients with knee OA in the short-term (Dunning et al., 2018). However, the effect size of PEDN when used as a stand-alone treatment has yet to be determined.

Electroacupuncture has been found to suppress the local release of proinflammatory cytokines (i.e., IL-1β and TNF-α) in cartilage, synovium, and subchondral bone of osteoarthritic joints, thereby attenuating pathological pain and cellular cascades associated with the degenerative process (Huang et al., 2007; Lou and Bu, 2025). In an animal model of knee OA, electroacupuncture has also been shown to decrease cartilage hypoxia by improving synovial microcirculation and fluid oxygen tension (Weiwei et al., 2024); moreover, electroacupuncture may stimulate cartilage repair in individuals with knee OA (Zhang, Bao, Wang, and Wu, 2016). Nevertheless, no prior PEDN or electroacupuncture clinical trials have incorporated intraarticular needle placements to evaluate whether this approach may augment the effectiveness of the intervention.

After completing a course of standard care for musculoskeletal conditions, there is a "pressing need to evaluate the effectiveness of regular follow-up via booster sessions for maintaining the beneficial effect of interventions" over longer periods of time (Abbott et al., 2015; Paterno and Fitzgerald, 2024). Moreover, extended care models, or a "booster visit care model," have been recommended to provide structured intermittent care for a more efficacious and cost-effective system of care for musculoskeletal pain conditions (Paterno and Fitzgerald, 2024). To date, there are just two prior randomized clinical trials that have investigated the sustained efficacy of PEDN boosters in patients with knee OA (Elbadawy, 2017; Weiner et al., 2013).

The purpose of this clinical trial was to compare the longer-term effects of three different dosing intervals of periosteal and intraarticular electrical dry needling (PIEDN) boosters on pain, stiffness, and disability in individuals with painful knee OA, and to quantify the effect size of PIEDN when used as a stand-alone treatment for knee OA.

Methods

Study design

This randomized, single-blinded, multi-center, parallel-group clinical trial compared three dosing intervals of PIEDN boosters for the management of knee OA. The primary outcome was related-disability as assessed by the Western Ontario and McMaster Universities (WOMAC total score) Osteoarthritis Index at 30 weeks. Secondary outcomes included knee pain

intensity as measured by the Numeric Pain Rating Scale (NPRS), all WOMAC subscales (pain: WOMAC-P; stiffness: WOMAC-S; physical function: WOMAC-PF) , medication intake, and the Global Rating of Change (GROC). The current clinical trial was conducted following the Consolidated Standards of Reporting Trials (CONSORT) extension for pragmatic clinical trials (Zwarenstein et al., 2008). The study was approved by the ethics committee at Universidad Rey Juan Carlos, Madrid, Spain (URJC-DPTO 47–2021) and the trial was registered (ClinicalTrials.gov:NCT05365061) on May 4, 2022. All participants provided written informed consent prior to enrollment.

Participants

Consecutive individuals with painful knee OA from 64 outpatient physical therapy clinics in 26 different U.S. states (Alabama, Arizona, Arkansas, Colorado, Connecticut, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Michigan, Minnesota, Mississippi, Montana, Nebraska, New Jersey, North Carolina, Ohio, Oklahoma, South Carolina, Tennessee, Texas, Wisconsin) and one British Overseas Territory (Anguilla) were screened for eligibility criteria and recruited over a 38-month period (from March 2021 to May 2024).

For patients to be eligible, they had to meet the American College of Rheumatology criteria for the diagnosis of knee OA (Altman, 1991; Altman et al., 1986) and have had chronic pain in the knee joint for more than 3 months. The clinical diagnosis of knee OA is typically made using the American College of Rheumatology clinical criteria developed by Altman, which has been found to be 89% sensitive and 88% specific (Altman, 1991; Altman et al., 1986; Wang et al., 2024). Patients had to have at least three of the following criteria to be included in the study: 1, >50 years of age; 2, less than 30 min of morning stiffness; 3, crepitus on active motion; 4, bony tenderness; 5, bony enlargement; and 6, no palpable warmth of synovium (Altman, 1991; Altman et al., 1986). In addition, the participants had to have a minimum knee pain intensity score of 2 points and be older than 18 years of age.

Patients were excluded from the study if they: 1, had received an injection to the affected knee in the last 4 weeks; 2, had a history of a partial or total knee replacement to the affected knee; 3, had a history of surgery to either lower extremity in the last 12 months; 4, had received physical therapy, massage therapy, acupuncture, or chiropractic for their knee pain in the previous 4 weeks; 5, were waiting for knee replacement surgery; 6, presented with two or more positive neurologic signs consistent with nerve root compression; 7, had a history of a psychiatric disorder or cognitive impairment; 8, presented with one or more contraindications to dry needling; 9, had pending litigation or worker's compensation regarding their knee pain; or 10, were currently pregnant. Additionally, before enrollment into the study, patients were instructed that treatment for their knee pain by other healthcare practitioners (i.e., injections, massage therapy, chiropractic, and physical therapy) was not permitted.

Treating therapists

Sixty-five physical therapists (mean age, 36.2 years, SD 7.6) participated in the delivery of treatment for patients in this study. They had an average of 10.1 (SD 8.1) years of clinical experience, an average of 3.9 (SD 2.6) years using dry needling, and all had completed a 54-hr post-graduate certification program that included practical training in periosteal and intraarticular electrical dry needling for knee OA. All participating physical therapists were required to study a manual of standard operating procedures and participate in a 4-hr training session. All treating therapists were Fellows-in-Training within a nationally accredited, post-graduate Fellowship program in Orthopaedic Manual Physical Therapy.

Randomization and blinding

Following a baseline examination, all patients received 8–10 sessions of PIEDN over 6 weeks using a 23-point standardized protocol. Patients were then randomly assigned to 1 of 3 dosing interval groups: (1) a PIEDN booster treatment once every 4 weeks for the next 6 months, (2) a PIEDN booster treatment once every 8 weeks for the next 6 months, or (3) no booster treatments over the next 6 months. Concealed allocation was conducted using a computer-generated randomized table of numbers created by a statistician who was not otherwise involved in the trial and did not participate in analysis or interpretation of the results. Individual and sequentially numbered index cards with the random assignment were prepared for each of the 64 data collection sites. The index cards were folded and placed in sealed opaque envelopes. Blinded to the baseline examination, the treating therapist opened the envelope and proceeded with treatment, according to the group assignment. The examining therapist remained blind to the patient's treatment group assignment; however, based on the nature of the interventions it was not possible to blind patients or therapists.

Interventions

All participants in all three groups received 8–10 treatment sessions of PIEDN at a frequency of 1–2 times per week over the initial 6-week period using a 23-point standardized dry needling protocol. At 6 weeks, participants were then randomized to receive PIEDN once every 4 weeks ($n = 195$) for the next 6 months, PIEDN once every 8 weeks ($n = 197$) for the next 6 months, or no further treatment sessions ($n = 194$) for the next 6 months. Each PIEDN treatment session included a 23-point standardized protocol as depicted in Figure 1. During the course of the study, patients were encouraged to continue to perform their normal daily activities, but were not permitted to receive any interventions for their knee pain by other healthcare practitioners including, but not limited to injections, massage therapy, chiropractic, and/or physical therapy.

Sterilized disposable stainless steel acupuncture needles were used, ranging from 30 mm to 75 mm in length and from 0.25 mm to 0.35 mm in diameter. The depth of needle insertion ranged from 25 mm to 70 mm and depended on the point selected (intramuscular, periosteal, intraarticular, joint line, periarticular), and the patient's physical constitution. Following insertion, all needles were manipulated and rotated bidirectionally to elicit a sensation of aching, tingling, deep pressure, heaviness, or warmth (Dunning et al., 2018; Zhou and Benharash, 2014).

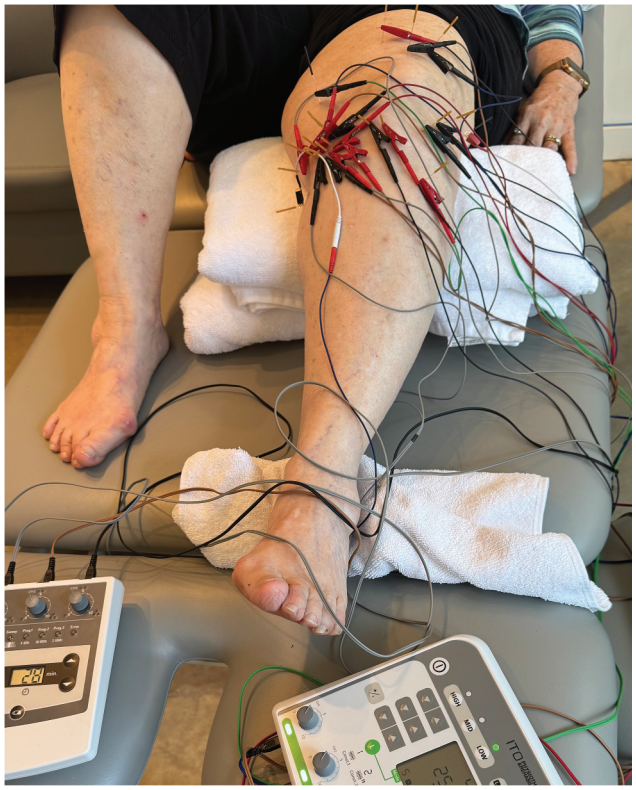

Figure 1. Standardized 23-point protocol of periosteal and intraarticular electrical dry needling (PIEDN) for knee OA.

Four of the 23 obligatory needles were intraarticular insertions via the medial infrapatellar sulcus (2 needles) and lateral infrapatellar sulcus (2 needles) to a 25–35-mm perpendicular depth using 30 mm ×0.25 mm or 40 mm ×0.30 mm needles (Delgado et al., 2019; Zhang, Bao, Wang, and Wu, 2016). Notably, in patients with knee OA, perpendicular needle insertions at the medial or lateral infrapatellar sulcus to a depth of 25–35 mm are considered intraarticular on ultrasound imaging (Delgado et al., 2019; Toda and Tsukimura, 2008; Zhang, Bao, Wang, and Wu, 2016). In addition, 8 needles passed through muscle, tendon, and/or connective tissue down to the periosteum of the femur or tibia (Dunning et al., 2018), and the remaining 11 needles were placed 1 cm above (3 needles) the anteromedial or anterolateral tibiofemoral joint line, 1 cm below (3 needles) the anteromedial or anterolateral tibiofemoral joint line, or at the anteromedial or anterolateral tibiofemoral joint line (5 needles). The decision to target the anteromedial versus anterolateral aspects of the tibiofemoral joint line area was based on each patient's symptoms. Notably, the 19 obligatory needles that targeted the periosteum were repeatedly thrusted and tapped on to the respective bone using a "periosteal stimulation" technique (Dunning et al., 2018; Weiner et al., 2013). In addition to the obligatory 23-point standardized protocol, clinicians were also permitted to insert needles at up to four additional locations based on the presence of the symptoms.

The needles were then left in situ for 30 mins with electric stimulation (two ES-160 electrostimulator ITO co.) in pairs to 22 of the needles using a low frequency (2 Hz), moderate pulse duration (250 microseconds), and biphasic continuous waveform at a maximum tolerable intensity (Dunning et al., 2018; Vas and White, 2007). Eleven channels of the two electroacupuncture units were used; thus, based on symptom distribution, the treating clinician left one needle without electrical stimulation. In cases of bilateral knee OA, both knees were treated, but only the most painful side at baseline was recorded and analyzed throughout the study to satisfy the assumption of independent data (Menz, 2005).

Outcome measures

The primary outcome was related-disability as assessed with the WOMAC total index score, whereas each WOMAC subscale [pain (WOMAC-

P), stiffness (WOMAC-S), and physical function (WOMAC-PF)] were considered secondary outcomes. The WOMAC is a valid and reliable instrument and has been used extensively to evaluate three dimensions (pain, stiffness, and physical function) in patients with hip or knee OA (Bellamy et al., 1988; McConnell, Kolopack, and Davis, 2001). In patients with knee OA, the minimum clinically important difference (MCID) for the WOMAC has been calculated to be 16.1 points (Kim et al., 2021).

Secondary outcomes included knee pain intensity, the 3 WOMAC subscales, medication intake, and the GROC. The NPRS was used to measure knee pain intensity. Patients were asked to indicate the average intensity of knee pain over the past week using an 11-point scale ranging from 0 ("no pain") to 10 ("worst pain imaginable") at baseline, 6 weeks, 14 weeks, 22 weeks, and 30 weeks following the initial treatment session (Jensen, Karoly, and Braver, 1986). The NPRS is a reliable and valid instrument to assess pain intensity (Farrar, Young, LaMoreaux, and Poole, 2001). The MCID for the NPRS has been shown to be 1.74 in patients with chronic pain conditions (Farrar, Young Jp, LaMoreaux, and Poole, 2001); however, the MCID for knee-related pain has not yet been established. Nevertheless, a change of 2 points or a 30% decrease in pain from baseline can be considered as a MCID in subjects with chronic musculoskeletal pain (Farrar, Young, LaMoreaux, and Poole, 2001; Salaffi et al., 2004).

Medication intake was measured as the number of times the patient had taken prescription or over-the-counter analgesic or anti-inflammatory medication in the past week for their knee pain, with five options: (1) not at all, (2) once a week, (3) once every couple of days, (4) once or twice a day, or (5) three or more times a day. Medication intake was assessed at baseline and at 30 weeks after the first treatment session.

At 6 weeks, 14 weeks, 22 weeks, and 30 weeks following the initial treatment session, patients completed a 15-point GROC question based on a scale described by Jaeschke, Singer, and Guyatt, (1989) to rate their self-perceived improved function. The MCID for the GROC has not been specifically reported but scores of +4 and +5 have typically been indicative of moderate changes in patient status (Jaeschke, Singer, and Guyatt, 1989).

Treatment side effects

Patients were asked to report adverse events that they experienced during any part of the study. In the current study, an adverse event was defined as a sequelae of one-week duration with any symptom perceived as distressing and unacceptable to the patient that required further treatment (Carlesso, Macdermid, and Santaguida, 2010). Particular attention was given to the presence of ecchymosis and post-needling soreness.

Sample size determination

The sample size calculations were based on detecting a between-group moderate effect size of 0.40 (Dunning et al., 2018) in related-disability (WOMAC total index score) at 30 weeks, assuming a 2-tailed test, an alpha level (α) of 0.01, and a desired power (β) of 90%. The estimated desired sample size was calculated to be at least 188 subjects per group. A dropout percentage of 10% was expected; therefore, 206 patients were required for each group.

Statistical analysis

Statistical analysis was performed using SPSS software, version 29.0 (Chicago, IL, USA) and it was conducted according to intention-to-treat analysis. We performed Little's Missing Completely at Random (MCAR) test (Rubin, Witkiewitz, Andre, and Reilly, 2007) to determine if missing data points associated with dropouts were missing at random or missing for systematic reasons. Intention-to-treat analysis was performed by using Expectation-Maximization whereby missing data was computed using regression equations.

The effects of treatment on pain, stiffness, physical function, and related-disability were each examined with a 3-by-5 mixed-model analysis of covariance (ANCOVA) with treatment group as the between-subjects factor, time as the within-subjects factor, and adjusted for baseline data (i.e., age, weight, height, and duration of symptoms). Separate ANCOVAs were performed with each outcome as the dependent variable. For each ANCOVA, the main hypothesis of interest was the 2-way interaction (group by time) with a Bonferroni-corrected alpha level of 0.01 (5 time points). We used $\chi 2$ tests to compare self-perceived improvement with GROC and changes in medication intake. To enable comparison of between-group effect sizes, standardized mean differences (SMDs) were calculated by dividing mean score differences between groups by the pooled standard deviation. Numbers needed to treat (NNT) and 95% confidence intervals (CI) were also calculated at the 30-week follow-up period using each definition for a successful outcome.

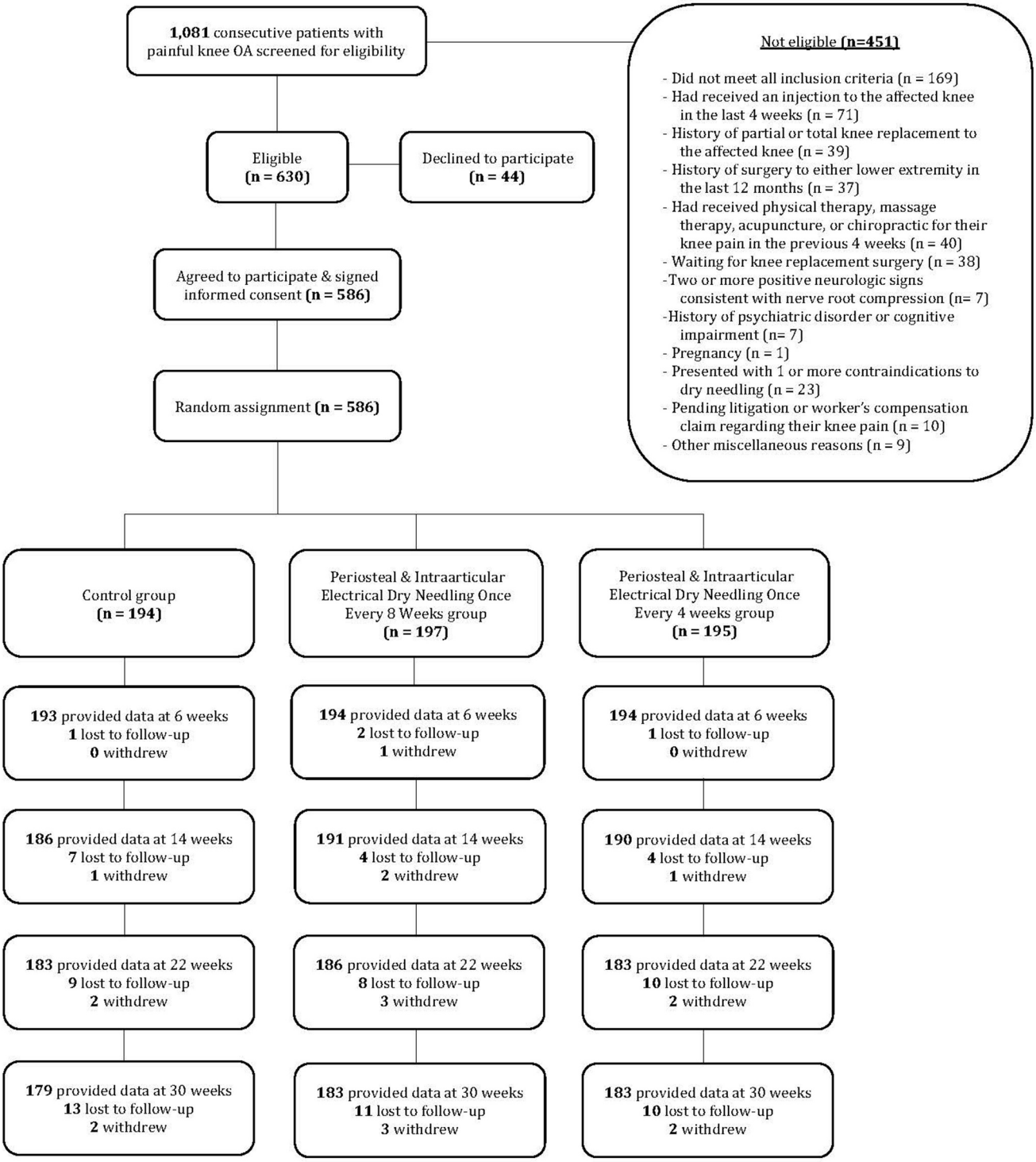

Figure 2. CONSORT flow diagram of patient recruitment and retention.

RESULTS

Between March 2021 and May 2024, 1,081 consecutive patients with knee OA pain were screened for eligibility (Figure 2). Five hundred and eighty-six (54.2%) satisfied all the inclusion criteria and agreed to participate. All participants ($n = 586$) received 8–10 sessions of PIEDN over the initial 6 weeks using a 23-point standardized periosteal and intraarticular electrical dry needling (PIEDN) protocol. At 6 weeks, participants were then randomly allocated to the PIEDN once every 4 weeks ($n = 195$) for the next 6 months, PIEDN once every 8 weeks ($n = 197$) for the next 6 months, or the control group

Table 1. Baseline characteristics by treatment assignment.

Baseline Variable	Control ($n = 194$)	PIEDN booster once every 8 weeks ($n = 197$)	PIEDN booster once every 4 weeks ($n = 195$)
Gender (male/female)	85/109	83/114	82/113
Age (years)	57.1 ± 12.7	56.9 ± 13.1	57.3 ± 11.6
Weight (kg)	85.1 ± 15.5	86.1 ± 16.3	86.2 ± 15.8
Height (cm)	171.5 ± 9.1	171.9 ± 9.3	172.1 ± 9.7
Years with knee pain	7.5 ± 7.4	7.7 ± 6.8	7.4 ± 7.8
Medication intake n (%)			
Not at all	13 (6.7%)	24 (12.2%)	15 (7.7%)
Once a week	24 (12.4%)	31 (15.7%)	37 (19.0%)
Once every couple of days	66 (34.0%)	58 (29.4%)	63 (32.3%)
Once or twice a day	76 (39.2%)	68 (34.5%)	60 (30.8%)
Three or more times a day	15 (7.7%)	16 (8.1%)	20 (10.3%)
Number of treatment sessions	7.9 ± 1.7	7.8 ± 1.6	7.9 ± 1.8
Mean intensity of knee pain (NPRS, 0–10)	5.8 ± 1.6	5.7 ± 1.8	5.7 ± 1.7
WOMAC Pain Scale (0–20)	9.5 ± 3.2	9.3 ± 3.2	9.5 ± 3.0
WOMAC Stiffness Scale (0–8)	4.2 ± 1.5	4.3 ± 1.6	4.3 ± 1.5
WOMAC Physical Function Scale (0–68)	31.9 ± 8.9	32.0 ± 9.7	32.1 ± 8.8
WOMAC Total Score (0–96)	45.6 ± 12.8	45.6 ± 13.7	45.9 ± 12.5

Data are mean (SD) except for gender and medication intake.
PIEDN = periosteal intraarticular electrical dry needling, NPRS = Numeric Pain Rating Scale, 0–10, lower scores indicate less pain; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, 0–96, lower scores indicate less pain and related-disability.

with no further treatment sessions ($n = 194$) for the next 6 months. Randomization resulted in similar baseline characteristics for all variables (Table 1). The reasons for ineligibility are found in Figure 2, which provides a flow diagram of patient recruitment and retention. From baseline to 6 weeks, there was no significant difference ($p = .776$) between the mean number of completed treatment sessions for the PIEDN once every 8 weeks group (mean: 7.8 ± 1.6), the PIEDN once every 4 weeks group (mean: 7.9 ± 1.8), and the control group (mean: 7.8 ± 1.7). In total, 545 of the 586 patients (93% follow-up) completed all outcome measures through 30 weeks (Figure 2). None of the participants in any group reported receiving other interventions during the study.

During the initial 6-week PIEDN intervention period, 341 of the 586 patients (58.2%) experienced post-needling muscle soreness and 184 (31.4%) experienced mild bruising (ecchymosis) that most commonly resolved spontaneously within 48 hr and 2–4 days, respectively. In addition, 8 of the 586 patients (1.4%) experienced drowsiness, headache, or nausea, which spontaneously resolved within several hours. No other adverse events were reported.

Adjusting for baseline outcomes, the mixed-model ANCOVA revealed a significant group-by-time interaction for the primary outcome of related-disability (WOMAC: $F = 33.060$; $p < .001$, Figure 3). Patients in the PIEDN-4 group experienced significantly greater improvements in related-disability at 22 weeks (Δ −9.4, 95% CI: −11.7, −7.0, $p < .001$) and 30 weeks (Δ −16.9, 95% CI: −19.4, −14.3, $p < .001$) than those in the control group (Tables 2 and 3).

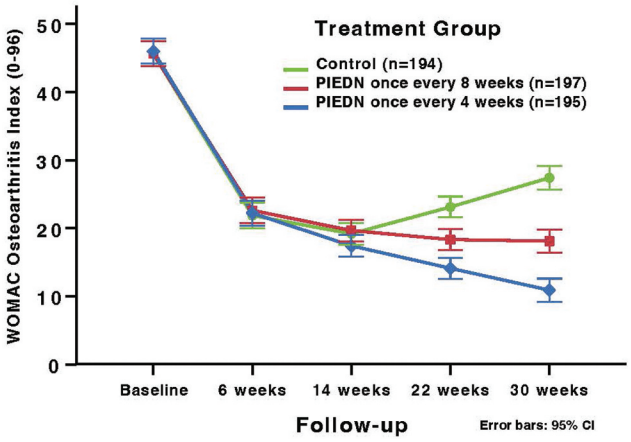

Figure 3. Evolution of the WOMAC Osteoarthritis Index (0–96) throughout the course of the study stratified by randomized treatment assignment. Data are means (standard error).

Notably, patients in the PIEDN-4 group experienced significantly greater improvements in related-disability at 22 weeks (Δ −4.2, 95% CI: −6.3, −2.2, $p < .001$) and 30 weeks (Δ −7.2, 95% CI: −9.4, −5.0, $p < .001$) than those in the PIEDN-8 group (Table 3). Likewise, patients in the PIEDN-8 group experienced significantly greater improvements in related-disability at 22 weeks (Δ −4.8, 95% CI: −7.2, −2.4, $p < .001$) and 30 weeks (Δ −9.3, 95% CI: −11.9, −6.7, $p < .001$) than those in the control group (Figure 3). For the WOMAC, the between-group effect size (compared with the control group) was medium (SMD: 0.72, 95% CI: 0.52, 0.93) at 30 weeks for the PIEDN-8 group and large (SMD: 1.32; 95% CI: 1.10, 1.54) at 30 weeks for the PIEDN-4 group (Table 3).

Table 2. Within-group mean scores by randomized treatment assignment*.

Outcomes	Timeline Scores: Mean ± SD (95% CI) Within-Group Change Scores: Mean (95% CI)		
	Control (*n* = 194) †	PIEDN booster once every 8 weeks (*n* = 197)	PIEDN booster once every **4 weeks (*n* = 195)**
WOMAC-P: Pain (0–20)			
Baseline	9.5 ± 3.2 (9.1, 10.0)	9.3 ± 3.2 (8.9, 9.8)	9.5 ± 3.0 (9.1, 9.9)
6 weeks	4.3 ± 3.1 (3.9, 4.8)	4.2 ± 2.8 (3.8, 4.6)	4.2 ± 2.7 (3.9, 4.6)
Change baseline → 6 weeks	−5.2 ± 3.0 (−5.6, −4.8)	−5.1 ± 3.0 (−5.5, −4.7); $p = .710$	−5.3 ± 2.7 (−5.7, −4.9); $p = .834$
14 weeks	3.6 ± 2.8 (3.2, 4.0)	3.5 ± 2.5 (3.2, 3.9)	3.1 ± 2.1 (2.8, 3.4)
Change baseline → 14 weeks	−5.9 ± 2.9 (−6.3, −5.5)	−5.8 ± 2.8 (−6.2, −5.4); $p = .738$	−6.4 ± 2.8 (−6.8, −6.0); $p = .077$
22 weeks	4.3 ± 2.8 (3.9, 4.7)	3.3 ± 2.4 (2.9, 3.6)	2.5 ± 2.2 (2.2, 2.9)
Change baseline → 22 weeks	−5.2 ± 2.7 (−5.6, −4.8)	−6.0 ± 2.9 (−6.5, −5.6); $p = .004$	−7.0 ± 3.0 (−7.4, −6.6); $p < .001$
30 weeks	5.3 ± 3.0 (4.9, 5.7)	3.4 ± 2.4 (3.1, 3.7)	2.2 ± 2.3 (1.9, 2.5)
Change baseline → 30 weeks	−4.2 ± 2.9 (−4.6, −3.8)	−5.9 ± 3.0 (−6.3, −5.5); $p < .001$	−7.3 ± 3.1 (−7.8, −6.9); $p < .001$
WOMAC-S: Stiffness (0–8)			
Baseline	4.2 ± 1.5 (4.0, 4.4)	4.3 ± 1.6 (4.1, 4.5)	4.3 ± 1.5 (4.1, 4.5)
6 weeks	2.1 ± 1.5 (1.9, 2.3)	2.2 ± 1.7 (2.0, 2.5)	2.3 ± 1.7 (2.1, 2.6)
Change baseline → 6 weeks	−2.1 ± 1.7 (−2.4, −1.9)	−2.1 ± 1.7 (−2.3, −1.8); $p = .892$	−2.0 ± 1.6 (−2.2, −1.8); $p = .534$
14 weeks	1.8 ± 1.4 (1.6, 2.0)	1.9 ± 1.5 (1.7, 2.2)	1.9 ± 1.5 (1.7, 2.1)
Change baseline → 14 weeks	−2.4 ± 1.7 (−2.2, −2.6)	−2.4 ± 1.6 (−2.6, −2.1); $p = .748$	−2.4 ± 1.6 (−2.7, −2.2); $p = .825$
22 weeks	2.2 ± 1.4 (2.0, 2.4)	1.8 ± 1.2 (1.6, 1.9)	1.4 ± 1.2 (1.2, 1.6)
Change baseline → 22 weeks	−2.0 ± 1.4 (−2.2, −1.8)	−2.5 ± 1.5 (−2.8, −2.3); $p < .001$	−2.9 ± 1.6 (−3.1, −2.7); $p < .001$
30 weeks	2.7 ± 1.4 (2.5, 2.9)	1.8 ± 1.3 (1.6, 2.0)	1.0 ± 1.2 (0.9, 1.2)
Change baseline → 30 weeks	−1.5 ± 1.3 (−1.7, −1.4)	−2.5 ± 1.6 (−2.7, −2.3); $p < .001$	−3.3 ± 1.5 (−3.5, −3.1); $p < .001$
WOMAC-PF: Physical Function (0–68)			
Baseline	31.9 ± 8.9 (30.6, 33.2)	32.0 ± 9.7 (30.7, 33.4)	32.1 ± 8.8 (30.9, 33.4)
6 weeks	15.4 ± 9.5 (14.1, 16.8)	16.2 ± 9.2 (14.9, 17.5)	15.6 ± 9.0 (14.4, 16.9)
Change baseline → 6 weeks	−16.5 ± 9.8 (−17.9, −15.1)	−15.8 ± 9.7 (−17.2, −14.5); $p = .519$	−16.5 ± 9.2 (−17.8, −15.2); $p = .965$
14 weeks	13.7 ± 8.6 (12.5, 15.0)	14.2 ± 7.8 (13.1, 15.3)	12.4 ± 7.2 (11.4, 13.5)
Change baseline → 14 weeks	−18.2 ± 8.5 (−19.4, −17.0)	−17.8 ± 9.0 (−19.1, −16.5); $p = .691$	−19.7 ± 8.9 (−21.0, −18.5); $p = .075$
22 weeks	16.6 ± 8.4 (15.4, 17.8)	13.4 ± 7.3 (12.3, 14.4)	10.2 ± 7.2 (9.2, 11.2)
Change baseline → 22 weeks	−15.3 ± 7.9 (−16.4, −14.2)	−18.7 ± 9.2 (−19.9, −17.4); $p < .001$	−22.0 ± 9.1 (−23.3, −20.7); $p < .001$
30 weeks	19.5 ± 9.8 (18.1, 20.9)	12.9 ± 8.1 (11.8, 14.1)	7.7 ± 7.6 (6.6, 8.7)
Change baseline → 30 weeks	−12.4 ± 8.6 (−13.6, −11.2)	−19.1 ± 9.9 (−20.5, −17.7); $p < .001$	−24.5 ± 9.7 (−25.9, −23.1); $p < .001$
WOMAC: Total Index (0–96)			
Baseline	45.6 ± 12.8 (43.8, 47.4)	45.6 ± 13.7 (43.7, 47.5)	45.9 ± 12.5 (44.2, 47.7)
6 weeks	21.9 ± 13.5 (20.0, 23.8)	22.6 ± 13.2 (20.8, 24.5)	22.2 ± 12.9 (20.4, 24.0)
Change baseline → 6 weeks	−23.7 ± 13.6 (−25.7, −21.8)	−23.0 ± 13.5 (−24.9, −21.1); $p = .587$	−23.8 ± 12.5 (−25.5, −22.0); $p = .981$
14 weeks	19.2 ± 12.2 (17.5, 20.9)	19.7 ± 11.1 (18.1, 21.2)	17.4 ± 10.2 (16.0, 18.9)
Change baseline → 14 weeks	−26.4 ± 11.9 (−28.1, −24.7)	−26.0 ± 12.4 (−27.7, −24.2); $p = .704$	−28.6 ± 12.1 (−30.3, −26.8); $p = .079$
22 weeks	23.1 ± 12.1 (21.4, 24.8)	18.3 ± 10.4 (16.9, 19.8)	14.1 ± 10.2 (12.7, 15.6)
Change baseline → 22 weeks	−22.5 ± 11.1 (−24.1, −20.9)	−27.3 ± 12.8 (−29.1, −25.5); $p < .001$	−31.9 ± 12.6 (−33.6, −30.1); $p < .001$
30 weeks	27.4 ± 13.8 (25.4, 29.4)	18.1 ± 11.5 (16.5, 19.7)	10.9 ± 10.7 (9.4, 12.4)
Change baseline → 30 weeks	−18.2 ± 12.1 (−19.9, −16.5)	−27.5 ± 13.7 (−29.4, −25.6); $p < .001$	−35.1 ± 13.4 (−37.0, −33.2); $p < .001$
Numeric Pain Rating Scale (0–10)			
Baseline	5.8 ± 1.6 (5.6, 6.0)	5.7 ± 1.8 (5.5, 6.0)	5.7 ± 1.7 (5.5, 6.0)
6 weeks	2.7 ± 1.8 (2.4, 2.9)	2.7 ± 1.7 (2.4, 2.9)	2.6 ± 1.6 (2.4, 2.9)
Change baseline → 6 weeks	−3.1 ± 2.1 (−3.4, −2.8)	−3.0 ± 2.0 (−3.3, −2.8); $p = .623$	−3.1 ± 1.8 (−3.4, −2.8); $p = .853$
14 weeks	2.2 ± 1.7 (2.0, 2.5)	2.3 ± 1.5 (2.1, 2.5)	1.8 ± 1.1 (1.7, 2.0)
Change baseline → 14 weeks	−3.6 ± 1.9 (−3.8, −3.3)	−3.4 ± 2.0 (−3.7, −3.1); $p = .465$	−3.9 ± 1.7 (−4.2, −3.7); $p = .052$
22 weeks	2.8 ± 1.6 (2.6, 3.0)	2.2 ± 1.5 (2.0, 2.4)	1.6 ± 1.5 (1.3, 1.8)
Change baseline → 22 weeks	−3.0 ± 1.7 (−3.2, −2.7)	−3.5 ± 1.9 (−3.8, −3.2); $p = .006$	−4.2 ± 1.8 (−4.5, −3.9); $p < .001$
30 weeks	3.4 ± 1.7 (3.2, 3.7)	2.2 ± 1.5 (1.9, 2.3)	1.3 ± 1.6 (1.1, 1.5)
Change baseline → 30 weeks	−2.4 ± 1.7 (−2.6, −2.1)	−3.6 ± 1.9 (−3.8, −3.3); $p < .001$	−4.5 ± 1.9 (−4.7, −4.2); $p < .001$

Timeline Scores: Mean ± SD (95% CI), Within-Group Change Scores: Mean (95% CI).
*p values are for tests of treatment effect comparative to those of the control group.
†No p values as inferential tests are comparative with those of the control group.
PIEDN = periosteal intraarticular electrical dry needling, NPRS, lower scores indicate less pain; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, 0–96, lower scores indicate less pain and related-disability.

Secondary outcomes

Significant group-by-time interactions were found for all the WOMAC subscales (WOMAC-P: F = 22.816, $p < .001$; WOMAC-S: F = 27.416, $p < .001$; WOMAC-PF: F = 32.856, $p < .001$) in favor of the PIEDN-4 group (Table 3). For the WOMAC subscales, the between-group effect sizes (compared with the control group) were medium ($0.57 < SMD < 0.72$) at 30 weeks for the PIEDN-8 group and large ($1.03 < SMD < 1.31$) at 30 weeks for the PIEDN-4 group (Table 3).

The intention-to-treat analysis also revealed a significant group-by-time interaction for knee pain

Table 3. Between-group differences and effect sizes comparative to the control group*.

	Between-Group Differences: Mean (95% CI) Standardized Mean Differences: Mean (95% CI)	
Outcome	PIEDN booster once every 8 weeks (n = 197)	PIEDN booster once every 4 weeks (n = 195)
WOMAC-P: Pain (0–20)		
Change baseline → 6 weeks	0.1 (−0.5, 0.7); SMD = 0.04 (−0.16, 0.24); p = .710	−0.1 (−0.6, 0.5); SMD = 0.02 (−0.17, 0.22); p = .834
Change baseline → 14 weeks	0.1 (−0.5, 0.6); SMD = 0.03 (−0.16, 0.23); p = .738	−0.5 (−1.1, 0.1); SMD = 0.18 (−0.02, 0.38); p = .077
Change baseline → 22 weeks	−0.8 (−1.4, −0.3); SMD = 0.30 (0.10, 0.49); p = .004	−1.8 (−2.3, −1.2); SMD = 0.62 (0.41, 0.82); p < .001
Change baseline → 30 weeks	−1.7 (−2.3, −1.1); SMD = 0.57 (0.36, 0.77); p < .001	−3.1 (−3.7, −2.5); SMD = 1.03 (0.81, 1.24); p < .001
WOMAC-S: Stiffness (0–8)		
Change baseline → 6 weeks	0.0 (−0.3, 0.4); SMD = 0.01 (−0.18, 0.21); p = .892	0.1 (−0.2, 0.4); SMD = 0.06 (−0.26, 0.14); p = .534
Change baseline → 14 weeks	0.1 (−0.3, 0.3); SMD = 0.03 (−0.17, 0.23); p = .748	0.0 (−0.4, 0.3); SMD = 0.02 (−0.18, 0.22); p = .825
Change baseline → 22 weeks	−0.5 (−0.8, −0.2); SMD = 0.35 (0.15, 0.55); p < .001	−0.9 (−1.2, −0.6); SMD = 0.61 (0.40, 0.81); p < .001
Change baseline → 30 weeks	−1.0 (−1.2, −0.7); SMD = 0.64 (0.43, 0.84); p < .001	−1.7 (−2.0, −1.4); SMD = 1.19 (0.98, 1.41); p < .001
WOMAC-PF: Physical Function (0–68)		
Change baseline → 6 weeks	0.6 (−1.3, 2.6); SMD = 0.07 (−0.13, 0.26); p = .519	0.0 (−1.9, 1.8); SMD = 0.01 (−0.20, 0.19); p = .965
Change baseline → 14 weeks	0.4 (−1.4, 2.1); SMD = 0.04 (−0.16, 0.24); p = .691	−1.6 (−3.3, 0.2); SMD = 0.18 (−0.02, 0.38); p = .075
Change baseline → 22 weeks	−3.4 (−5.1, −1.7); SMD = 0.39 (0.19, 0.59); p < .001	−6.7 (−8.4, −5.0); SMD = 0.78 (0.57, 0.99); p < .001
Change baseline → 30 weeks	−6.7 (−8.5, −4.8); SMD = 0.72 (0.51, 0.92); p < .001	−12.1 (−13.9, −10.3); SMD = 1.31 (1.09, 1.53); p < .001
WOMAC: Total Index (0–96)		
Change baseline → 6 weeks	0.7 (−1.9, 3.4); SMD = 0.06 (−0.14, 0.25); p = .587	0.0 (−2.6, 2.5); SMD = 0.00 (−0.20, 0.20); p = .981
Change baseline → 14 weeks	0.5 (−2.0, 2.9); SMD = 0.04 (−0.16, 0.24); p = .704	−2.1 (−4.5, 0.3); SMD = 0.18 (−0.02, 0.37); p = .079
Change baseline → 22 weeks	−4.8 (−7.2, −2.4); SMD = 0.40 (0.20, 0.60); p < .001	−9.4 (−11.7, −7.0); SMD = 0.79 (0.58, 0.99); p < .001
Change baseline → 30 weeks	−9.3 (−11.9, −6.7); SMD = 0.72 (0.52, 0.93); p < .001	−16.9 (−19.4, −14.3); SMD = 1.32 (1.10, 1.54); p < .001
Numeric Pain Rating Scale (0–10)		
Change baseline → 6 weeks	0.1 (−0.3, 0.5); SMD = 0.05 (−0.15, 0.25); p = .623	0.0 (−0.3, 0.4); SMD = 0.02 (−0.18, 0.22); p = .853
Change baseline → 14 weeks	0.1 (−0.2, 0.5); SMD = 0.07 (−0.12, 0.27); p = .465	−0.4 (−0.7, 0.0); SMD = 0.20 (−0.01, 0.40); p = .052
Change baseline → 22 weeks	−0.5 (−0.9, −0.1); SMD = 0.28 (0.08, 0.48); p = .006	−1.2 (−1.6, −0.9); SMD = 0.69 (0.49, 0.90); p < .001
Change baseline → 30 weeks	−1.2 (−1.5, −0.8); SMD = 0.64 (0.44, 0.85); p < .001	−2.1 (−2.4, −1.7); SMD = 1.14 (0.93, 1.36); p < .001

Between-Group Differences: Mean (95% CI), Standardized Mean Differences: Mean (95% CI).

*p values and SMD values are for tests of treatment effect comparative to the control group.

PIEDN = periosteal intraarticular electrical dry needling; NPRS, lower scores indicate less pain; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, 0–96, lower scores indicate less pain and related-disability.

Large between-group effect size: Cohen's d = .8 or greater. Medium effect size: Cohen's d = .5 or greater. Small effect size: Cohen's d = .2 or greater. Effect size provides information about the magnitude or strength of the difference between two groups.

(NPRS) intensity (F = 25.678; p < .001) in favor of the PIEDN-4 group (Table 2). For knee pain intensity (NPRS), the between-group effect size (compared with the control group) was medium (SMD: 0.64; 95% CI: 0.44, 0.85) at 30 weeks for the PIEDN-8 group and large (SMD = 1.14; 95% CI: 0.93, 1.36) at 30 weeks for the PIEDN-4 group (Table 3).

At 30 weeks, significantly more patients in the PIEDN-4 group (n = 123, 63.1%) had completely stopped taking medication for their pain compared to the control group (X^2 = 70.158; p < .001; n = 41, 21.1%), or the PIEDN-8 group (X^2 = 14.950; p < .001; n = 77, 39.1%). At the 30-week follow-up and based on the cutoff score of ≥ +5 on the GROC, significantly more patients (n = 142, 72.8%) within the PIEDN-4 group achieved a successful outcome when compared to the control (X^2 = 88.028; p < .001; n = 49, 25.3%) group or the PIEDN-8 (X^2 = 35.553; p < .001; n = 108, 54.8%) group. Therefore, compared with the control group and based on the cutoff score of ≥ +5 on the GROC, the NNT was 2.10 (95% CI: 1.78, 2.58) in favor of the PIEDN-4 group at 30-week follow-up. Likewise, compared with the control group and based on a 50% improvement from baseline to 30 weeks in the primary outcome (WOMAC), the NNT was 1.83 (95% CI: 1.59, 2.14) in favor of the PIEDN-4 group at 30-week follow-up.

Discussion

In individuals with painful knee OA, the PIEDN dosing interval of once every 4 weeks was a more effective dosage regimen for maintaining improvements in pain, stiffness, physical function, medication intake, and related-disability at long-term (30 weeks) than the dosing interval of once every 8 weeks or no further treatment sessions. For middle-aged or older adults with painful knee OA, PIEDN with monthly boosters may provide an alternative and cost-effective treatment option for those wanting to avoid adverse drug reactions or surgery.

For the primary outcome (WOMAC), the between-group effect size (compared with the control group) was medium (SMD: 0.72, 95% CI: 0.52, 0.93) at 30 weeks for the PIEDN-8 group and large (SMD: 1.32; 95% CI: 1.10, 1.54) at 30 weeks for the PIEDN-4 group. The point estimate (16.9 points, 95% CI: 14.3, 19.4) for the between-group difference (PIEDN-4 group comparative to the control group) of the WOMAC, exceeded the

MCID (i.e., 16.1 points) for that instrument at 30 weeks (Kim et al., 2021). For the NPRS, the point estimate for the between-group change (2.1 points, 95% CI: 1.7, 2.4) exceeded the reported MCID (i.e., 1.74 points (Farrar, Young, LaMoreaux, and Poole, 2001; Salaffi et al., 2004)) at 30 weeks.

To date, there are just two randomized clinical trials that have investigated the sustained efficacy of PEDN and boosters in patients with painful knee OA (Elbadawy, 2017; Weiner et al., 2013). Similar to the findings of our study, after an initial 10-week (once per week) treatment protocol of periosteal stimulation therapy (with acupuncture needles touching the bone over the medial femoral condyle, lateral femoral condyle, medial tibial condyle, and head of the fibula) and following monthly boosters for 6 months in patients with advanced knee OA, Elbadawy (Elbadawy, 2017) ($n = 60$) reported statistically and clinically meaningful improvements in pain (VAS) and all 5 KOOS subscales (i.e., pain, symptoms, activities of daily living, sport and recreation function, knee-related quality of life) compared to TENS and a home exercise program. Additionally, after 6 months of periosteal stimulation boosters, large within-group effect sizes (SMD: 1.30 to 5.62) were reported for pain, function, and quality of life (i.e., all 5 KOOS subscales) (Elbadawy, 2017).

In contrast to the findings of our study, after an initial 10-week treatment period in patients with advanced knee OA (i.e., KL grade 3 and grade 4 disease), although Weiner et al. (2013) found periosteal stimulation ($n = 190$) with monthly boosters was superior to periosteal stimulation without boosters or with placebo boosters at 6 months, only "modest reductions" in pain were reported. Notably, neither within-group nor between-group effect sizes were reported (Weiner et al., 2013). However, the authors concluded their sample size was insufficient to achieve statistical significance (Weiner et al., 2013). Compared with the large effect size found in the present study, Weiner et al. (2013) used only four needles and did not place any needles through the synovium to target inside the knee joint. Notably, in an individual patient meta-analysis of 17,922 patients with chronic pain in 29 randomized controlled trials, superior pain outcomes were observed when a higher number of needles were used (MacPherson et al., 2013). Moreover, "adequate" dosage of acupuncture (i.e., higher number of needles, the use of electroacupuncture rather than manual acupuncture, strong intensity of electric stimulation, a course of 8–10 treatment sessions, treatment durations of 20–30 min, and "deep needling" at the medial and lateral infrapatellar sulcus) may explain why some clinical trials found larger effect sizes on pain and disablity in patients with knee OA (Dunning et al., 2018; Vas and White, 2007; Vas et al., 2004; White, Foster, Cummings, and Barlas, 2007). Additionally, in our study, we utilized a low frequency (2 Hz) electrical stimulation at a high intensity (i.e., "maximum tolerable intensity") (Ahsin et al., 2009; Dunning et al., 2018; Sangdee et al., 2002; Taechaarpornkul et al., 2009; Yuan et al., 2024) in comparison to the low intensity ("perceptible but not painful") and high frequency (100 Hz) periosteal stimulation used in the (Weiner et al., 2013) protocol. Notably, according to a recent meta-analysis of patients with knee OA, low-frequency (2 Hz) and high-intensity electroacupuncture provides superior pain relief and has a more profound effect on emotional scale scores than low-intensity electroacupuncture (Yuan et al., 2024). Lastly, in the short/intermediate term follow-up, exercise for knee OA has been reported to have a small effect size for function (SMD = 0.15), a small effect size for pain (SMD; range = 0.24 to 0.36) (Fransen et al., 2015; Serrano-García et al., 2025), and effect sizes of "questionable clinical importance" on pain and disability (Holden et al., 2023). Manual therapy is reported to have a large effect size (SMD = 0.79) in the immediate/short-term (Serrano-García et al., 2025), while the addition of manual therapy to exercise has a medium effect size (SMD = 0.56) in the long term (Runge, Aina, and May, 2022). However, the large between-group effect size found in the current trial (WOMAC: SMD = 1.32; 95% CI: 1.10, 1.54) should not be directly compared to the aforementioned studies that are considered "conservative" interventions, as dry needling (more specifically intraarticular and periosteal needling) is classified by the American Medical Association as an "invasive procedure" rather than a conservative intervention (American Medical Association, 2016).

Although the current study did not investigate the underlying neurophysiological mechanisms of PIEDN, electroacupuncture has been found to: (1) block the local release of proinflammatory cytokines (i.e., IL-1β and TNF-α) in cartilage, synovium, and subchondral bone of osteoarthritic joints (Huang et al., 2007; Lou and Bu, 2025), (2) decrease cartilage hypoxia by improving synovial microcirculation and fluid oxygen tension in knee OA (Weiwei et al., 2024), (3) significantly lower T2 values in tibial weightbearing cartilage on MRI, suggesting a role in cartilage repair (Weiwei et al., 2024; Zhang, Bao, Wang, and Wu, 2016), (4) reduce IL-6 mRNA expression in bone marrow, thereby limiting inflammation and inhibiting myelogenic osteoclast activity driving degeneration (Liu et al., 2004; Zhang et al., 2017), (5) stimulate sympathetic fibers in

proximity to the periosteum to modulate knee joint microcirculation (Loaiza, Yamaguchi, Ito, and Ohshima, 2002), and (6) inhibit the NLRP3 inflammasome-associated protein in the synovial membrane, thereby downregulating the release of proinflammatory cytokines (Han et al., 2023; Zhang et al., 2023).

The major strengths of the current study include the inclusion of a large sample size with 65 treating physical therapists from 64 clinics in 26 different geographical states and one British Overseas Territory, and the use of the same standardized 23-point needling protocol and dosage parameters.

Limitations

There are five important limitations to the current trial. First, the present study did not use a placebo-needling or control group. Although the authors recognize the use of a placebo-needling group as an ideal situation (Kamper, 2018), the purpose of this clinical trial was to compare the longer-term effects of three different dosing intervals of PIEDN boosters on pain, stiffness, and disability in individuals with painful knee OA, and to quantify the effect size of PIEDN when used as a stand-alone treatment for knee OA (Durlak, 2009; Faraone, 2008), without the potential for an inflated between-group effect size (Faraone, 2008; Kamper, 2019). Trials measure relative efficacy of a treatment compared to a control, placebo, or usual care (Kamper, 2018). Further, the authors believe the question of how frequently PIEDN booster sessions are needed for maintaining the beneficial effect of the intervention over longer periods of time is meaningful to clinicians and to patients with knee OA (Abbott et al., 2015; Paterno and Fitzgerald, 2024). In addition, a recent secondary analysis of an individual patient data meta-analysis of 29 trials ($n = 19{,}827$) of acupuncture for chronic pain concluded that real acupuncture was superior to sham needling irrespective of the subtype of control or sham procedure (penetrating or non-penetrating) (MacPherson et al., 2014). Moreover, a recent systematic review and network meta-analysis of 15 trials found real acupuncture to be more effective than nonpenetrating or penetrating sham acupuncture for improving pain (SMD −0.56) and function (SMD −0.73) in patients with knee OA (Lee et al., 2022). Second, the current trial was retrospectively registered, as it was submitted to clinicaltrials.gov after data collection had already begun. Although the majority of the data collected occurred after trial registration, classification as a retrospectively registered trial is appropriate, promotes transparency, incorporates all valuable data from subjects who volunteered for the trial, and reduces the risk of bias (Holst and Carlisle, 2024). Third, we cannot be certain that the results are generalizable to other dry needling techniques or protocols that do not involve periosteal and/or intraarticular stimulation. Fourth, therapist and patient treatment preferences were not collected and could potentially affect the results. Fifth, while two prior studies (Weiner et al., 2007, 2013) have reported successful outcomes following periosteal stimulation in patients with advanced knee OA (i.e., Kellgren-Lawrence grade 4, bone on bone) and although disease severity measured by radiography (i.e., the KL 0–4 scale) has previously been found to not affect treatment response of periosteal stimulation in patients with knee OA (Weiner et al., 2013), our study did not use imaging to classify disease severity; therefore, the results may not be indicative of an equal response across all five radiological grades of disease severity in knee OA.

Conclusion

In individuals with painful knee OA, the PIEDN dosing interval of once every 4 weeks was a more effective dosage regimen for maintaining improvements in pain, stiffness, physical function, medication intake, and related-disability at long-term (30 weeks) than the dosing interval of once every 8 weeks or no further treatment sessions. For adults with painful knee OA, PIEDN with monthly boosters may provide an alternative and cost-effective treatment option for those wanting to avoid adverse drug reactions or surgery.

Author contributions

CRediT: **James Dunning:** Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Resources, Writing – original draft, Writing – review & editing; **Ian Young:** Formal analysis, Methodology, Project administration, Writing – original draft, Writing – review & editing; **Norman Taylor:** Methodology, Supervision, Writing – original draft, Writing – review & editing; **Firas Mourad:** Conceptualization, Methodology, Writing – review & editing; **Paul Bliton:** Data curation, Resources, Supervision, Writing – review & editing; **James Escaloni:** Data curation, Supervision, Visualization, Writing – review & editing; **Patrick Gorby:** Methodology, Project administration, Supervision, Writing – review & editing; **Rejoy Varghese:** Investigation, Methodology, Visualization; **Filippo Maselli:** Investigation, Methodology, Validation, Writing – review & editing; **César Fernández-de-Las-Peñas:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing.

Disclosure statement

J.D. is the Director of the American Academy of Manipulative Therapy Fellowship in Orthopaedic Manual Physical Therapy. The American Academy of Manipulative Therapy is an accredited post-doctoral fellowship program that provides post-graduate training in musculoskeletal sonography, vestibular rehabilitation, spinal manipulation/mobilisation, dry needling, extremity manipulation/mobilisation, exercise prescription, and differential diagnosis to licensed physical therapists and medical physicians. J.D., I.Y., P.B., R.B., J.E., and P.G. are senior faculty of the American Academy of Manipulative Therapy Fellowship. The other authors declare that they have no competing interests.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

ORCID

James Dunning PhD, DPT, MSc http://orcid.org/0000-0002-1194-0108
Ian Young DSc, PT http://orcid.org/0000-0001-6559-993X
Norman Taylor MD, PhD http://orcid.org/0000-0001-5961-6641
Firas Mourad PhD, PT http://orcid.org/0000-0002-8981-2085
Filippo Maselli PhD, PT http://orcid.org/0000-0001-9683-9975
César Fernández-de-Las-Peñas PhD, PT http://orcid.org/0000-0003-3772-9690

References

Abbott JH, Chapple CM, Fitzgerald GK, Fritz JM, Childs JD, Harcombe H, Stout K 2015 The incremental effects of manual therapy or booster sessions in addition to exercise therapy for knee osteoarthritis: A randomized clinical trial. Journal of Orthopaedic & Sports Physical Therapy 45: 975–983. 10.2519/jospt.2015.6015

Ahsin S, Saleem S, Bhatti AM, Iles RK, Aslam M 2009 Clinical and endocrinological changes after electro-acupuncture treatment in patients with osteoarthritis of the knee. Pain 147: 60–66. 10.1016/j.pain.2009.08.004

Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald RHochberg M, et al. 1986 Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. diagnostic and therapeutic criteria committee of the American rheumatism association. Arthritis & Rheumatism 29: 1039–1049. 10.1002/art.1780290816

Altman RD. 1991 Criteria for classification of clinical osteoarthritis. The Journal of Rheumatology 27: 10–12.

American Medical Association Chicago, USA https://policysearch.ama-assn.org/policyfinder/detail/dry%20needling?uri=%2FAMADoc%2FHOD-410.949.xml

Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. 1988 Validation study of WOMAC: A health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. Journal of Rheumatology 15: 1833–1840.

Carlesso LC, Macdermid JC, Santaguida LP 2010 Standardization of adverse event terminology and reporting in orthopaedic physical therapy: Application to the cervical spine. Journal of Orthopaedic & Sports Physical Therapy 40: 455–463. 10.2519/jospt.2010.3229

Corbett MS, Rice SJ, Madurasinghe V, Slack R, Fayter DA, Harden M, Sutton AJ, Macpherson H, Woolacott NF 2013 Acupuncture and other physical treatments for the relief of pain due to osteoarthritis of the knee: Network meta-analysis. Osteoarthritis and Cartilage 21: 1290–1298. 10.1016/j.joca.2013.05.007

Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, Bridgett L, Williams S, Guillemin FHill CL, et al. 2014 The global burden of hip and knee osteoarthritis: Estimates from the global burden of disease 2010 study. Annals of Rheumatic Diseases 73: 1323–1330.

Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H 2020 Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. EClinicalMedicine 29–30: 10.1016/j.eclinm.2020.100587

Deadman P, Al-Khafaji M, Baker K 2011 A manual of acupuncture Hove, East Sussex, UK: Journal of Chinese Medicine Publications.

Delgado D, Garate A, Vincent H, Bilbao AM, Patel R, Fiz N, Sampson S, Sánchez M 2019 Current concepts in intraosseous platelet-rich plasma injections for knee osteoarthritis. Journal of Clinical Orthopaedics and Trauma 10: 36–41. 10.1016/j.jcot.2018.09.017

Dunning J, Butts R, Mourad F, Young I, Flannagan S, Perreault T 2014 Dry needling: A literature review with implications for clinical practice guidelines. Physical Therapy Reviews 19: 252–265. 10.1179/108331913X13844245102034

Dunning J, Butts R, Young I, Mourad F, Galante V, Bliton P, Tanner M, Fernández-de-Las-Peñas C 2018 Periosteal electrical dry needling as an adjunct to exercise and manual therapy for knee osteoarthritis: A multicenter randomized clinical trial. Clinical Journal of Pain 34: 1149–1158. 10.1097/AJP.0000000000000634

Durlak JA 2009 How to select, calculate, and interpret effect sizes. Journal of Pediatric Psychology 34: 917–928. 10.1093/jpepsy/jsp004

Elbadawy MA. 2017 Effectiveness of periosteal stimulation therapy and home exercise program in the rehabilitation of patients with advanced knee osteoarthritis. Clinical Journal of Pain 33: 254–263.

Faraone SV. 2008 Interpreting estimates of treatment effects: Implications for managed care. Pharmacy and Therapeutics T33: 700–711.

Farrar JT, Young JP Jr., LaMoreaux JL, Poole MR 2001 Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain 94: 149–158. 10.1016/S0304-3959(01)00349-9

Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL 2015 Exercise for osteoarthritis of the knee. Cochrane Database of Systematic Reviews 2015: 10.1002/14651858.CD004376.pub3

Han X, Lin D, Huang W, Li D, Li N, Xie X 2023 Mechanism of NLRP3 inflammasome intervention for synovitis in knee osteoarthritis: A review of TCM intervention. Frontiers in Genetics 14: 1159167. 10.3389/fgene.2023.1159167

Holden MA, Hattle M, Runhaar J, Riley RD, Healey EL, Quicke J, van der Windt DA, Dziedzic K, van Middelkoop MBurke D, et al. 2023 Moderators of the effect of therapeutic exercise for knee and hip osteoarthritis: A systematic review and individual participant data meta-analysis. The Lancet Rheumatology 5: e386–e400.

Holst M, Carlisle BG 2024 Trials that turn from retrospectively registered to prospectively registered: A cohort study of "retroactively prospective" clinical trial registration using history data. Trials 25: 189. 10.1186/s13063-024-08029-5

Huang J, Zhuo LS, Wang YY, Peng ZL, Huang YR, Wang Y, Yang L. 2007 Effects of electroacupuncture on synovia IL-1beta and TNF-alpha contents in the rabbit with knee osteoarthritis. Zhen Ci Yan Jiu 32: 115–118.

Jaeschke R, Singer J, Guyatt GH 1989 Measurement of health status. Ascertaining the minimal clinically important difference. Controlled Clinical Trials 10: 407–415. 10.1016/0197-2456(89)90005-6

Jansen MJ, Viechtbauer W, Lenssen AF, Hendriks EJ, de Bie RA. 2011 Strength training alone, exercise therapy alone, and exercise therapy with passive manual mobilisation each reduce pain and disability in people with knee osteoarthritis: A systematic review. Journal of Physiotherapy 57: 11–20.

Jensen MP, Karoly P, Braver S 1986 The measurement of clinical pain intensity: A comparison of six methods. Pain 27: 117–126. 10.1016/0304-3959(86)90228-9

Kamper SJ 2018 Control groups: Linking evidence to practice. Journal of Orthopaedic & Sports Physical Therapy 48: 905–906. 10.2519/jospt.2018.0706

Kamper SJ. 2019 Interpreting outcomes 2-statistical significance and clinical meaningfulness: Linking evidence to practice. Journal of Orthopaedic & Sports Physical Therapy 49: 559–560.

Kim MS, Koh IJ, Choi KY, Sung YG, Park DC, Lee HJ. 2021 The minimal clinically important difference (MCID) for the WOMAC and factors related to achievement of the MCID after medial pening wedge high tibial osteotomy for knee osteoarthritis. American Journal of Sports Medicine 49: 2406–2415.

Lee B, Kim TH, Birch S, Alraek T, Lee HW, Nielsen A, Wieland LS, Lee MS 2022 Comparative effectiveness of acupuncture in sham-controlled trials for knee osteoarthritis: A systematic review and network meta-analysis. Frontiers in Medicine (lausanne) 9: 10.3389/fmed.2022.1061878

Lin X, Huang K, Zhu G, Huang Z, Qin A, Fan S 2016 The effects of acupuncture on chronic knee pain due to osteoarthritis: A meta-analysis. Journal of Bone and Joint Surgery American 98: 1578–1585. 10.2106/JBJS.15.00620

Liu X, Shen L, Wu M, Wu B, Gao L, Hu W, Zhang A. 2004 Effects of acupuncture on myelogenic osteoclastogenesis and IL-6 mRNA expression. Journal of Traditional Chinese Medicine 24: 144–148.

Loaiza LA, Yamaguchi S, Ito M, Ohshima N 2002 Electroacupuncture stimulation to muscle afferents in anesthetized rats modulates the blood flow to the knee joint through autonomic reflexes and nitric oxide. Autonomic Neuroscience 97: 103–109. 10.1016/S1566-0702(02)00051-6

Lou Z, Bu F 2025 Recent advances in osteoarthritis research: A review of treatment strategies, mechanistic insights, and acupuncture. Medicine (Baltimore) 104: e41335. 10.1097/MD.0000000000041335

MacPherson H, Maschino AC, Lewith G, Foster NE, Witt CM, Vickers AJ 2013 Acupuncture trialists, C 2013 characteristics of acupuncture treatment associated with outcome: An individual patient meta-analysis of 17,922 patients with chronic pain in randomised controlled trials. PLOS ONE 8: e77438. 10.1371/journal.pone.0077438

MacPherson H, Vertosick E, Lewith G, Linde K, Sherman KJ, Witt CM, Vickers AJ 2014 Acupuncture trialists, C 2014 influence of control group on effect size in trials of acupuncture for chronic pain: A secondary analysis of an individual patient data meta-analysis. PLOS ONE 9: e93739. 10.1371/journal.pone.0093739

McConnell S, Kolopack P, Davis AM. 2001 The Western Ontario and McMaster Universities osteoarthritis Index (WOMAC): A review of its utility and measurement properties. Arthritis and Rheumatology 45: 453–461.

Menz HB 2005 Analysis of paired data in physical therapy research: Time to stop double-dipping? Journal of Orthopaedic & Sports Physical Therapy 35: 477–478. 10.2519/jospt.2005.0108

Paterno MV, Fitzgerald GK 2024 Booster visits in the management of the acute musculoskeletal injuries: Transforming care to improve outcomes-A perspective review. Journal of Orthopaedic Research 42: 1151–1158. 10.1002/jor.25852

Rubin LH, Witkiewitz K, Andre JS, Reilly S. 2007 Methods for handling missing data in the behavioral neurosciences: Don't throw the baby rat out with the bath water. Journal of Undergraduate Neuroscience Education: JUNE: A Publication of FUN, Faculty for Undergraduate Neuroscience 5: A71–77.

Runge N, Aina A, May S. 2022 The benefits of adding manual therapy to exercise therapy for improving pain and function in patients with knee or hip osteoarthritis: A systematic review with meta-analysis. Journal of Orthopaedic & Sports Physical Therapy 52: 675–a613.

Salaffi F, Stancati A, Silvestri CA, Ciapetti A, Grassi W 2004 Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. European Journal of Pain 8: 283–291. 10.1016/j.ejpain.2003.09.004

Sangdee C, Teekachunhatean S, Sananpanich K, Sugandhavesa N, Chiewchantanakit S, Pojchamarnwiputh S, Jayasvasti S 2002 Electroacupuncture versus diclofenac in symptomatic treatment of osteoarthritis of the knee: A randomized controlled trial. BMC Complementary Alternative Medicine 2: 3. 10.1186/1472-6882-2-3

Serrano-García B, Martínez-Cepa CB, Forriol F, Angulo-Díaz-Parreño S, Mesa-Jiménez JA, Zuil-Escobar J 2025 Effects of manual therapy and strengthening exercise on pain in patients with knee osteoarthritis: A systematic review and meta-analysis. Applied Sciences 15: 215. 10.3390/app15010215

Taechaarpornkul W, Suvapan D, Theppanom C, Chanthipwaree C, Chirawatkul A 2009 Comparison of the effectiveness of six and two acupuncture point regimens in

osteoarthritis of the knee: A randomised trial. Acupuncture in Medicine 27: 3–8. 10.1136/aim.2008.000067

Toda Y, Tsukimura N 2008 A comparison of intra-articular hyaluronan injection accuracy rates between three approaches based on radiographic severity of knee osteoarthritis. Osteoarthritis and Cartilage 16: 980–985. 10.1016/j.joca.2008.01.003

Vas J, Mendez C, Perea-Milla E, Vega E, Panadero MD, Leon JM, Borge MA, Gaspar O, Sanchez-Rodriguez FAguilar I, et al. 2004 Acupuncture as a complementary therapy to the pharmacological treatment of osteoarthritis of the knee: Randomised controlled trial. The British Medical Journal 329: 1216. 10.1136/bmj.38238.601447.3a

Vas J, White A 2007 Evidence from rcts on optimal acupuncture treatment for knee osteoarthritis – an exploratory review. Acupuncture in Medicine 25: 29–35. 10.1136/aim.25.1-2.29

Wang Q, Runhaar J, Kloppenburg M, Boers M, Bijlsma JWJ, Bierma-Zeinstra SMA 2024 CREDO expert group 2024. Evaluation of the diagnostic performance of American college of rheumatology, EULAR, and national institute for health and clinical excellence criteria against clinically relevant knee osteoarthritis: Data from the CHECK cohort. Arthritis Care & Research (Hoboken) 76: 511–516. 10.1002/acr.25270

Weiner DK, Moore CG, Morone NE, Lee ES, Kent Kwoh C. 2013 Efficacy of periosteal stimulation for chronic pain associated with advanced knee osteoarthritis: A randomized, controlled clinical trial. Clinical Therapeutics 35: 1703–1720.

Weiner DK, Rudy TE, Morone N, Glick R, Kwoh CK 2007 Efficacy of periosteal stimulation therapy for the treatment of osteoarthritis-associated chronic knee pain: An initial controlled clinical trial. Journal of the American Geriatrics Society 55: 1541–1547. 10.1111/j.1532-5415.2007.01314.x

Weiwei M, Mei D, Juan L, Longfei X, Xilin C, Tingyao H, Wenting Z, Changqing G 2024 Electroacupuncture improves articular microcirculation and attenuates cartilage hypoxia in a male rabbit model of knee osteoarthritis. Journal of Traditional and Complementary Medicine 14: 414–423. 10.1016/j.jtcme.2024.01.002

White A, Foster NE, Cummings M, Barlas P 2007 Acupuncture treatment for chronic knee pain: A systematic review. Rheumatology (Oxford) 46: 384–390. 10.1093/rheumatology/kel413

Yuan SG, Chen J, Chen MX, Zheng NS, Zhang ZW, Wang HJ, Li J, Li L, Gao YP 2024 High-intensity electroacupuncture is superior to low-intensity electroacupuncture for knee osteoarthritis: A meta-analysis of randomized controlled trials. Acupuncture in Medicine 42: 303–310. 10.1177/09645284241298718

Yunus MH, Nordin A, Kamal H 2020 Pathophysiological perspective of oteoarthritis. Medicina (Kaunas) 56: 614. 10.3390/medicina56110614

Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, Bierma-Zeinstra S, Brandt KD, Croft PDoherty M, et al. 2010 OARSI recommendations for the management of hip and knee osteoarthritis: Part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis and Cartilage 18: 476–499.

Zhang W, Zhang L, Yang S, Wen B, Chen J, Chang J 2023 Electroacupuncture ameliorates knee osteoarthritis in rats via inhibiting NLRP3 inflammasome and reducing pyroptosis. Molecular Pain 19: 10.1177/17448069221147792

Zhang Y, Bao F, Wang Y, Wu Z. 2016 Influence of acupuncture in treatment of knee osteoarthritis and cartilage repairing. American Journal of Translational Research 8: 3995–4002.

Zhang Z, Lai Q, Li Y, Xu C, Tang X, Ci J, Sun S, Xu B, Li Y 2017 Acidic pH environment induces autophagy in osteoblasts. Scientific Reports 7: 46161. 10.1038/srep46161

Zhou K, Ma Y, Brogan MS 2015 Dry needling versus acupuncture: The ongoing debate. Acupuncture in Medicine 33: 485–490. 10.1136/acupmed-2015-010911

Zhou W, Benharash P 2014 Significance of "deqi" response in acupuncture treatment: Myth or reality. Journal of Acupuncture and Meridian Studies 7: 186–189. 10.1016/j.jams.2014.02.008

Zwarenstein M, Treweek S, Gagnier JJ, Altman DG, Tunis S, Haynes B, Oxman AD, Moher D, Group C 2008 Pragmatic trials in healthcare, g 2008 improving the reporting of pragmatic trials: An extension of the CONSORT statement. The British Medical Journal 337: a2390. 10.1136/bmj.a2390