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**Title Page**

**Running head:** TENS, education and exercise for knee OA

**Title:** Transcutaneous Electrical Nerve Stimulation as an adjunct to education and exercise for knee osteoarthritis: a randomised controlled trial

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## ABSTRACT

**Objective.** To determine the additional effects of Transcutaneous Electrical Nerve Stimulation (TENS) for knee osteoarthritis (OA) when combined with a group education and exercise programme ('knee group').

**Methods.** The study was a randomised sham-controlled clinical trial. Patients referred for physiotherapy with suspected knee OA (confirmed using the American College of Rheumatology clinical criteria) were invited. Exclusion criteria included co-morbidities preventing exercise, previous TENS experience and TENS contraindications. Prospective sample size calculations required n=67 in each trial arm. 224 participants (mean age 61 years, 37% men) were randomised to three arms: TENS & knee group (n=73); Sham TENS & knee group (n=74); knee group (n=77). All patients entered an evidence-based six-week group education and exercise programme ('knee group'). Active TENS produced a "strong but comfortable" paraesthesia within the painful area and was used as much as needed during the six-week period. Sham TENS used dummy devices with no electrical output. Blinded assessment took place at baseline, 3, 6, 12 and 24 weeks. The primary outcome was the Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) function subscale at 6 weeks. Secondary outcomes included WOMAC pain, stiffness and total scores; extensor muscle torque; global assessment of change; exercise adherence; and exercise self-efficacy. Data analysis was by intention to treat.

**Results.** All outcomes improved over time ($p<0.05$) but there were no differences between trial arms ($p>0.05$). All improvements were maintained at 24-week follow-up.

**Conclusion.** There were no additional benefits of TENS, failing to support its use as a treatment adjunct within this context.

## SIGNIFICANCE AND INNOVATION

- People with knee OA improved over time with a group education and exercise intervention.
- Improvements included pain, stiffness, function, strength, exercise adherence, exercise self-efficacy and global assessment of change.
- TENS failed to provide any additional clinical benefit and cannot be recommended as a treatment adjunct in this context.

## INTRODUCTION

Knee osteoarthritis (OA) is associated with pain, decreased range of movement and muscle weakness which over time may lead to functional loss (1) and substantial economic burden (2). 16.3% of men and 29.1% of women over 55 years exhibit radiographic evidence of knee OA, with age, pain and stiffness contributing to locomotor disability (3). Knee OA thus presents a significant source of morbidity. Cochrane reviews of the evidence for knee OA interventions have indicated that exercise is effective for both pain and function (4, 5). The latest Cochrane review exploring Transcutaneous Electrical Nerve Stimulation (TENS), however, was unable to support its effectiveness for pain relief (6). The latter review highlighted poor methodological quality and inadequate statistical power of existing trials, supporting the need for more robust randomised controlled trials (RCTs).

Therapists often employ complex intervention packages but research into the effectiveness of combining treatments has been neglected (7). TENS has specifically been advocated as an adjunct to other treatments (8-10) and those who use TENS often do so in conjunction with exercise (7). Clinical guidelines also recommend exercise and patient education as core treatments, with TENS as an adjunct (9). Elucidation of the effects of TENS when combined with exercise and education is therefore an important clinical research question. Such effects have yet to be clearly established, with a limited number of previous studies in knee OA.

One study found that TENS in combination with exercise was no better for OA knee pain intensity than either in isolation (11). Another trial, which met its prospectively calculated sample size, found that neither TENS nor interferential current provided additional benefits (on pain and function) over exercise alone (12). A third trial reported a trend towards TENS and exercise producing better

improvements in a range of physical outcome measures (isometric peak torque, gait parameters and knee range of movement) when compared with either intervention in isolation or sham (no current) stimulation (13), although the results failed to reach statistical significance. Common features of these studies are low participant numbers (total n=46-62; n=15-16 per trial arm) and the intermittent and brief (20-60min) application of TENS when effectiveness may be maximised when used for extended periods throughout the day (10). Each study applied TENS for only four weeks, shorter than the minimum six weeks suggested by an earlier Cochrane review (14). Further, TENS was administered by therapists in the clinic when TENS is designed for self-administration at home (6). Suboptimal TENS dosing and inappropriate outcome assessment have been identified as particularly prevalent weaknesses indicating low fidelity in RCTs and this contributes to negative findings (15). A high quality trial was therefore required, with close attention to issues of statistical power, TENS application and outcomes assessment.

This study is a randomised sham-controlled clinical trial designed to determine the additional effects of TENS in knee OA when combined with a six-week group education and exercise regime ('knee group').

## PATIENTS AND METHODS

The study was conducted in accordance with the Declaration of Helsinki and received a favourable opinion from the Cambridgeshire 2 Research Ethics Committee (07/H0308/209).

**Design.** This was a randomised, sham-controlled trial with 3 parallel arms: 1) TENS and knee group; 2) sham TENS and knee group; or 3) knee group.

**Study population.** Patients referred to physiotherapy at University Hospitals Bristol (UHBristol) with confirmed or suspected knee OA were eligible. Referrals were screened by a research associate (MD). Telephone screening was then conducted by MD or one of two other therapists trained in the recruitment procedure. The telephone interview offered referral into the knee group (routine care for knee OA patients at UHBristol) and gave initial verbal information about the research and an opportunity to ask questions. Patients who confirmed that they were interested were sent a patient information sheet and an appointment for a full standardised physiotherapy assessment with MD.

The physiotherapy assessment aimed to ensure the knee group was clinically appropriate, to screen for study inclusion and exclusion criteria, and to provide patients with an opportunity to ask further questions. Those agreeing to enter the trial provided formal written consent, completed the baseline outcome measures (see later details), and were assigned a consecutive study number in the order in which they attended for assessment. They were given a date to commence the knee group and the participant's study number and contact details were forwarded to the TENS instructors. The inclusion criteria comprised being 18 years of age or older with knee OA confirmed by the American College of Rheumatology (ACR) clinical criteria (16). The ACR criteria are knee pain accompanied by at least three from six signs and symptoms (age > 50 years, stiffness < 30 minutes, crepitus, bony tenderness, bony enlargement, no palpable warmth). Exclusion criteria were co-morbidities preventing participation in the knee group (17); contraindications to TENS (18); and previous TENS experience. Those not fulfilling the eligibility criteria or declining entry to the trial were referred either for individual physiotherapy treatment or to the knee group

as normal (but not as a study participant) according to which was considered most clinically appropriate.

**Randomisation.** Participants were randomly assigned to one of the three trial arms. An independent monitor prepared sealed opaque envelopes containing treatment allocations. 261 envelopes were prepared with 87 allocations to each of the 3 treatment arms. Envelopes were mixed and then mixed again before being numbered consecutively. Once prepared, the trained TENS instructors were the only individuals to have access to the envelopes and were responsible for assigning all participants by opening the appropriately numbered envelope corresponding to their study number. All other members of the research team and clinical staff were blinded to allocation throughout. Before participants commenced the knee group, the TENS instructors contacted those allocated to active or sham TENS to arrange TENS training. Participants allocated to only receive the knee group intervention simply attended the knee group as originally scheduled.

**TENS Interventions.** 'TouchTENS' devices (Model XL-Y1, TensCare, UK) were used throughout. Sham devices were deactivated by the manufacturer. All devices were checked by the Medical Equipment Management Organisation at UHBristol and were randomly assigned a device number before being employed in the trial. Only the TENS instructors and one member of the research team (FC) had access to the identity (active or sham) of individual devices. FC provided all training for the TENS instructors according to standardised operating procedures. FC also audited the processes associated with randomisation and treatment allocation, including periodic observation of TENS instruction sessions.

TENS instructors were all physiotherapy technical instructors working with patients with musculoskeletal disorders. Four TENS instructors were employed on

the project to reflect the pragmatic nature of the trial. TENS instruction comprised a thirty-minute appointment during which patients were also assessed for competency to self-administer. Patients received a TENS device for their personal use from the date of TENS instruction and throughout the six-week duration of the knee group. Written and verbal information detailed the existence of different TENS devices, that some do not produce perceptible sensations, and that participants may receive an active or inactive device (in line with principles of fully informed consent). Patients were taught to position four electrodes around the knee joint, two on the medial and two on the lateral aspect either side of the joint line (such that each of the two electrical circuits diagonally crossed the knee). For the purposes of instruction, devices were set to a continuous mode (Programme A - 110Hz, 50μs). All electrical pulses were asymmetrical biphasic. Dummy devices (the displays were active but there was no current output) were used to administer sham TENS. All written and verbal instructions were standardised as far as possible, although patients were allowed to ask questions and received further instruction as required to ensure adequate understanding. Due to lack of evidence for the specific effects of many TENS parameters (19, 20, 21, 22), patients were instructed to use the device as much as needed (23, 24) and encouraged to try different TENS programmes. TENS could be used before, during or after exercise or physical function. Stimulus intensity is one parameter related to treatment efficacy (19, 22) therefore those receiving active TENS were instructed to select a stimulation intensity that generated a 'strong but comfortable' tingling sensation within or close to the site of pain. Those receiving sham TENS were instructed to select an intensity of seven or eight (within the middle range of the 15 settings available). TENS devices were returned to the TENS instructor at the end of the six-week intervention. Participants were requested not to

discuss their TENS treatment with research staff, clinical staff or fellow patients during the trial.

**Exercise intervention.** Full details of the evidence-based education and exercise programme have previously been reported by Domaille et al (17) and it has been shown to be as effective as similar programmes. To reflect the pragmatic nature of the trial, seven therapists were trained to facilitate the knee groups. To maximise consistency, the same therapist aimed to lead all six sessions of each group. The education component was supported by a standardised presentation and protocol. All participants took part in the six-week knee group (17). This involved a group of up to 12 patients attending for one hour (30 minutes education and 30 minutes group exercise) on six consecutive weeks. The education programme aimed to enhance patients' abilities to self-manage their condition. It included information on setting personal objectives, pacing, managing flare-ups, diet, medical management of OA, local community exercise opportunities and long-term exercise adherence. The exercise component included five minutes warm up, followed by a circuit of exercises aimed at improving lower limb strength, proprioception and function. Each exercise had specific ideas for progression which patients advanced as able over the six-week programme. During the first session each exercise was performed for one minute, with one minute between exercises to move to the next station. On the subsequent five sessions each exercise was performed for two minutes which included the time to move to the next station. All patients were taught home exercises during the second session and advised to perform them daily. These included step-ups, sit to stand, balancing on one leg and heel to toe walking. Increase in general physical function was a key aim of the intervention and was supported by individual action plans. The knee group was supported by a booklet

containing written advice on the topics covered in the education session, details of the home exercises and tools to aid goal setting.

**Outcomes.** Baseline outcome measures were taken by MD at the end of the initial physiotherapy assessment. Two blinded assessors (MD and another senior physiotherapist specialising in Rheumatology) took all other outcome measures at weeks 3, 6, 12 and 24. Assessments took place in the same treatment cubicle to standardise the environment. Participants were asked to complete all paper-based outcome measures prior to attending. Outcomes were chosen to meet the recommendations of the Outcome Measures in Rheumatology (OMERACT) core set (25).

The primary outcome measure was the function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (26) at 6 weeks. Although TENS is primarily used for pain relief, function was chosen to reflect the overall aim of the combined TENS, education and exercise package to enhance physical function. The total WOMAC score and pain and stiffness subscales were included as secondary outcome measures. The WOMAC was administered at all outcome points.

Maximum knee extensor torque (as a measure of quadriceps strength) was measured in upright sitting (knees and hips at $90^{o}$ flexion) at all outcome points using a digital myometer (MIE Medical Research Ltd, UK). One knee was tested, chosen by the patient as being the most painful. Participants undertook one practice followed by one assessment measure (to avoid aggravating patients' pain). The assessor and participant were blinded to the myometer reading by a flap which was later uncovered, recorded (in Newtons) and divided by the moment arm length to give a torque value (in Nm). Extensor torque was the only outcome measure that was not

patient-reported therefore an inter-rater reliability study was conducted using the first 12 participants entering the trial. Reliability was found to be excellent (ICC = 0.95) and supported the use of two blinded assessors.

A patient global assessment of change scale (27) was used at weeks 3, 6, 12 and 24. Patients were asked to state whether they were the same, better or worse compared to when they first attended the knee group. If patients chose 'better' or 'worse' they were asked to indicate on a seven-point Likert scale by how much (ranging from 'a tiny bit, almost the same' to 'a very great deal').

Self-efficacy for exercise (28) was assessed at baseline and at week 24. Patients were asked to respond to 4 statements about their ability and confidence to exercise using a five-point Likert scale (ranging from 'strongly disagree' to 'strongly agree').

Self-reported exercise adherence was assessed by asking patients to indicate how often they undertook the daily exercises using a five-point Likert scale ranging from 'never' to 'always'.

Unknown to patients, TENS devices logged the cumulative duration of use which was retrieved on return of the device. A brief questionnaire about the settings used was also completed by all TENS users.

To assess the effectiveness of blinding, assessors and exercise therapists were asked to guess whether or not each participant had received a TENS machine.

**Sample size.** Sample size calculations were based on the WOMAC function subscale data presented by Tubach and colleagues (29), with data converted to scores out of 68 (the WOMAC function subscale total) rather than 100. This gave values of mean 29.1 (SD 10.9), with the minimal clinically significant improvement being 6.2 out of 68. At an alpha level of 0.05 and 90% power, a minimum sample

size of 67 in each trial arm was calculated. Allowing for 30% attrition, a target recruitment of 261 participants was set (87 in each trial arm).

**Statistical analysis.** Primary data analysis was by intention to treat using IBM SPSS Statistics Version 19. Missing values were imputed using multiple imputation techniques. With the exception of age and the WOMAC function subscale and WOMAC total score, data were not normally distributed. Log, square root and reciprocal transformation techniques were applied with little improvement in data distributions. Although deviation from normality does not preclude parametric analysis, a more conservative approach was taken and it was decided to use non-parametric analyses on all data which deviated from a normal distribution. Changes over time and between trial arms were investigated using a general linear model repeated measures or non-parametric Kruskal Wallis and Friedman tests as appropriate. All data analysis was performed blind to trial arm allocations.

## RESULTS

**Recruitment and retention.** Figure 1 illustrates the recruitment and retention of study participants. Telephone screening effectively identified potential participants who were ineligible, no longer needed treatment, were unwilling, or had difficulty attending. Table 1 illustrates that randomisation resulted in largely comparable trial arms (on the basis of demographic information and baseline outcome measures). The only potential exception was extensor torque, with participants receiving active TENS displaying slightly lower baseline values. Total loss to follow-up was 13% at six weeks and 22% at 24 weeks. Loss to follow-up was slightly higher in the knee group when compared to either of the TENS groups. The reasons for withdrawal failed to identify why, although more people in this trial arm failed to give a reason

and some may have been disappointed not to have received TENS. Five patients were not issued with TENS devices – one (active TENS) due to scheduling problems and four (two active and two sham TENS) who withdrew after baseline assessment. All were still included as part of an intention to treat analysis.

**Primary Outcome.** Results for the primary outcome measure of WOMAC function, along with the total WOMAC score, are presented in Table 2. There was a clear trend of improvement over time in both outcomes but little obvious difference between groups. Improvements over time for each score were statistically significant (both $p<0.001$) but differences between trial arms or time x arm interaction effects were not (all $p>0.05$). Table 3 presents the proportion of patients in each trial arm who met the clinically significant threshold of improvement of >6.2 points on the WOMAC function subscale at the primary outcome point of six weeks. A slightly greater proportion of those who received exercise in isolation achieved this magnitude of improvement. The pooled standardised effect size from baseline (using data for all n=224 participants) was 0.30 at both week 6 and week 24.

**Secondary outcomes.** Table 4 shows clear improvements over time in the secondary outcomes of WOMAC pain, WOMAC stiffness, extensor torque, self-reported global change and exercise self-efficacy, but no obvious differences between groups. Reported exercise adherence did not seem to change over time. Statistical analysis confirmed that there were no statistically significant differences between trial arms (all $p>0.05$ at each time point), although each of the secondary outcomes improved over time (all $p<0.05$).

**Blinding.** Questionnaires about how patients used TENS were returned by 74% (n=54/73) of participants in the active TENS arm and 81% (n=60/74) in the sham TENS arm. Of those who predicted whether they had received an active or

inactive device (participants had to choose one or the other), 92% (n=46/50) of active TENS users guessed correctly. Correct identification in the sham TENS arm was only slightly better than chance at 60% (n=36/60). Data on blinding of the assessor and exercise therapists were available for 51% (n=114/224) and 35% (n=78/224) respectively. They were asked whether or not they thought individual participants had a TENS machine (regardless of whether it was active or sham). The proportion of correct responses was worse than chance, at 43% for the assessor (n=49/114) and 30% (n=23/78) for the exercise therapists.

**TENS usage.** TENS usage (as logged by the devices) was available for 88% of active TENS users (n=64/73) and 93% (n=69/74) of sham TENS users. Median logged usage was 46.5 and 39.0 hours for active and sham TENS respectively (Mann-Whitney U Test p=0.861). The self-reported settings *"normally used"* used by participants are presented in Table 5. Data for this question was available for 67% (n=49/73) and 72% (n=53/74) of active and sham TENS users respectively. The results show a large variation in settings used by participants in each trial arm.

## DISCUSSION

This investigation found that using TENS as an adjunct to a six-week group education and exercise programme failed to elicit additional clinical benefits. 33% of active TENS users achieved the pre-specified clinically significant improvement in function, slightly lower than sham TENS (36%) or the knee group in isolation (42%).

These results support previous but inconclusive findings of a lack of additional effect of TENS when combined with exercise for pain intensity (11) and for pain and function (12). Another study observed a non-statistically significant trend towards TENS and exercise improving a range of physical outcome measures (13). The

present investigation failed to substantiate those trends. The present findings concur with those of the most recent Cochrane review on the effectiveness of TENS for OA knee pain (6), although it should be noted that our study focussed on identifying adjunctive rather than isolated benefits of TENS.

Alternative explanations for the findings could be that the trial was not sensitive enough to detect any additional benefit of TENS from that achieved by the knee group, or that the knee group reduced symptoms to a level that would not benefit from TENS. However, although the variability of baseline WOMAC function scores was slightly greater than the values used for the prospective sample size calculation (reducing statistical power to 80%), this was considered acceptable and there was certainly no trend suggestive of TENS benefits.

The knee group intervention seems effective, with improvements in all outcome measures over time, although it should be noted that this investigation was not specifically designed to assess the efficacy of the knee group. Nonetheless, the standardised effect size of 0.30 for the primary function outcome at both week six and week 24 suggests moderate treatment effects, similar in magnitude to nonsteroidal anti-inflammatory drugs (30). It is slightly less than the effect size of 0.37 at six weeks observed by Domaille and colleagues (17) using the same knee group intervention, although the present cohort was slightly less disabled and arguably had less scope for improvement. The effect size was comparable to that observed by Hurley and colleagues (31) (0.28 at six months) whose intervention was adapted (17) and employed in the present investigation.

The study blinded the outcome assessor and exercise therapists effectively to treatment allocation. Blinding patients to the sham intervention was relatively successful, with 40% believing that it was active (compared to 50% expected by

chance). This was, however, much less than the 92% of active TENS users who correctly identified that their device was active and the 84% of sham TENS users who thought they had an active device achieved by Deyo and colleagues (32). Due to the lack of additional effect of either active or sham TENS, patient blinding issues are not thought to have affected the trial outcome. Interestingly, the logged usage of sham and active TENS devices was comparable and a wide range of programmes were used (Table 5), suggesting a high level of interaction with, and use of, sham TENS devices.

The lack of standardisation of TENS parameters may be seen by some as a limitation but was designed to encourage patients to engage with the devices. It is known that individual patients experiment with TENS devices to find settings that suit them (19) and this was evidenced by the wide range of settings used in the present study (Table 5). There is currently a lack of evidence for the effects of many specific parameters (19, 20, 21, 22) and therefore prescribed use may discourage engagement with TENS devices. More formal verification of device parameters than was conducted in this study would be required to identify their importance.

It would be interesting in the future to more fully explore the interaction between TENS use and exercise adherence. Anecdotal evidence suggested some practical issues with TENS use, such as leads pulling and pads peeling off. It is also conceivable that TENS use might engender a slightly more passive approach to self-management. Both issues have the potential to reduce engagement with exercise. Although the limited data suggested no difference in exercise adherence between groups, a much more nuanced approach to assessing exercise adherence might help to determine if and how TENS affects engagement with exercise. Identification

of predictors of TENS outcome could be a further important focus for future research (33, 34).

In conclusion, the findings fail to support the use of TENS as an adjunct to a group education and exercise intervention.

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**REFERENCES**

1. Bijlsma JW, Berenbaum F, Lafeber FP. Osteoarthritis: an update with relevance for clinical practice. Lancet 2011;377:2115-2126.

2. Leardini G, Salaffi F, Caporali R, Canesi B, Rovati L, Montanelli R; Italian Group for Study of the Costs of Arthritis. Direct and indirect costs of osteoarthritis of the knee. Clin Exp Rheumatol 2004;22:699-706.

3. Odding E, Valkenburg HA, Algra D, Vandenouweland FA, Grobbee DE, Hofman A. Associations of radiological osteoarthritis of the hip and knee with locomotor disability in the Rotterdam Study. Ann Rheum Dis 1998;57:203-208.

4. Brosseau L, MacLeay L, Welch V, Tugwell P, Wells GA. Intensity of exercise for the treatment of osteoarthritis. Cochrane Database of Systematic Reviews 2003, Issue 2.

5. Fransen M, McConnell S. Exercise for osteoarthritis of the knee. Cochrane Database of Systematic Reviews 2008, Issue 4.

6. Rutjes AWS, Nüesch E, Sterchi R, Kalichman L, Hendriks E, Osiri M, et al. Transcutaneous electrostimulation for osteoarthritis of the knee. Cochrane Database of Systematic Reviews 2009, Issue 4.

7. Turner PA, Whitfield TWA. A multidimensional scaling analysis of the techniques that physiotherapists use. Physiother Res Int 1997;2:237-254

8. Watson T. The role of electrotherapy in contemporary physiotherapy practice. Manual Ther 2000;5:132-141.

9. National Institute for Health and Clinical Excellence (NICE). Osteoarthritis. The care and management of osteoarthritis in adults. NICE clinical guideline 59. 2008.

10. Johnson MI, Bjordal JM. Transcutaneous electrical nerve stimulation for the management of painful conditions: focus on neuropathic pain. Expert Rev Neurother 2011;11:735-753.

11. Cheing GLY, Hui-Chan CWY, Chan KM. Does four weeks of TENS and/or isometric exercise produce cumulative reduction of osteoarthritic knee pain? Clin Rehabil 2002;16:749-760.

12. Adedoyin RA, Olaogun MO, Oyeyemi AL. Transcutaneous electrical nerve stimulation and interferential current combined with exercise for the treatment of knee osteoarthritis: a randomised controlled trial. Hong Kong Physiother J 2005;23:13-19.

13. Cheing GLY, Hui-Chan CWY. Would the addition of TENS to exercise training produce better physical performance outcomes in people with knee oateoarthritis than either intervention alone? Clin Rehabil 2004;18:487-497.

14. Osiri M, Welch V, Brosseau L, Shea B, McGowan J, Tugwell P, et al. Transcutaneous electrical nerve stimulation for knee osteoarthritis. Cochrane Database of Systematic Reviews 2000, Issue 4.

15. Bennett MI, Hughes N, Johnson MI. Methodological quality in randomised controlled trials of transcutaneous electric nerve stimulation for pain: low fidelity may explain negative findings. Pain 2011;152:1226-1232.

16. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. 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 Rheum 1986;29:1039-1049.

17. Domaille M, Mascarenhas R, Dayal N, Kirwan J. Evaluation of the Bristol Royal Infirmary physiotherapy programme for the management of patients with osteoarthritis of the knee. Musculoskeletal Care 2006;4:78-87.

18. Chartered Society of Physiotherapy. Guidance for the clinical use of electrophysical agents. Chartered Society of Physiotherapy, London; 2006.

19. Johnson MI, Ashton CH, Thompson JW. An in-depth study of long-term users of transcutaneous electrical nerve stimulation (TENS). Implications for clinical use of TENS. Pain 1991;44:221-229.

20. Johnson MI, Ashton CH, Thompson JW. The consistency of pulse frequencies and pulse patterns of transcutaneous electrical nerve stimulation (TENS) used by chronic pain patients. Pain 1991;44:231-234.

21. Chen C-C, Tabasam G, Johnson MI. Does the pulse frequency of transcutaneous electrical nerve stimulation (TENS) influence hypoalgesia? A systematic review of studies using experimental pain and healthy human participants. Physiotherapy 2008;94:11-20.

22. Claydon LS, Chesterton LS, Barlas P, Sim J. Dose-specific effects of transcutaneous electrical nerve stimulation (TENS) on experimental pain. A systematic review. Clin J Pain 2011;27(7):635-647.

23. Walsh DM. TENS: clinical applications and related theory. New York: Churchill Livingstone; 1997.

24. Johnson M. Transcutaneous Electrical Nerve Stimulation (TENS). In: Kitchen S (Editor) Electrotherapy: evidence based practice (11th Edition). Edinburgh: Churchill Livingstone; 2002. p. 259-286.

25. Bellamy N, Kirwan J, Boers M, Brooks P, Strand V, Tugwell P, et al. Recommendations for a core set of outcome measures for future phase III clinical trials in knee, hip and hand osteoarthritis. Consensus development at OMERACT III. J Rheumatol 1997;24:799-802.

26. Kennedy D, Stratford PW, Pagura MC, Wessel J, Gollish JD, Woodhouse LJ. Exploring the factorial validity and clinical interpretability of the Western Ontario and McMaster universities osteoarthritis index (WOMAC). Physiother Can 2003;55:160-168.

27. Stratford PW, Binkley JM, Riddle DL. Health status measures: strategies and analytic methods for assessing change scores. Phys Ther 1996;76:1109-1123.

28. Lorig K, Chastain R, Ung E, Shoor S, Holman HR. Development and evaluation of a scale to measure the perceived self-efficacy of people with arthritis. Arthritis Rheum 1989;32:37-44.

29. Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, et al. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimally clinically important improvement. Ann Rheum Dis 2005;64:29-33.

30. Bjordal JM, Ljunggren AE, Klovning A, Slørdal L. Non-steroidal anti-inflammatory drugs, including cyclo-oxygenase-2 inhibitors, in osteoarthritic knee pain: meta-analysis of randomised placebo controlled trials. BMJ 2004;329(7478):1317.

31. Hurley MV, Walsh NE, Mitchell HL, Pimm TJ, Patel A, Williamson E, et al. Clinical effectiveness of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain: a cluster randomized trial. Arthritis Rheum 2007;57:1211-1219.

32. Deyo RA, Walsh NE, Schoenfeld LS, Ramamurthy S. Can trials of physical treatments be blinded? The example of transcutaneous electrical nerve stimulation for chronic pain. Am J Phys Med Rehabil 1990;69:6-10.

33. Lampl C, Kreczi T, Klinger D. Transcutaneous electrical nerve stimulation in the treatment of chronic pain: predictive factors and evaluation of the method. Clin J Pain 1998;14:134-142.

34. Oosterhof J, Samwel HJA, de Boo TM, Wilder-Smith OHG, Oostendorp RAB, Crul BJP. Predicting outcome of TENS in chronic pain: a prospective, randomized, placebo controlled trial. Pain 2008;136:11-20.

**TABLES**

| Variable | Active TENS & knee group (n=73) | Sham TENS & knee group (n=74) | Knee group (n=77) | Total (n=224) |
|---|---|---|---|---|
| **Sex, women:men** | 47:26 | 49:25 | 45:32 | 141:83 |
| **Study knee, left:right** | 37:36 | 36:38 | 38:39 | 111:113 |
| **Age, years, mean (SD)** | 61.2 (11.4) | 60.9 (10.8) | 62.0 (9.4) | 61.4 (10.5) |
| **Body Mass Index** | 29.7 (11.1) | 29.1 (9.0) | 29.8 (7.4) | 29.6 (8.4) |
| **Pain duration, years** | 4.4 (8.7) | 4.0 (8.7) | 3.8 (9.8) | 4.0 (8.7) |
| **WOMAC total, max 96, mean (SD)** | 41.7 (19.2) | 41.0 (17.6) | 39.0 (18.1) | 40.5 (18.2) |
| **WOMAC function, max 68, mean (SD)** | 29.3 (14.0) | 28.8 (13.0) | 27.5 (13.5) | 28.5 (13.5) |
| **WOMAC pain** | 9.0 (6.0) | 9.0 (5.0) | 8.0 (5.8) | 9.0 (6.0) |
| **WOMAC stiffness** | 4.0 (2.0) | 4.0 (2.0) | 4.0 (2.0) | 4.0 (2.0) |
| **Extensor torque, Nm** | 42.0 (40.2) | 47.8 (34.9) | 45.1 (54.6) | 45.0 (45.1) |
| **Exercise self-efficacy, max 20** | 14.6 (4.0) | 15.0 (3.9) | 14.6 (3.5) | 15.0 (4.0) |
| **Exercise beliefs** | 62.2 (8.1) | 63.0 (10.2) | 62.0 (10.8) | 63.0 (9.6) |

**Table 1. Participant characteristics and median baseline values for outcome measures.** All figures are median (IQR) except where otherwise specified.

| Outcome | Trial arm | Baseline | Week 3 | Week 6 | Week 12 | Week 24 | Effects |
|---|---|---|---|---|---|---|---|
| **WOMAC function, max 68** | Active TENS & knee group (n=73) | 29.3 (14.0) | 26.2 (13.8) | 26.4 (15.0) | 25.3 (14.1) | 25.8 (13.8) | **Time p<0.001*** **Arm p=0.413** **Time x arm p=0.528** |
| | Sham TENS & knee group (n=74) | 28.8 (13.0) | 26.9 (14.0) | 25.1 (13.9) | 25.7 (14.1) | 25.3 (15.0) | |
| | Knee group (n=77) | 27.5 (13.5) | 24.4 (11.6) | 22.2 (12.1) | 24.3 (11.9) | 22.6 (13.4) | |
| **WOMAC total, max 96** | Active TENS & knee group (n=73) | 41.7 (19.2) | 37.4 (18.8) | 37.3 (20.4) | 36.2 (19.4) | 36.7 (19.5) | **Time p<0.001*** **Arm p=0.363** **Time x arm p=0.541** |
| | Sham TENS & knee group (n=74) | 41.0 (17.6) | 38.7 (18.4) | 35.7 (18.9) | 36.4 (19.5) | 35.7 (20.6) | |
| | Knee group (n=77) | 39.0 (18.1) | 34.9 (15.9) | 31.7 (16.7) | 34.4 (16.6) | 31.8 (18.4) | |

**Table 2. WOMAC function (the primary outcome measure) and WOMAC total scores over time for each trial arm.** All figures are mean (SD). A reduction in scores indicates an improvement in the condition. Effects of time, trial arm and time x arm interaction were tested using a general linear model repeated measures. *Statistically significant. Post hoc analyses of changes over time did not provide any novel findings and have therefore been excluded in the interests of brevity and because this was not the primary

focus of investigation. As the overall effect of trial arm was non-significant, between-group comparisons at each time point have not been explored.

| Variable | Active TENS & knee group (n=73) | Sham TENS & knee group (n=74) | Knee group (n=77) |
|---|---|---|---|
| % improving by >6.2 points | 33.2% | 35.9% | 41.6% |

**Table 3. Proportion of patients in each trial arm who met the clinically significant difference of 6.2/68 points on the WOMAC function subscale at six weeks.**

| Outcome | Trial arm | Baseline | Week 3 | Week 6 | Week 12 | Week 24 | Effect of time |
|---|---|---|---|---|---|---|---|
| **WOMAC Pain** | Active TENS & knee group (n=73) | 9.0 (6.0) | 7.5 (7.0) | 6.0 (5.0) | 7.0 (7.8) | 7.0 (8.0) | |
| | Sham TENS & knee group (n=74) | 9.0 (5.0) | 8.0 (6.0) | 8.0 (7.0) | 7.0 (7.0) | 6.0 (8.0) | **p<0.001*** |
| | Knee group (n=77) | 8.0 (5.8) | 7.0 (5.8) | 6.0 (5.0) | 6.0 (6.3) | 6.0 (7.0) | |
| | **Effect of trial arm** | **p=0.590** | **p=0.537** | **p=0.465** | **p=0.386** | **p=0.226** | |
| **WOMAC Stiffness** | Active TENS & knee group (n=73) | 4.0 (2.0) | 4.0 (2.0) | 3.0 (3.0) | 4.0 (3.0) | 3.5 (3.0) | |
| | Sham TENS & knee group (n=74) | 4.0 (2.0) | 4.0 (3.0) | 4.0 (2.0) | 4.0 (3.0) | 3.0 (3.0) | **p<0.001*** |
| | Knee group (n=77) | 4.0 (2.0) | 3.0 (2.0) | 3.0 (2.5) | 3.0 (3.0) | 3.0 (2.5) | |
| | **Effect of trial arm** | **p=0.503** | **p=0.538** | **p=0.201** | **p=0.527** | **p=0.510** | |
| **Extensor torque,** | Active TENS & knee | 42.0 (40.2) | 47.6 (56.0) | 49.2 (51.5) | 51.5 (45.2) | 53.9 (44.6) | **p<0.001*** |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Nm** | group (n=73) | | | | | | |
| | Sham TENS & knee group (n=74) | 47.8 (34.9) | 49.4 (41.9) | 56.6 (35.8) | 53.9 (44.4) | 58.9 (39.7) | |
| | Knee group (n=77) | 45.1 (54.6) | 55.6 (52.6) | 62.0 (60.5) | 58.7 (53.0) | 62.2 (62.2) | |
| | **Effect of trial arm** | **p=0.440** | **p=0.748** | **p=0.788** | **p=0.660** | **p=0.419** | |
| **Global assessment of change, -7 to +7** | Active TENS & knee group (n=73) | - | 2.0 (3.1) | 3.0 (3.5) | 2.0 (5.6) | 2.8 (5.8) | **p<0.001*** |
| | Sham TENS & knee group (n=74) | - | 2.0 (3.7) | 2.9 (4.4) | 2.7 (5.4) | 2.9 (6.4) | |
| | Knee group (n=77) | - | 2.0 (3.0) | 3.0 (4.8) | 2.0 (5.0) | 3.2 (5.3) | |
| | **Effect of trial arm** | **-** | **p=0.212** | **p=0.590** | **p=0.785** | **p=0.595** | |
| **Exercise Self-Efficacy, 5 to 20** | Active TENS & knee group (n=73) | 14.6 (4.0) | - | - | - | 15.8 (4.5) | **p=0.031*** |
| | Sham TENS & knee group (n=74) | 15.0 (3.9) | - | - | - | 16.0 (4.1) | |
| | Knee group (n=77) | 14.6 (3.5) | - | - | - | 16.0 (5.5) | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Effect of trial arm** | **p=0.693** | **-** | **-** | **-** | **p=0.259** | |
| **Exercise Adherence, 0 to 4** | Active TENS & knee group (n=73) | - | 3.0 (1.1) | 3.0 (1.0) | 3.0 (1.0) | 3.0 (1.0) | **p<0.001*** |
| | Sham TENS & knee group (n=74) | - | 3.0 (1.0) | 3.0 (0.3) | 3.0 (1.0) | 3.0 (1.0) | |
| | Knee group (n=77) | - | 3.0 (1.6) | 3.0 (1.9) | 3.0 (1.0) | 3.0 (1.2) | |
| | **Effect of trial arm** | **-** | **p=0.555** | **p=0.391** | **p=0.292** | **p=0.159** | |

**Table 4. Secondary outcome scores over time for each trial arm.** All figures are median (IQR). A reduction in WOMAC pain and stiffness scores indicates an improvement in the condition. An increase in all other scores indicates improvement. Effects of trial arm were tested using Kruskal Wallis tests and time effects using Friedman tests. As there were no trial arm effects for any outcome measure, the effects of time were calculated using all participants (n=224). *Statistically significant. Post hoc analyses of changes over time did not provide any novel findings and have therefore been excluded in the interests of brevity and because this was not the primary focus of investigation.

| TENS Programme | Active TENS | Sham TENS |
|---|---|---|
| A. Continuous - 110Hz (50μs)* | 22% | 17% |
| B. Continuous - 4Hz (200μs) | 8% | 8% |
| C. Burst - Frequency within burst=100Hz (200μs); Repetition Frequency of bursts=2Hz | 20% | 8% |
| D. Continuous - 10Hz (200μs) | 12% | 11% |
| E. Continuous - 110Hz (200μs) | 2% | 6% |
| F. Intensity Modulation - 110Hz (200μs) | 2% | 9% |
| G. Frequency Modulation - 2Hz, 10Hz, 50Hz, 80Hz, 90Hz, 100Hz and 110Hz (200μs) | 4% | 21% |
| Combination | 29% | 21% |

**Table 5. Settings reported by TENS users as those that they *"normally used"*.** Please note that patients were asked to choose the TENS programme letter identifier as this was all that was visible to participants on the device display. Additional TENS parameter details are included here for clarity. *Setting A was used for initial instruction but participants were encouraged to try other settings throughout the six-week TENS intervention.

## FIGURE LEGEND

**Figure 1. Flowchart of recruitment and retention of study participants.** Data analysis was by intention to treat using multiple imputation therefore n=224 data sets were available for analysis.

**FIGURE**

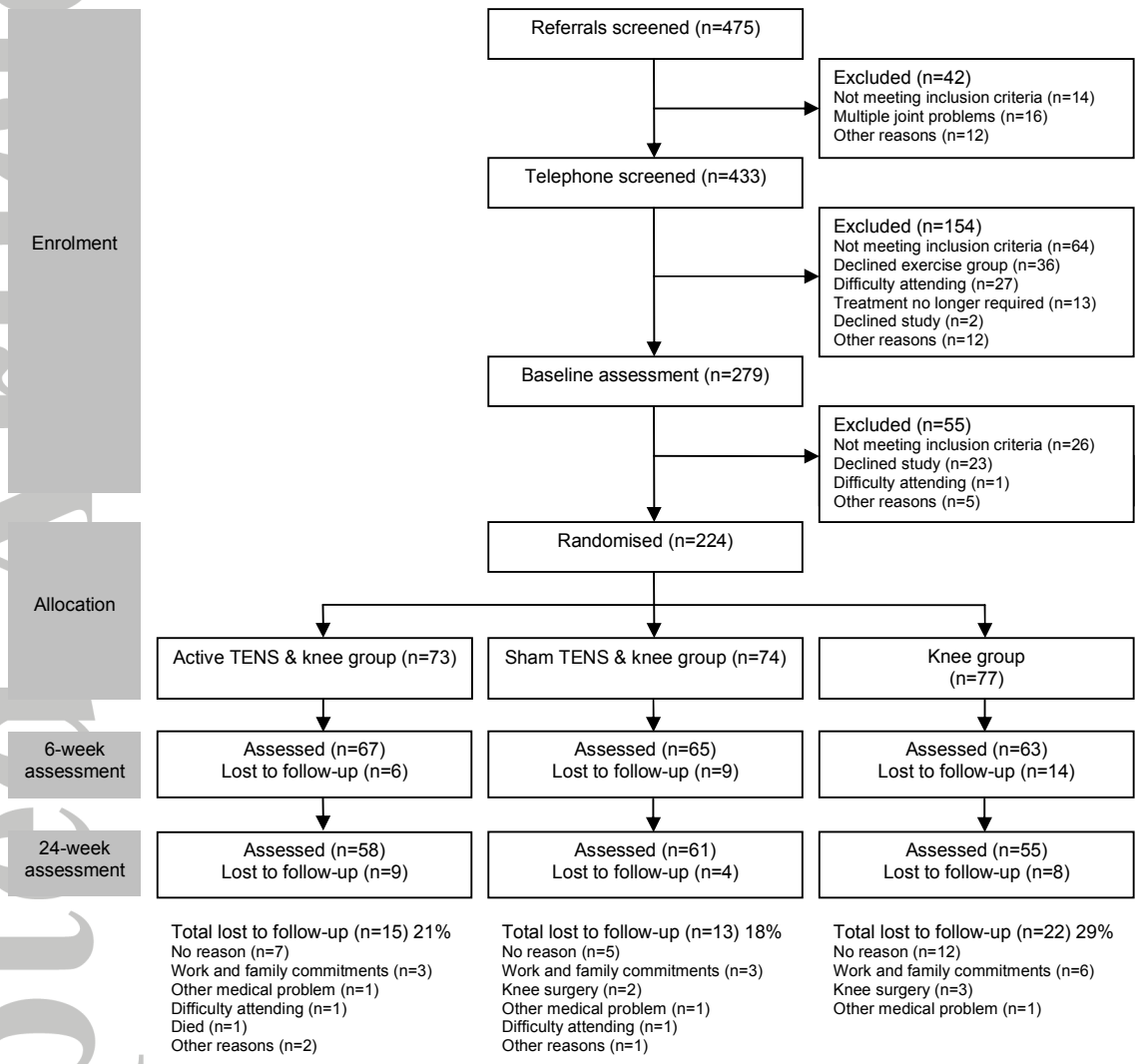


**Figure 1. Flowchart of recruitment and retention of study participants.** Data analysis was by intention to treat using multiple imputation therefore n=224 data sets were available for analysis.