**TITLE**

Manual therapy, therapeutic patient education and therapeutic exercise, an effective multimodal treatment for nonspecific chronic neck pain; a randomised controlled trial.

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Manual therapy, therapeutic patient education and therapeutic exercise, an effective multimodal treatment for nonspecific chronic neck pain; a randomised controlled trial

**Objective:** The aim of this study was to determine the effectiveness of a multimodal treatment in the short and medium term for disability in non-specific chronic neck pain (CNP).

**Design:** A single blinded randomised controlled trial carried out in a University research laboratory. Forty-five patients between 18 and 65 years old with non-specific CNP. Each patient was treated eight times over a four-week period. The sample was divided into three groups. (Control) A protocol of manual therapy (MT), (Experimental 1) a protocol of MT and therapeutic patient education (TPE) and (Experimental 2) MT, TPE and a therapeutic exercise protocol. Assessments were performed at baseline, at 4, at 8 and 16 weeks using the following measurements: The Neck Disability Index (NDI), Tampa Scale of Kinesiophobia (TSK), Fear Avoidance Beliefs Questionnaire (FABQ), Neck Flexor Muscle Endurance Test (NFME) and Visual Analogue Fatigue Scale (VAFS) were used as outcome measures.

**Results:** The non-parametric Kruskal-Wallis test for NDI showed statistically significant differences between baseline outcomes and all follow-up periods ($P<0.01$). In the Kruskal-Wallis test, differences were found for the VAFS and NFME in the follow-ups at 8 and 16 weeks ($P<0.05$). ANOVA for group x time interaction showed statistically significant changes [TSK ($F=3.613$; $P=0.005$); FABQ ($F=2.803$; $P=0.022$)]. Minimal detectable changes were obtained in both experimental groups for the TSK-11, but not in the control group.

**Conclusion:** No differences were found between the experimental groups in the short and medium term. However, the treatment protocol used in experimental group 2 showed a greater effect in the medium term than the treatment protocol used in experimental group 1 for the treatment of disability in patients with non-specific CNP.

**Keywords:** Neck pain; manual therapy; exercise; education.

## Introduction

Non-specific chronic neck pain has a high prevalence and is commonly in clinical practice.[1] This condition is often accompanied by significant levels of disability and pain, and these levels have shown a moderate correlation with fear of movement.[2] Consequently, inactivity is thought to lead to deconditioning.[3] Moreover, as the pain is chronic, there are psychosocial risk factors associated with the disability, such as depression and anxiety, that should be taken into account during treatment by a physiotherapist.[4] These approaches should be integrated into a biopsychosocial approach.

Several studies have demonstrated the effectiveness of techniques for the treatment of pain and disability in the neck, including mobilisation, manipulation and therapeutic exercise.[5–8] For non-specific neck pain, the combination of manual therapy with exercise produced greater reductions in pain and improvements of function than manual therapy alone, exercise alone, medications or passive interventions regardless of follow-up duration.[9–11] Moreover, no advantage was found in exercise alone versus manual therapy alone, and mobilization was not better than exercise for nonspecific neck pain, irrespective of follow-up duration.[6,12,13]

There is a lack of evidence of therapeutic patient education (TPE) concerning for non-specific neck pain. In a recent review of patient education for neck pain it was suggested that TPE has no effectiveness with different educational interventions.[14] But for other clinical conditions such as whiplash and associated disorders a systematic review reported that education was superior to other interventions for reducing pain and disability.[15] However, these conclusions were based on heterogeneous patient education, including education as part of a multimodal intervention.[14,15] Thus, there is a need to determine the effectiveness of a protocolled TPE intervention combined with manual therapy. We are not aware of any studies that have researched the effects of TPE combined with manual therapy and exercise for nonspecific chronic neck pain patients.[14–16]

Therefore, the aim of this study was to determine the effectiveness of a multimodal intervention treatment in the short and medium term for disability associated in non-specific chronic neck pain patients as well as to determine if therapeutic exercise (TEX) and TPE influence disability outcomes compared with TPE alone.

## Methods

### *Design*

The study was a single-blinded RCT. People with nonspecific chronic neck pain were recruited by referral from La Salle University and at a primary health care ambulatory in Coslada, Madrid. The trial was conducted in accordance with the CONSORT statement; the study was approved by the ethical committee of the Hospital Universitario La Princesa and was registered with the United States Clinical Trials Registry as registration number NCT02033460.

After meeting the eligibility criteria for the study, the patients each signed an informed consent form. Each participant was randomly allocated by a therapist to one of three groups according to a computer-generated random allocation list. The protocol for each group lasted four weeks with two sessions of treatment per week for a total of eight sessions. All sessions were one-on-one patient-therapist encounters. The outcomes were recorded at 0, 4, 8 and 16 weeks.

The RCT consisted of physical therapists, including four assessors and two therapist. The assessors made the telephone calls, verbally discussed inclusion and exclusion criteria with enquirers, made appointments, and prepared files. Also, one therapist was tasked with generating the randomisation schedule using a Web-based random number generator (GraphPad) and allocating each participant to one of the three groups. This therapist kept the schedule to which the assessors were blinded. The therapists' role was to perform the interventions. The assessors collected all baseline and outcome data. The therapist was blinded to the assessment outcomes until the end of the entire data collection. Also, the participants were specifically told not to discuss their interventions with the outcome assessor. During the treatment and follow-up periods, they were advised not to use medication or take other manual therapies so that the effect of the therapy could be seen. In the cases where the patient did not follow that advice, they were counted as lost.

*Participants*

Men and women aged between 18 and 65 years of age with neck pain for at least 12 weeks were included in the study. On the university campus, the study was publicly advertised so that university staff, students and relatives could participate. If they did, the assessor asked screening questions and cited them for the first assessment. The subjects for the study were selected if they fulfilled the following inclusion criteria: they were aged between 18 and 65 years; they understood, wrote, and spoke Spanish fluently; they had experienced neck pain for at least 12 weeks; they were willing to undergo the treatment and complained of pain localised in the neck region. Patients were not considered if they reported any of the following conditions: neck pain associated with whiplash injuries, medical red flag history (i.e., tumour, fracture, metabolic diseases, rheumatoid arthritis, osteoporosis), neck pain with cervical radiculopathy, neck pain associated with externalized cervical disc herniation, fibromyalgia syndrome, previous neck surgery, neck pain accompanied by vertigo caused by vertebrobasilar insufficiency or accompanied by non-cervicogenic headaches. People were also not considered if they were undergoing any type of pain treatment, had received physical therapy in the previous three months, or had pending legal action (e.g., compensation for injury, labour), psychiatric disorders or other problems that could contraindicate the use of techniques in this study

*Interventions*

In a one-month period, all participants received eight treatment sessions (twice per week) regardless of their allocation group. Each session was one-on-one, and there was a rest period of 48 to 72 hours between them. To enter the analysis, each patient had to receive at least seven sessions; everyone fulfilled this criterion.

The control group received various MT techniques that were focussed on decreasing neck pain. The effectiveness of these techniques has been demonstrated previously.[5,17,18] The protocol of the MT is described in **Supplemental Digital Content 1**. The duration of each session was about 25 minutes.

Experimental group 1 (Exp1) received the same treatment as the control group but with the addition of TPE in two sessions. The TPE was based on a biobehavioural approach and divided into three parts: cognitive, operant and respondent. A summary of the TPE is provided in **Table 1**. The purpose of the TPE was to modify any erroneous beliefs about pain and disability and to promote coping strategies and self-efficacy through a graded activity. The duration of the two TPE sessions was about 20 minutes each. The first TPE session was held after the first treatment intervention, in which the cognitive part was explained. The second TPE session was held after the fifth treatment intervention, in which we reviewed the concepts viewed in the first session, and also the operant and respondent parts were explained. It was held after the fifth treatment intervention because the participant needed to have assimilated and understood the cognitive part. Furthermore, the respondent part utilised techniques (e.g. autotraction) that make it preferable for the patient not to have much pain, which in the fifth session is expected to be somewhat reduced compared to the beginning of the treatment.

In the first session, with the support of a PowerPoint presentation using diagrams, images and texts, the physiotherapist explained the cervical engine behaviour, the neurophysiological basis of pain, the importance of the participant's involvement in the treatment (e.g., coping, motivation), and the maintenance of good ergonomics. Furthermore, the patients were given an information booklet containing the most relevant aspects of the educational session talk and were encouraged by the physiotherapist to ask any questions about it.

In the second session, the content covered in the first session was reviewed and continued with the respondent section, which was aimed at modifying the physiological response to pain system. Then it continued with the operant section, in which the physiotherapist explained self-treatment techniques, such as stretching, autotraction, diaphragmatic breathing and relaxation techniques (Jacobson relaxation technique) to provide the patients with coping strategies and reduce their attention to pain. In addition, patients received another booklet that contained a detailed description of these self-treatment techniques. Finally, it was determined that the patients had understood everything that was explained and the physiotherapist urged the patients to ask any questions about any doubts they may have had.

Experimental group 2 (Exp2) received the same treatment as Exp1 but with the addition of a TEX programme. This programme was based on motor control exercises of the cervical region and neural self-mobilisation. These motor control exercises were targeted at the deep neck flexors and extensors to provide them with strength and resistance. A physiotherapist, in line with the detailed written protocol shown in **Supplemental Digital Content 2**, taught and supervised the exercise programme. All exercises were pain-free provocation, so patients were asked to cease activity if they felt any pain. The TEX programme was progressive and added in sessions 5 to 8, in which exercises were undertaken with physiotherapist supervision. For the integration of TEX in the treatment sessions, the time spent on MT techniques was halved. Patients were asked to perform the exercises at least once per day at home for the next eight weeks.

*Outcome measures*

***Primary outcome:*** The primary outcome was the change in the scores of the Neck Disability Index (NDI) between the baseline assessment and at the 16-week follow-up. The NDI is a well-validated 10-item questionnaire, where each item is rated on a 0 to 5-point scale.[19] The NDI has sufficient support in the literature as the most commonly used instrument for reporting neck pain.[19,20] A Spanish validation of the index was used.[21] Scores of <4 indicate no disability, 5–14 mild disability, 15–24 moderate disability, 25–34 severe disability and >35 complete disability. The minimum detectable change is 5 points out of 50, and it is recommended that 7 points be considered the minimum clinically important difference.[20]

***Secondary outcomes:*** To evaluate the participants pain-related fear of movement and (re)injury, a Spanish validated Tampa Scale of Kinesiophobia (TSK) was used.[22] We used an 11-item version that has shown good psychometric reliability for chronic pain.[23] Each item is scored on a four-point Likert-type scale that ranges from “strongly agree” to “strongly disagree”. Total scores range from 11 to 44, and higher scores indicate more fear of movement and/or (re)injury. For chronic pain, the minimal detectable change is 5.6.[24]

To assess patient beliefs with regard to the effect of physical activity and work on their pain we used the Fear Avoidance Beliefs Questionnaire (FABQ). This consists of 16 items and patients rate their agreement with each statement on a seven-point Likert scale (0=completely disagree, 6=completely agree).[25,26] This test showed excellent test-retest reliability (ICC=0.97) for the Spanish validation.[26]

The Neck Flexor Muscle Endurance Test (NFME) and the Visual Analogue Fatigue Scale (VAFS) were used to measure endurance and the sensation of fatigue in the deep neck flexors. The test was performed in the supine and crook lying positions.[27] With the patient's chin maximally tucked and maintained isometrically, the therapist lifted their head and neck until the occipital bone was approximately 2.5 cm off the plinth while keeping the chin retracted to the chest. Prior to the test, the verbal command "keep the chin tucked and breathe" was given, but during the test verbal commands were not given. The test was stopped whenever there was a loss of chin tuck or if the participant wanted to stop because of fatigue or pain. We took only one measurement to avoid inducing patient fatigue. This test showed a moderate reliability for neck pain (ICC=0.67) with 24.1±12.8 seconds.[27] Also, the minimal detectable change for this test is 17.8 seconds.[27] Immediately after the NFME test, participants were asked to rate their experiencied fatigue intensity with a VAFS.[28] The VAFS contains a 100mm-long line that is  marked with "No fatigue" on the left and "Worst fatigue ever experienced" on the right.

*Data analysis*

The NDI was chosen as the primary outcome measure. The effect size (ES) of the NDI was estimated to be medium (ES=0.25). With a power of 0.90 and an alpha level of 0.05, it was estimated that 13 participants would be required for each group (39 participants altogether) by using the software G*power 3.[29] The enrolment goal was set at 45 participants in order to account for a 15% possible dropout rate. Baseline demographic characteristics are reported with descriptive statistics.

The Statistical Package for the Social Sciences (SPSS 21, SPSS Inc., Chicago, IL USA) was used for statistical analysis. The normal distribution of all primary and secondary measures data was assessed using the Shapiro-Wilk test ($P>0.05$). The data showed a normal distribution, with the exception of age, pain duration, NDI, VAFS and NFME test. An independent t-test and one-way ANOVA were used to compare variables from the three groups to baseline data, including the analysis of self-reported psychological variables (TSK and FABQ) and the subjects' sociodemographic data (weight, height). Analyses were performed according to the intention-to-treat principle.

For outcome variables, a two-way repeated-measures within-between interaction factors ANOVA was performed; the factors analysed were group (i.e. control group, Exp1 and Exp2) and time (0, 4, 8 and 16 weeks). The hypothesis of interest was the group x time interaction. Post hoc analysis with Bonferroni correction was performed in the case of significant ANOVA findings for multiple comparisons between variables. Effect sizes (Cohen's *d*) were calculated for the primary and secondary outcome variables. The magnitude of the effect was classified as small (0.20 to 0.49), medium (0.50 to 0.79) or large (0.8) according to Cohen's method.[30]

We used non-parametric statistics for the NDI, VAFS and NFME variables, because they were not normally distributed. Descriptive statistics were used to summarise data, including means and SDs, medians, and interquartile ranges (IQR) for continuous data. The Kruskal-Wallis test was used for the analysis of pain duration and the NDI, VAFS and NFME were used to compare the three groups to baseline data. For comparisons across and between groups we used the Kruskal-Wallis test. The Friedman test was used to analyse the change from the intra-group results, and the Wilcoxon signed rank test was used for post hoc intra-group comparisons.

**Results**

Participants were recruited from November 2011 to May 2013, and 45 took part in the trial. The study flow chart and the reasons why one participant from the control group (7%) and one participant from the Exp1 group (7%) were lost to follow-up are presented in **Figure 1**. Baseline demographic characteristics data are presented in **Table 2**. No significant differences existed between groups in any of the baseline measurements ($P>0.05$).

*NDI outcome*

All groups presented statistically significant differences between baseline outcomes and all follow-up periods (P<0.01). In comparisons between groups using the Kruskal-Wallis test, differences were found at 4, 8 and 16 weeks (P<0.01). The results for the NDI are presented in **Table 3**.

*VAFS and NFME outcomes*

In the Kruskal-Wallis test, differences were found for the VAFS and NFME in the follow-ups at 8 and 16 weeks (P<0.05) as observed in **Table 3.** The Wilcoxon test showed significant differences for VAFS and NFME outcomes when the baseline data were compared with the follow-up periods at 8 and 16 weeks (P<0.05) for Exp1 and Exp2, but not for the control group. The Friedman test showed that in the Exp1, the following variables were found to be statistically significant (P<0.01): VAFS and NFME. In Exp2, NFME was found to be statistical significant (P<0.01), but not VAFS.

*TSK and FABQ outcomes*

The results of the ANOVA revealed a significant effect for the group factor [TSK (F=5.348; P=0.009) and FABQ (F=4.15; P=0.009)]. There were differences for the group x time interaction [TSK (F=3.613; P=0.005) and FABQ (F=2.803; P=0.022)]. The effect size (*d*) for baseline outcomes at the four-month follow-up was significantly greater for Exp2 in the FABQ (*d*=1.13) than for Exp1 (*d*=0.78). The TSK showed better changes in Exp1 (*d*=1.22) than in Exp2 (*d*=1.02). Results are presented in **Table 4.1.** In the comparison between groups, no differences existed between Exp1 and Exp2 in the short and medium term. There were differences in the short and medium term between the experimental groups and the control group. Comparisons between groups of the baseline and post-treatment follow-ups are presented in **Table 4.2.**

## Discussion

The aim of this study was to determine the effectiveness of a multimodal intervention treatment in the short and medium term for disability associated with non-specific chronic neck pain patients. The findings suggest that both experimental and control treatments reduced disability in these patients in the short and medium term. Furthermore, the inclusion of TPE and TPE plus TEX in the same protocol treatment showed a greater effect. For several years we have known that biobehavioural factors affect disability in chronic pain patients. Although they have been studied more in relation to low back pain, we know that they also affect patients with neck pain.[31–34]

In this study, the NDI scores for the short term (4 and 8 weeks) and medium term (16 weeks) in Exp1 and Exp2 revealed greater changes when compared with the control group. These changes in Exp2 may be justified by the inclusion of TEX in the treatment protocol, as has been seen in recent studies that combine MT and exercise.[18,35] Furthermore, in Exp1 the inclusion of TPE with a biobehavioural approach and MT obtained the same results as in Exp2. Therefore, not only did the inclusion of exercise show great improvement in the disability of chronic neck pain patients in the medium term, but so did the combination of MT and TPE. According to the authors' knowledge of chronic non-specific neck pain, this is the first study to analyse the effect of TPE in the short and medium term, although it is true that this effect of TPE with a focus on neurophysiology has been observed in other clinical conditions such as chronic non-specific low back pain.[33] Exp2 obtained a small improvement over Exp1 for the neck disability; this may be due to the combination of TPE and TEX. The control group obtained statistically significant changes in the short and medium term. But by looking at the medians and quartiles, these changes are very small in terms of disability, and we do not know whether this would have a real impact in the clinic. Furthermore, we know from the literature that MT becomes more statistically significant in short-term changes.[10,18,35,36] The combination of several MT techniques may have medium-term disability effects, but they were not as powerful as a multimodal intervention and as explained later did influence other variables in the same way.

The VAFS and NFME test for the experimental groups showed better outcomes than the control group, which did not demonstrate statistical significance for the short and medium term. Exp2, which included exercise, showed better medians and quartiles in comparison with Exp1 in the short and medium term; this corresponds with the findings observed in the literature on exercise for neck pain[27] and with the hypothesis that the Exp2 group will have a greater improvement because of the inclusion of exercise. For Exp1 there was statistical significance in the short to medium term and the authors believe this may be due to an increased sense of well-being and a decreasing sense of kinesiophobia and fear of movement. This is discussed further in the next paragraph, but this statistical significance is not clinically relevant.

In the medium term, minimally detectable changes were found in the two experimental groups for the TSK. Exp1 showed minimal detectable changes in the short term, but Exp2, which had TPE and TEX instead of TPE alone, did not. It is unclear as to why the TPE alone had better short-term TSK outcomes. But C.G. Ryan et al.,[34] referring to chronic low back pain, also reported that patient education alone was better than the combination of education and exercise in the short term. C.G. Ryan et al.[34] suggested that the purpose of the educational session was to "demedicalise" the person's condition and to shift attitudes towards a more biopsychosocial self-management approach. Attending the exercise classes with a clinical instructor (physiotherapist) may have detracted from that message and reinforced the concept of the participants being patients. Moreover, this changed in the current study in the eight-week follow-up when the patients had to performed their exercises on their own for four weeks. In the control group, no differences were found between follow-ups. Our results in Exp1 agree with the study by Linton and Ryberg, who reported that cognitive behavioural therapy produced more beneficial effects than conventional treatment to reduce the fear of motion in patients with chronic neck pain.[37] However, previous studies have found on the one hand that a higher fear of motion correlate with poor neck kinematics and higher disability, and on the other hand that patients who have recovered poorly from neck pain maintain the same level of kinesiophobia during 12 months of follow-up.[38,39]

In our research the FABQ showed statistically significant differences in all follow-ups of the experimental groups but not in the control group; this may be due to the lack of inclusion of TPE in the control group. In relation to that lack, a recent study among patients with chronic low back pain found that an exercise programme with a cognitive behavioural TPE showed an improvement in fear avoidance beliefs in the long term in contrast to an exercise programme alone.[40] This is in agreement with previous literature that has shown that a higher level of fear of movement is predictive of a higher risk of prolonged disability.[41] So this could be a justification for the inclusion of TPE in a MT treatment for chronic pain patients.

### *Study limitations*

There are several limitations to consider in this study. For one thing, we did not collect information about the patients' failure with previous treatments. This issue could limit potential gains in the current study because the patients' expectations may be affected, especially in the control group. Also, the inclusion criteria vary greatly; it would be interesting to use more concrete inclusion criteria for a specific neck pain.

Another limitation is the medium-term follow-up. We do not know what the long-term effectiveness of this protocol treatment would be, but previous literature has shown positive long-term effects in patients with chronic neck pain.[5] It would be interesting for future research to observe these long-term changes and determine the long-term clinical effectiveness of TPE.

## Conclusions

A multimodal treatment is a good method for reducing disability in patients with nonspecific chronic neck pain in the short and medium term. No differences were found between the experimental groups in the short and medium term. But a treatment protocol with MT, TPE and TEX showed a greater improvement in the medium term than only MT plus TPE for the treatment of neck disability in patients with chronic non-specific neck pain.

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**Figures legend:**

*Figure 1 footnotes:*

Figure 1. Study flow chart diagram.

**Supplemental Digital Content legend:**

A. Techniques used in the manual therapy protocol.

B. Exercises used in the therapeutic exercise protocol.

Table 1

Table 1.Therapeutic patient education summary.

| | Method | Approach | Skills |
|---|---|---|---|
| Cognitive | -Education on the basic physiology of pain and chronic pain.<br>-Education on basic anatomy of the cervical region.<br>-Physiological and biomechanical bases of motor behaviour. | -Explanation of maladaptive belief about pain and disability | -Reinforce positive beliefs.<br>-Ergonomic<br>-Interrupting and reversing of maladaptive craniocervical postures. |
| Operant | -Eliminate inappropriate behaviour (e.g. sedentary lifestyle)<br>-Promoting positive behaviours (e.g. exercise, return to work) | -Exposure to graded activity | -Gradual progression of cervical movements.<br>-Gradual progression of low-intensity aerobic exercise (e.g. walking 30 minutes a day) |
| Respondent | | -Self-treatment techniques | - Auto-traction techniques.<br>-Diaphragmatic breathing and relaxation techniques (e.g. Jacobson relaxation technique) |

Table 2

| Characteristic | Randomised (n = 45) | | | | | | P value of independent samples ANOVA or $\chi^2$ test |
|---|---|---|---|---|---|---|---|
| | Control (n = 15) | Shapiro-Wilk (P value) | Experimental 1 (n = 15) | Shapiro-Wilk (P value) | Experimental 2 (n = 15) | Shapiro-Wilk (P value) | |
| Participants | | | | | | | |
| Age(yr), mean (SD) | 43.5 (15.9) | **0.01†** | 40.9 (16.2) | **0.02*** | 39.8 (13.4) | **0.14** | **0.76** |
| Gender, n females(%) | 12 (80) | - | 13 (86.7) | - | 10 (66.7) | - | **0.40** |
| Weight (kg), mean (SD) | 64.4 (13.2) | **0,66** | 64.2 (10.2) | **0.50** | 70.4 (17.9) | **0.33** | **0.40** |
| Height (mts), mean (SD) | 1.72 (0.18) | **0.82** | 1.68 (0.14) | **0.66** | 1.75 (0.18) | **0.96** | **0.50** |
| Pain Duration (month), mean (SD) | 95.8 (77.5) | **0.08** | 54.9 (57.1) | **0.13** | 83.4 (94.1) | **0.00†** | **0.28** |
| NDI, mean (SD) | 14.1 (4.2) | **0.34** | 12.9 (4.1) | **0.76** | 13 (3.8) | **0.68** | **0.73** |
| TSK-11, mean (SD) | 30(5.9) | **0.36** | 28 (6) | **0.52** | 25.4 (5.8) | **0.77** | **0.11** |
| FABQ, mean (SD) | 41.2 (14.6) | **0.71** | 34.7(20.7) | **0.1** | 34.9(16) | **0.6** | **0.51** |
| VAFS (mm), mean (SD) | 50.5(20.1) | **0.96** | 45.1(13.8) | **0.53** | 46.2 (22.3) | **0.7** | **0.58** |
| NMFE (sec), mean (SD) | 16.3(8.4) | **0.71** | 17 (7.9) | **0.02*** | 16.4(5.7) | **0.01†** | **0.88** |

**Table 2.** Baseline characteristics of participants.

**Footnotes:** NDI, Neck disability index; TSK, Tampa Scale of Kinesiophobia; FABQ, Fear Avoidance Beliefs Questionnaire; NFME, Neck Flexor Muscle Endurance Test; VAFS, Visual Analogue Fatigue Scale; * p≤0.05; † p≤0.01

Table 3

Table 3. Non-parametric tests of outcome data.

| | Group | Median (first and third quartiles) | | | | Friedman ANOVA | Wilcoxon a) Pre vs. Post b) Pre vs. 8 weeks c) Pre vs. 16 weeks |
|---|---|---|---|---|---|---|---|
| | | Baseline | Post-treatment | 8 weeks | 16 weeks | | |
| **NDI (0-50)** | **Con** | 14 (11 and 18) | 9 (5 and 11) | 10 (5 and 14) | 8 (5 and 14) | < 0.001 | **a)** 0.001<br>**b)** 0.006<br>**c)** 0.007 |
| | **Exp1** | 13 (11 and 15) | 2 (1 and 6) | 2 (0 and 8) | 5 (0 and 8) | < 0.001 | **a)** 0.001<br>**b)** 0.001<br>**c)** 0.001 |
| | **Exp2** | 13 (12 and 16) | 2 (0 and 5) | 4 (0 and 7) | 3 (1 and 5) | < 0.001 | **a)** 0.001<br>**b)** 0.001<br>**c)** 0.001 |
| **Kruskal-Wallis** | | 0.735 | 0.003 | 0.001 | 0.006 | | |
| **VAFS (mm)** | **Con** | 48 (32 and 68) | 46 (20 and 70) | 47 (30 and 53) | 50 (24 and 60) | 0.128 | **a)** 0.088<br>**b)** 0.123<br>**c)** 0.798 |
| | **Exp1** | 45 (35 and 60) | 20 (5 and 51) | 23 (18 and 38) | 20 (0 and 40) | 0.003 | **a)** 0.041<br>**b)** 0.013<br>**c)** 0.003 |
| | **Exp2** | 46 (25 and 62) | 28 (9.5 and 40) | 25 (17 and 41) | 27 (16 and 40) | 0.113 | **a)** 0.033<br>**b)** 0.033<br>**c)** 0.006 |
| **Kruskal-Wallis** | | 0.588 | 0.108 | 0.04 | 0.009 | | |
| **NFME (secs)** | **Con** | 15 ( 10 and 25) | 20 (13 and 40) | 26 (13 and 33) | 21 (14 and 34) | 0.056 | **a)** 0.018<br>**b)** 0.038<br>**c)** 0.033 |
| | **Exp1** | 17 (11 and 18) | 28 (20 and 45) | 30 (24 and 50) | 33 (23 and 45) | 0.003 | **a)** 0.006<br>**b)** 0.001<br>**c)** 0.003 |
| | **Exp2** | 15 (14.5 and 18.5) | 30 (24.5 and 47.5) | 32 (25.5 and 45.5) | 35 (29.5 and 48.5) | < 0.001 | **a)** 0.001<br>**b)** 0.001<br>**c)** 0.001 |
| **Kruskal-Wallis** | | 0.883 | 0.14 | 0.047 | 0.006 | | |

**Footnotes**: Con, control group; Exp1, Experimental group 1; Exp2, Experimental group 2; NDI, Neck disability index; NFME, Neck Flexor Muscle Endurance Test; VAFS, Visual Analogue Fatigue Scale.

Table 4

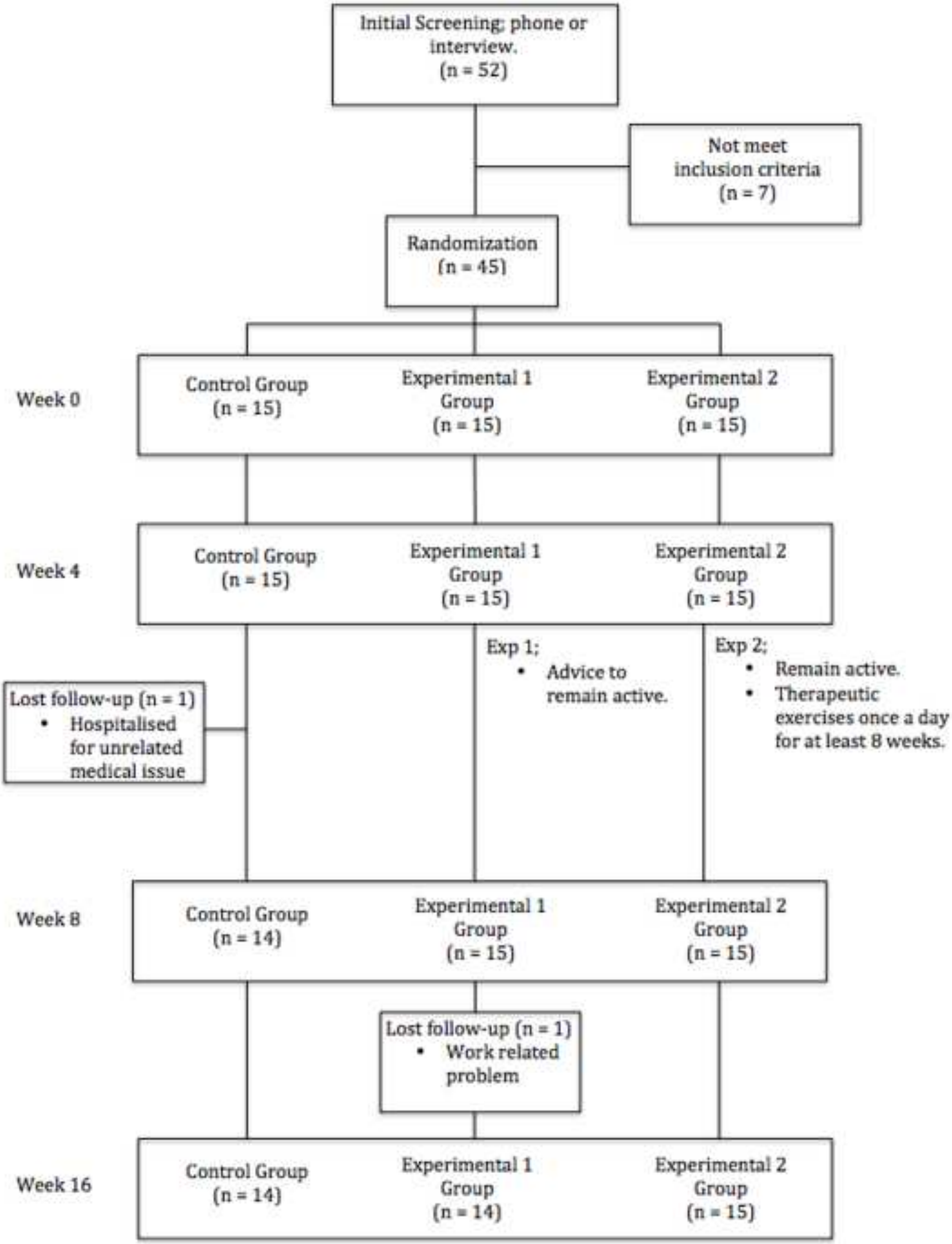
**Table 4**. 1. Mean of groups (SD), mean (95% CI) difference between groups for outcomes, effect size (*d*) of interventions in follow-ups. 2. Comparison between groups, baseline versus post-treatment. Mean difference (95% CI) and significance of interventions in follow-ups.

| **1** | | Mean (SD) | | | | Mean difference (95% CI); Effect size (*d*) |
|---|---|---|---|---|---|---|
| | Group | Baseline | Post-treatment (4 weeks) | 8 weeks | 16 weeks | a) Base vs. Post-treatment<br>b) Base vs. 8 weeks<br>c) Base vs. 16 weeks |
| TSK (0 to 44) | Con | 30 (6) | 25 (6) | 26 (6) | 26 (6) | a) 4 (1 to 7)†; 0.7<br>b) 3 (-1 to 7.); 0.6<br>c) 3 (-1 to 7); 0.5 |
| | Exp1 | 28 (6) | 19.8 (4) | 19.3 (6.3) | 19.3 (8) | a) 8 (5 to 11)†; 1.6<br>b) 8 (5 to 12)†; 1.4<br>c) 8 (5 to 12)†; 1.2 |
| | Exp2 | 25.4 (5.8) | 23 (5) | 20 (5) | 19.5 (5.4) | a) 2 (-1 to 5); 0.4<br>b) 5 (1 to 9)†; 1<br>c) 6 (2 to 10)†; 1 |
| FABQ (0 to 96) | Con | 41.2 (14.6) | 40.9 (18.1) | 33.4 (16.5) | 36.8 (15.9) | a) 1 (-7 to 8); 0<br>b) 7 (-1 to 16); 0.5<br>c) 4 (-4 to 12); 0.2 |
| | Exp1 | 34.7 (20.7) | 23.9 (16.5) | 21.4 (16.1) | 20.6 (14.9) | a) 11 (3 to 18)†; 0.5<br>b) 13 (5 to 21)†; 0.7<br>c) 14 (5 to 22)†; 0.7 |
| | Exp2 | 34.9 (16) | 23.8 (12.2) | 20.9 (12) | 18.6 (12.5) | a) 11 (3 to 19)†; 0.7<br>b) 14 (6 to 22)†; 0.9<br>c) 16 (8 to 24)†; 1.1 |

| **2** | | Mean difference (95% CI) | | | | Significance (p) |
|---|---|---|---|---|---|---|
| | Group | Baseline | Post-treatment (4 weeks) | 8 weeks | 16 weeks | a) vs Post-treatment<br>b) vs 8 weeks<br>c) vs 16 weeks |
| TSK (0 to 44) | Con vs Exp1 | 2.1 (-3.3 to 7.5) | 5.7 (1.1 to 10) | 7.1 (1.7 to 12.5) | 7.2 (1.1 to 13.3) | a) 0.009†<br>b) 0.006†<br>c) 0.01† |
| | Con vs Exp2 | 4.6 (-0.7 to 10) | 2.4 (-2 to 7) | 6.4 (1 to 11.8) | 7 (0.9 to 13.1) | a) 0.5<br>b) 0.01†<br>c) 0.02* |
| | Exp1 vs Exp2 | 2.5 (-2.8 to 7.9) | -3.2 (-7.8 to 1.2) | -0.6 (-6 to 4.7) | -0.2 (-6.3 to 5.9) | a) 0.2<br>b) 1<br>c) 1 |
| FABQ (0 to 96) | Con vs Exp1 | 6.4 (-9.3 to 22.2) | 17 (2.6 to 31.4) | 12 (-1.6 to 25.6) | 16.2 (3 to 29.5) | a) 0.01†<br>b) 0.1<br>c) 0.01† |
| | Con vs Exp2 | 6.2 (-9.5 to 22) | 17 (2.6 to 31.4) | 12.4 (-1.2 to 26.1) | 18.2 (5 to 31.5) | a) 0.01†<br>b) 0.08<br>c) 0.004† |
| | Exp1 vs Exp2 | -0.2 (-16 to 15.6) | -5.6 (-14.4 to 14.4) | 0.4 (-13.2 to 14.1) | 2 (-11 to 15) | a) 1<br>b) 1<br>c) 1 |

**Footnotes**: Con, control group; Exp1, Experimental group 1; Exp2, Experimental group 2; TSK, Tampa Scale of Kinesiophobia; FABQ, Fear Avoidance Beliefs Questionnaire; * p≤0.05; † p≤0.01

Figure 1



Initial Screening; phone or interview. (n = 52)
Not meet inclusion criteria (n = 7)
Randomization (n = 45)
Week 0
Control Group (n = 15)
Experimental 1 Group (n = 15)
Experimental 2 Group (n = 15)
Week 4
Control Group (n = 15)
Experimental 1 Group (n = 15)
Experimental 2 Group (n = 15)
Exp 1; • Advice to remain active.
Exp 2; • Remain active. • Therapeutic exercises once a day for at least 8 weeks.
Lost follow-up (n = 1) • Hospitalised for unrelated medical issue
Week 8
Control Group (n = 14)
Experimental 1 Group (n = 15)
Experimental 2 Group (n = 15)
Lost follow-up (n = 1) • Work related problem
Week 16
Control Group (n = 14)
Experimental 1 Group (n = 14)
Experimental 2 Group (n = 15)