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Is a combined programme of manual therapy and exercise more effective than usual care in patients with non-specific chronic neck pain? A randomized controlled trial

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Abstract

Objective: The aim of this study was to compare the effectiveness of a combined intervention of manual therapy and exercise (MET) versus usual care (UC), on disability, pain intensity and global perceived recovery, in patients with non-specific chronic neck pain (CNP).
Design: Randomized controlled trial.
Setting: Outpatient care units.
Subjects: Sixty-four non-specific CNP patients were randomly allocated to MET ($n = 32$) or UC ($n = 32$) groups.
Interventions: Participants in the MET group received 12 sessions of mobilization and exercise, whereas the UC group received 15 sessions of usual care in physiotherapy.
Main measures: The primary outcome was disability (Neck Disability Index). The secondary outcomes were pain intensity (Numeric Pain Rating Scale) and global perceived recovery (Patient Global Impression Change). Patients were assessed at baseline, three weeks, six weeks (end of treatment) and at a three-month follow-up.

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Results: Fifty-eight participants completed the study. No significant between-group difference was observed on disability and pain intensity at baseline. A significant between-group difference was observed on disability at three-week, six-week and three-month follow-up (median (P_{25}–P_{75}): 6 (3.25–9.81) vs. 15.5 (11.28–20.75); $P < 0.001$), favouring the MET group. Regarding pain intensity, a significant between-group difference was observed at six-week and three-month follow-up (median (P_{25}–P_{75}): 2 (1–2.51) vs. 5 (3.33–6); $P < 0.001$), with superiority of effect in MET group. Concerning the global perceived recovery, a significant between-group difference was observed only at the three-month follow-up ($P = 0.001$), favouring the MET group.

Conclusion: This study's findings suggest that a combination of manual therapy and exercise is more effective than usual care on disability, pain intensity and global perceived recovery.

Keywords

Physiotherapy, randomized controlled trial, manual therapy, neck pain

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Introduction

Chronic neck pain is a common musculoskeletal disorder worldwide, with an increased disability-adjusted life-years from 17 million (95% confidence interval (CI): 11.4–23.7) in 1990 to 29 million (95% CI: 19.5–40.5) in 2016.[1–4] A specific cause of neck pain symptoms cannot be assigned in the majority of patients, ultimately being described as non-specific chronic neck pain.[5–7]

Manual therapy and exercise have been identified in the literature as effective approaches on disability, pain intensity, quality of life and global perceived effect, at short and long term in patients with non-specific chronic neck pain, when applied whether as a combination or alone.[8–15] However, the effect size and clinically important differences achieved in the outcomes are small to modest, with considerable heterogeneity among the studies.[16–19]

Moreover, the interpretation and application of these findings in real-world clinical practice are difficult, since they usually come from exploratory trials. These exploratory trials were performed under ideal and controlled conditions and did not measure the effect of an intervention in real routine clinical practice, considering the absence of the control groups with usual care.[20] In this sense, the pragmatic trials are being recommended to evaluate the effectiveness in real-world.[21] Although the effectiveness of physiotherapy intervention in patients with non-specific chronic neck pain was extensively evaluated in previous studies, the pragmatic studies are scarce and the effects of physiotherapy intervention in real-world clinical practice remain unknown.[22]

Therefore, the aim of this study was to perform a pragmatic randomized controlled trial to compare the effects of a six-week manual therapy and exercise programme with those of usual care in physiotherapy intervention, on disability, pain intensity and global perceived recovery, in patients with non-specific chronic neck pain.

Methods

This was a prospective, parallel single-blinded randomized controlled trial. The study is reported following the guidance of the Consolidated Standards of Reporting Trials (CONSORT statement)[23] and is registered with ClinicalTrials.gov, with the number NCT03560947. Ethical approval was obtained from the ethics committee of the NOVA Medical School, Faculdade de Ciências Médicas by Nova University of Lisbon, with reference number 20/2016/CEFCM. NOVA Medical School, Faculdade de Ciências Médicas by Nova University of Lisbon was responsible for oversight of study conduct and governance. Recruitment was conducted between May and October 2018.

Participants were recruited consecutively from the waiting list of the outpatient care unit from two Portuguese hospitals, located in the Lisbon area.

Eligible participants were adults aged 18- to 65 years with non-specific neck pain (defined as pain in the cervical region with no specific anatomopathological diagnosis[5–7]) with or without arm pain, for at least three months, and able to read and speak European Portuguese. They were excluded if they had a specific cause for neck pain (e.g. clinical signs of infection, inflammatory disorder, tumour, osteoporosis, fracture or a traumatic injury, and disc herniation with medical indication for surgical treatment), were pregnant or had undergone neck surgery in the previous six months. The inclusion/exclusion criteria were confirmed by a trained physician, blinded to the study's procedures. The participants who met the criteria were referred to physiotherapy treatment. Eligible patients gave their written informed consent after receiving oral and written information about the study.

Each participant was randomly assigned to one of two parallel groups, with an allocation ratio of 1:1, to receive a manual therapy and exercise programme (manual therapy group) or usual care (usual care group). A computer-generated randomization list with balanced blocks of eight participants was used for the allocation of the participants to the groups. Participants were allocated to a group by the central telephone registration service of the participating hospitals, thus ensuring allocation concealment. The sample size and power calculations were performed with ClinCal software statistical online programme[24] and based on our previous pilot study with a sample of 39 participants. The calculations were based on detecting a mean difference of 4.21 points on the Neck Disability Index, assuming a standard deviation of 5.58 points, a two-tailed test, an alpha level of 0.05, a desired power of 80% and an estimated loss of follow-up of 15%. These assumptions generated a sample size of a minimum of 32 participants per group.

Outcomes measures

The primary outcome was disability measured by the Portuguese version of Neck Disability Index.[25] The Neck Disability Index is a 10-item self-administered questionnaire measuring the patients' limitations in managing everyday-life activities due to neck pain. Total score ranges between 0 and 50 points, with higher values indicating higher levels of disability.[26] A decrease of at least 27% in the score was identified as the minimal clinically important difference in a sample of chronic neck pain Portuguese patients.[27]

The secondary outcomes were pain intensity measured by the Numeric Pain Rating Scale and global perceived recovery measured by the Portuguese version of Patient Global Improvement Change Scale.

The Numeric Pain Rating Scale is an 11-point numeric pain intensity ranging from 0 ('no pain') to 10 ('as much pain as possible'). A change of two points or more was identified as the minimal clinically important difference in patients with chronic neck pain.[28]

The Patient Global Improvement Change Scale is a 7-point transition scale designed to assess the patient's perception of their overall change in their neck condition since the start of the physiotherapy treatment. The scores ranged from 1 (no change or condition has worsened) to 7 (a great deal better and a considerable improvement that has made all the difference); a score of 6 or 7 was identified as a clinically important difference.[29]

In addition, the participants completed a questionnaire booklet containing sociodemographic and clinical data. Participants were assessed at baseline, three weeks (middle of treatment), six weeks (end of treatment) and at a three-month follow-up (after the end of treatment) by a physiotherapist blinded to the participants' groups.

An external assistant physiotherapist, blinded to the participants' allocation groups, was responsible for collecting patient data. All the questionnaires were filled by the participants, on their own, without the presence of the physiotherapist. The completed questionnaires were given to the physiotherapist and then delivered to the researcher.

Interventions protocol

Manual therapy and exercise group. All participants carried out a six-week programme consisting of 12 sessions of manual therapy and exercise. Patients received individualized treatment by a physiotherapist for approximately 45 minutes twice a week.

Participants did not receive other forms of treatment. The treatment was performed according to the description below.

The manual therapy technique was performed in a set of three passive physiological mobilizations in flexion, rotation, lateral flexion and extension to end-of-range in supine position. Then, in prone position, the patients received passive intervertebral joint mobilizations applied to stiff or painful joints in the upper and lower cervical spine as described by Maitland et al.[30] The degree of vigour (grade according to Maitland) and duration of the application were determined by clinical judgement within grade II or III, by 30-second applications, repeated three times at each spinal level treated.

The exercise for deep neck flexors muscles consisted of three phases and was structured according to what was described by Jull et al.,[31] based on the principles of motor control learning.

The main task of the first stage was incremental cranio-cervical flexion in a relaxed supine lying position performed by deep flexors of the upper cervical region, the longus capitis and colli, rather than the superficial flexors, sternocleidomastoid and anterior scalene muscles. The patients were instructed to perform and hold progressively inner range positions of cranio-cervical flexion guided by feedback from a pressure unit (Stabilizer Pressure Biofeedback; Chattanooga, Hixson, TN, USA) placed behind the neck to monitor the slight flattening of the cervical lordosis, which occurs with contraction of deep neck flexors muscles. Patients who achieved 10 repetitions/10 seconds in 26 mmHg moved to the second phase of the exercise programme.

The objective of the second phase was to start the movement in a loading position, maintaining the neutral position of the upper cervical spine. The patients continued their strength training in upper levels (28 and 30 mmHg) and performed the cranio-cervical rotation in 4-point kneeling and sitting position while maintaining the cervical spine in a neutral position.

The third stage of the programme involved higher load exercises with head weight or load in movements of the upper limb. During this stage, the patients performed upper limb flexion and head lift up to a maximum of 15 repetitions in the supine position. Before the exercise, the patients were instructed to perform cranio-cervical flexion followed by cervical flexion to lift the head from the bed.

Although all patients followed the general programme of exercises, the level and number of repetitions of each exercise were individually tailored to each patient to ensure that they could perform the exercises in a pain-free manner and without muscle fatigue. Patients were asked to refrain from seeking any other form of specific intervention for neck pain during the trial.

Three physiotherapists, involved in manual therapy and exercise treatment, received training for all procedures of the intervention throughout the three face-to-face sessions scheduled before the beginning of the trial. All participating therapists had a minimum work experience of 7 years in neck pain conditions.

Usual care group. Participants received usual care in physiotherapy, which is the current practice in physiotherapy treatment, without any influence or specific restriction from the researchers. The treatment was performed in the same clinical setting as the manual therapy and exercise group. The patients were clinically evaluated by a physician and a physiotherapist, both blinded to the specific study's aims, participant allocation group and procedures of the study, and received the treatment based on the clinical judgement concerning the clinical presentation. The usual care consisted of a multimodal approach with a combination of different techniques, such as electrotherapy, massage, stretching, postural correction exercises, aerobic exercise and education. On average, the treatment had a duration of six weeks, with three sessions a week, each with a duration of 45–60 minutes.

Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences Version 21.0 (IBM Corporation, Chicago, IL). A level of significance of $P \leqslant 0.05$ was set for this study.

Clinical and sociodemographic baseline variables, including disability and pain intensity scores,

were compared between groups using the independent *t* tests for continuous data and chi-square tests of independence for categorical data.[32]

Data were assessed for outliers, normality, homogeneity of variances and covariances. The changes in Neck Disability Index, Numeric Pain Rating Scale and Patient Global Improvement Change Scale scores were examined using Friedman's test and Mann–Whitney *U* test for analysis within- and between groups, respectively. The non-parametric tests were used, considering that normality and homogeneity of variances criteria were not observed at all time-points.[32] The data were analysed according to the intention-to-treat analysis principle using expectation maximization method to estimate the missing values.[33]

Finally, number needed to treat, relative risks and the corresponding 95% CI were calculated to assess the differences between groups for the perceived benefit of physiotherapy, taking into consideration the minimal clinically important difference established for disability, pain intensity, and global perceived recovery. In addition, chi-square tests were also used to determine whether or not there was a difference between the groups for the proportion of participants reporting global perceived benefits.

Results

Participants

A total of 88 participants were assessed according to the established eligibility criteria; 24 were excluded for not meeting the inclusion/exclusion criteria ($n = 22$) or not accepting to integrate the study ($n = 2$) (Figure 1).

Baseline characteristics of the 64 participants included in the study are presented in Table 1. At the baseline, there were no significant differences between groups in any of the demographic and clinical variables.

Of the 64 participants who were randomized, three in each group withdrew sometime during the study period. All dropouts were either due to issues of scheduling incompatibility or to personal problems. There was no adverse effect associated with the intervention programmes.

The participants lost during the study showed similar characteristics to those completing the study, except for the age variable. The dropout patients showed a slightly lower mean age either in the manual therapy and exercise group (45.33 ± 20.31 vs. 49.72 ± 7.99) or in the usual care group (44 ± 10.39 vs. 49.76 ± 10.08).

To be included in the statistical analyses, participants had to complete at least 10 sessions (80%) of the treatment programme, in a six-week period. None of the participants were excluded for this reason. Participants in the manual therapy and exercise group attended a mean of 11.97 (± 1.19) out of the 12 planned sessions, whereas the participants from the usual care group attended a mean of 15.07 ($\pm$ 2.37) sessions.

Treatment outcomes

There was a statistically significant reduction on disability and pain intensity, and an improvement on global perceived recovery within each group.

Significant differences between groups were found for disability at three weeks, six weeks and at the three-month follow-up. The reduction in disability was statistically significantly greater in the manual therapy and exercise group in comparison with the usual care group. (Table 2 and Supplemental Figure S1)

In what concerns to the decrease of pain intensity, significant differences between groups were found at six-week and three-month follow-up, in favour of the manual therapy and exercise group. No statistically significant difference was found at three weeks (Table 2 and Supplemental Figure S1).

Regarding global perceived recovery, a significant difference between groups was found at the three-month follow-up, and no statistical differences were found at three and six weeks (Table 2 and Supplemental Figure S1).

Regarding Individual Responder Analysis (i.e. the proportion of participants achieving a minimal clinically important change in the outcomes), the data showed that participants in the manual therapy and exercise group were more likely to report benefits from treatment on disability, pain intensity and global perceived recovery at all time-points than participants in the usual care group.

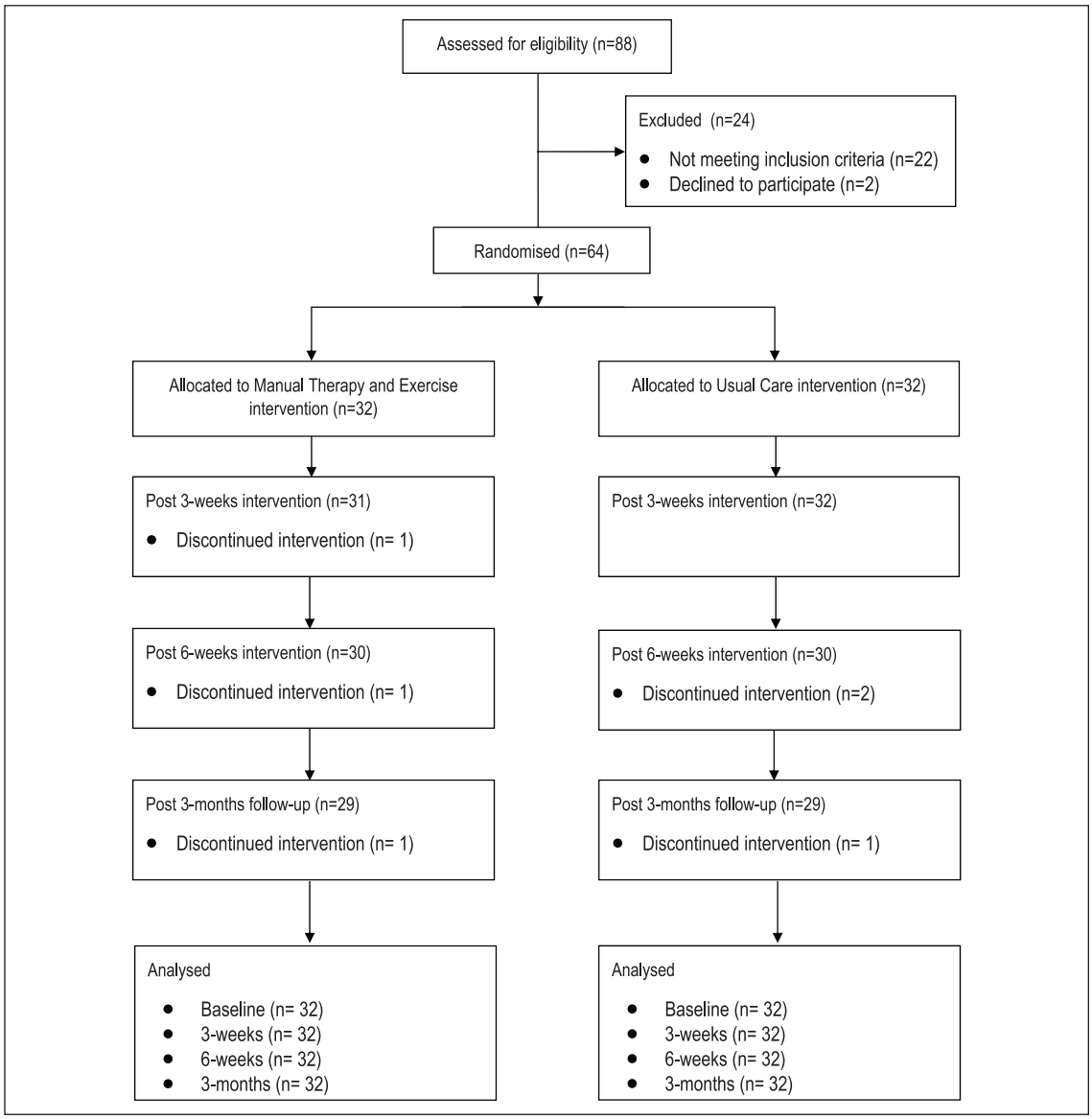

Figure 1. Flowchart of the study.

The only exception was on global perceived recovery at three weeks. Significant differences between groups were found in all moments for benefit on disability. However, on pain intensity, at three weeks, and on global perceived recovery, at three and six weeks, no significant differences between groups were found concerning the proportion of participants that achieved the criteria of the minimal clinically important difference (Supplemental Table S1).

Discussion

The findings of this study found that a combination of spinal mobilization and low load cranio-cervical flexion exercise results in greater pain, disability

Table 1. Baseline demographics and clinical characterization for both groups.

Variables	Categories	MET group ($n = 32$)	UC group ($n = 32$)	*P* value
Age (years), mean (SD)		49.31 (9.28)	49.22 (10.08)	0.969[a]
Gender, *n* (%)	Female	24 (75%)	27 (84%)	0.268[b]
	Male	8 (25%)	5 (16%)	
Absenteeism, *n* (%)	Yes	9 (28%)	7 (22%)	0.387[b]
	No	23 (72%)	25 (78%)	
Duration of pain, *n* (%)	3–24 months	9 (28%)	12 (37.5%)	0.298[b]
	>24 months	23 (72%)	20 (62.5%)	
Pain referred to head or/ and upper limb, *n* (%)	Yes	27 (84.4%)	29 (90.6%)	0.354[b]
	No	5 (15.6%)	3 (9.4%)	
Headache, *n* (%)	Yes	21 (65.6%)	21 (65.6%)	0.604[b]
	No	11 (34.4%)	11 (34.4%)	
Dizziness, *n* (%)	Yes	20 (65.6%)	20 (65.6%)	0.602[b]
	No	12 (37.5%)	12 (37.5%)	
Pain in other regions of the vertebral column	Yes	27 (84.4%)	28 (87.5%)	0.500[b]
	No	5 (15.6%)	4 (12.5%)	
Medication	Yes	9 (28.1%)	10 (31.3%)	0.500[b]
	No	23 (71.9%)	22 (68.7%)	
Previous neck pain	Yes	29 (90.6%)	24 (75%)	0.092[b]
	No	3 (9.4%)	8 (25%)	
Disability (NDI 0–50)		21.34 ± 8.71	22.75 ± 5.53	0.444[a]
Pain intensity (NPRS 0–11)		6.47 ± 1.39	6.75 ± 1.46	0.433[a]

MET: manual therapy and exercise; UC: usual care; NDI: neck disability index; NPRS: Numeric Pain Rating Scale.
[a]Analysed by Student's *t* test.
[b]Analysed by the chi-square test.

and global perceived recovery improvement compared with usual care in patients with non-specific chronic neck pain.

Participants in the manual therapy and exercise group achieved better disability outcomes over time, not only at the group level but also at the individual level. The recovery criteria established for disability at the three-month follow-up was achieved by all the participants in the manual therapy and exercise group compared with 59% of participants in the usual care group. Therefore, it is likely that 41% of the participants in the usual care group did not perceive a clinical important change with impact in their daily functional activities. The complementary report of the benefits found at individual level improves the relevance and clinical interpretability of the findings of this study and facilitates their applicability in the real clinical contexts.[23,34] However, despite being important relative and absolute measures of effect, measures like relative risk and number needed to treat are rarely reported in studies with neck pain patients, and for this reason the comparison of our findings with others is limited.[34,35]

Although non-significant differences between groups were found at three weeks in pain intensity, participants in the manual therapy and exercise group had significantly more improvement in pain intensity at six weeks (end of treatment) and at the three-month follow-up. Moreover, all the participants in the manual therapy and exercise group perceived a clinically important improvement at posttreatment (six weeks) that remained at three months, compared to 80% and 62% in the control group, respectively.

Regarding global perceived recovery, differences between groups are less evident with significant gains only observed at the three-month follow-up. However, these findings are consistent with the results of previous studies where pain

Table 2. Disability, pain intensity and global perceived recovery scores at three-week, six-week (end of treatment) and three-month follow-up.

Time	MET group median (P_{25}–P_{75})	UC group median (P_{25}–P_{75})	*P* value
Disability (NDI 0–50)[a]			
Baseline ($n = 64$)	22.5 (13.5–26.75)	24 (19–25.75)	0.576
3 weeks ($n = 64$)	14 (10.25–16.88)	19.5 (15–22)	0.001[b]
6 weeks ($n = 64$)	8.5 (6–11)	15 (10.25–20)	<0.001[b]
3 months ($n = 64$)	6 (3.25–9.81)	15.5 (11.28–20.75)	<0.001[b]
Pain intensity (NPRS 0–11)[a]			
Baseline ($n = 64$)	6 (6–7.75)	7 (6–8)	0.404
3 weeks ($n = 64$)	4.93 (4–5)	5 (4–6)	0.199
6 weeks ($n = 64$)	2.29 (2–3)	3.33 (2–5)	0.002[b]
3 months ($n = 64$)	2 (1–2.51)	5 (3.33–6)	<0.001[b]
Global perceived recovery (PGIC 1–7)[a]			
3 weeks ($n = 64$)	5 (4.25–5.75)	5 (3.25–6)	0.548
6 weeks ($n = 64$)	6 (5–6)	5.5 (3.25–6)	0.227
3 months ($n = 64$)	6 (5–6.75)	4 (2–6)	0.001[b]

MET: manual therapy and exercise; UC: usual care; NDI: Neck Disability Index; NPRS: Numeric Pain Rating Scale; PGIC: Patient Global Improvement Change.
Data are presented as median (P25–P75) and *P* value
[a]Significant at $P < 0.05$ for differences within group.
[b]Significant at $P < 0.05$ for differences between groups.

intensity and disability changes during the intervention only showed a modest contribution to the self-perception of global recovery.[36]

The results of this trial are consistent with other trials that showed the benefits of a combined programme of mobilization and low-load cranio-cervical flexion for disability, pain intensity and global perceived recovery, compared with the use of other different treatment modalities in chronic neck pain.[8,13,22] However, the findings of this study contrast with the results reported in a recent systematic review and meta-analysis where only small and non-significant between-group differences in effect sizes on neck disability at different follow-up periods were found when a combination of mobilization and exercise was compared to exercise alone.[37]

Reasons for this difference might be related to the kind of exercise used in our study and those reported in the different studies included in this systematic review. The exercise programmes of those studies include general strengthening and range of motion exercises (neck and scapulothoracic exercises), stretching and postural advice,[37] but recent research has shown that the persistence of neck pain and disability in chronic neck pain patients has been associated with significant changes in motor control, such as reductions in the recruitment, endurance, delays in feedforward activity and reduced specificity of the cervical flexor muscles activity.[38–41] Spinal mobilization[42] and task-specific exercises like low-load cranio-cervical flexion have been found to be effective in altering deep cervical flexor muscles recruitment, and increases on the recruitment of these muscles have been found to be associated with improvements in pain and disability in chronic neck pain patients.[10,15,43,44] Thus, the consistent greater benefits of the manual therapy and exercise group over usual care on disability and pain intensity found in this study might be explained by the increase in deep flexor activity following spinal mobilization and task-specific training with the consequent decrease in activity of the superficial flexors.[42–44]

There are some potential limitations in this study. First, the limited base of recruitment, (only

two outpatient hospitals) may limit the external validity of this study. Second, it is possible that important variables related to the outcomes may not have been assessed, such as anxiety, depression, pain catastrophizing and environmental factors. Previous studies have found a relationship between psychosocial factors and self-reported disability.[45] Moreover, other forms of physical activity, such as activity during leisure time or work, were not monitored during this study. Although it was expected that the potential effect of these factors was diluted or minimized through randomization, they may have influenced and/or mediated the outcomes achieved by the patients. Finally, this study's findings are limited to short-term outcomes. It is not possible to anticipate whether the differences found between treatments will remain in the long-term.

Despite these potential limitations, this study has important strengths to emphasize. The treatment that has been applied to the control group was not planned by the researchers but represents the usual care received by these patients in two real contexts of clinical practice. The between-group differences found at group and individual level shows a clear benefit for the non-specific chronic neck pain patients that could easily be implemented in a routine day to day practice. Moreover, this study also showed that the differences found correspond to meaningful reductions of disability, pain intensity and global perceived recovery.

In conclusion, this study indicates that the mobilization and low-load cranio-cervical flexion exercises seem to be more clinically effective for patients with non-specific chronic neck pain than usual care received in physiotherapy. Therefore, the findings seem to support the inclusion of the specific intervention programme in real-world clinical practice. However, further studies are necessary to evaluate the cost-effectiveness of manual therapy and exercise intervention in comparison with usual care and to better understand the underlying action mechanisms involved in pain and disability improvements when a combined programme of mobilization and low-load cranio-cervical flexion is used.

Clinical message

- A combined programme of mobilization and exercise with a duration of six weeks led to greater improvement on disability, pain intensity and global perceived recovery when compared with current practice.

Author contributions

The manuscript was drafted by Lucia Maria Amaral Domingues and was critically revised by Fernando Manuel Pimentel-Santos, Eduardo Brazete Cruz, Ana Cristina Sousa, Ana Santos, Ana Cordovil, Anabela Correia, Laura Sa Torres, Antonio Silva, Pedro Soares Branco and Jaime Cunha Branco. Ana Cristina Sousa, Ana Santos, Ana Cordovil, Anabela Correia, Laura Sa Torres, Antonio Silva and Pedro Soares Branco were involved in the acquisition of the data. Lucia Maria Amaral Domingues, Eduardo Brazete Cruz, Fernando Manuel Pimentel-Santos, Pedro Soares Branco and Jaime Cunha Branco contributed to the development of the selection criteria, design of the study, statistical analysis and interpretation of the findings. All the authors approved the final version of the manuscript.

Declaration of conflicting interests

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Supplemental material

Supplemental material for this article is available online.

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