

Manual therapy and neck-specific exercise are equally effective for treating non-specific neck pain but only when exercise adherence is maximised: A randomised controlled trial

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ABSTRACT

Objective: To assess the effectiveness of manual therapy versus a progressive, tailored neck-specific exercise program with high adherence for treating non-specific chronic neck pain (NSNP) and to examine the relationship between exercise adherence and treatment outcome.

Design: Single-blind, parallel, randomized clinical trial with two treatment arms, adhering to CONSORT guidelines.

Methods: 65 NSNP participants were randomly allocated to manual therapy or exercise. They received four treatment sessions of either manual therapy or neck-specific exercise, once a week for four weeks. Outcomes measured at baseline, two weeks, four weeks, and 12 weeks post-treatment included pain intensity, disability, patient-perceived improvement, quality of life, kinesiophobia and the craniocervical flexion test (CCFT) performance. In addition to evaluating each individual outcome, patients were categorized into either *responders* or *non-responders* according to pain intensity, disability and patient-perceived improvement. Exercise adherence was recorded.

Results: There were no differences between groups in individual outcomes. Treatment outcome in the exercise group was associated with exercise adherence. Patients receiving manual therapy were more likely to be classified as responders than those receiving exercise at all measured time points (odds ratio, 2 weeks: 0.14; 95 % CI: 0.02–0.79; treatment completion: 0.31; 95 % CI: 0.12–0.82; 12 weeks after treatment completion: 0.19; 95 % CI: 0.05–0.65), however these differences were no longer present when only patients whose exercise adherence was $\geq 95\%$ were analysed. Exercise was more effective than manual therapy in improving CCFT performance but only if patients with $\geq 95\%$ adherence were considered.

Conclusion: A four-week intervention of manual therapy was more effective than exercise, however when exercise adherence was $\geq 95\%$, the interventions were equally effective. Manual therapy may only be superior to specific-exercise when high exercise adherence cannot be assured.

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1. Introduction

Neck pain is a prevalent condition (Safiri et al., 2020), ranks as the sixth leading cause of disability worldwide (GBD 2019 Diseases and Injuries Collaborators, 2020) and the recurrence rate of neck pain is high (Carroll et al., 2008; Childs et al., 2008). In the absence of identifiable pathoanatomical causes, most patients are classified as having nonspecific chronic neck pain (NSNP) (Farrell et al., 2019).

Clinical practice guidelines and systematic reviews advocate the use of manual therapy and specific exercise for the treatment of NSNP (Bier et al., 2018; Blanpied et al., 2017; Côté et al., 2016; Guzman et al., 2009; Kjaer et al., 2017; Monticone et al., 2013; Parikh et al., 2019; Villanueva-Ruiz et al., 2021). However, a recent network meta-analysis comparing the effectiveness of different conservative treatments for NSNP (Castellini et al., 2022) reported low to very low certainty of evidence for the relative effectiveness of different interventions, highlighting the need for further good quality research. Furthermore, the authors concluded that the heterogeneity among current guideline recommendations creates uncertainty for clinicians when deciding the best treatment option and, while multimodal approaches combining both therapies appear promising, it is unclear whether one intervention may be more effective than the other, for it to either be used independently or receive greater weighting in the overall treatment approach. Therefore, conducting a direct comparison between manual therapy and exercise could provide additional critical insights for optimizing treatment strategies for NSNP.

Increased knowledge about the relative effectiveness of manual therapy and specific exercise would help clinicians in their clinical decision-making (Fredin and Lörås, 2017). Furthermore, given the dose-effect relationship of exercise and treatment outcomes in people with neck pain (Mueller et al., 2023; Nikander et al., 2006; Pedersen et al., 2013; Price et al., 2020), it is possible that the true effect of exercise may have been underestimated previously if adherence to treatment was low.

The primary aim of this study was to assess the relative effectiveness of manual therapy and neck specific exercise, for the treatment of NSNP. The secondary aim was to assess the relationship between exercise adherence and treatment outcome.

2. Methods

A single-blind, parallel, randomized clinical trial with two treatment arms was conducted (ACTRN12620000711910). There was one deviation from the registered protocol. At the inception of the study, the plan was to enrol 80 participants, however, the COVID-19 pandemic considerably reduced access to patients for research purposes. Nevertheless, data on the first 30 participants of the study (coded, to blind the statistician for the final analysis) were used to obtain context-specific estimates of the effect size and perform a power calculation to determine the final sample size to detect differences in our primary outcome measures. Calculations revealed that in a two-sided test, assuming an alpha risk of 5 %, maximum indeterminacy and with a sample size of 60 patients, the statistical power was 80 %. Patients with NSNP attending a secondary care spinal unit in Donostia (Spain) were invited to participate. The inclusion criteria required participants to be aged 18 years or older, with a primary complaint of neck pain, and a non-traumatic, insidious onset of symptoms. Participants who exhibited radicular pain, signs of central hyperexcitability—such as widespread, non-anatomical or nonspecific pain distribution or stimulus-independent spontaneous pain—were excluded. Additionally, individuals with a history of whiplash injury, those who had undergone or were awaiting neck surgery, and those with inflammatory diseases or other spinal conditions were excluded from the study (Lascrain-Aguirrebeña et al., 2018a,b).

2.1. Randomization

Participants were allocated randomly to one of two treatment groups: manual therapy or neck specific exercise. A computer-generated random sequence was used for allocation, the treating physical therapist opened a sealed envelope and provided the intervention according to the allocation. The same physical therapist with 15 years of clinical experience and postgraduate training in neuromusculoskeletal physiotherapy administered all interventions.

2.2. Interventions

2.2.1. Manual therapy

Patients in this group underwent four (once a week) 30-min sessions of manual therapy involving both myofascial and articular techniques. Treatment commenced with a suboccipital inhibition manual technique (Guo et al., 2023; Zabala-Mata et al., 2024) and cervical longitudinal intermittent traction (Binder, 2008). Subsequently, at the discretion of the physiotherapist and based on clinical reasoning, grade II-III segmental postero-anterior mobilizations to the upper thoracic spine (Griswold et al., 2015) and postero-anterior and/or antero-posterior mobilizations to the cervical spine were applied; these were applied following the movement plane of the zygapophyseal joints (Lascrain-Aguirrebeña et al., 2018a,b, 2021).

2.2.2. Exercise

Patients in the exercise group completed a program of neck-specific exercises adapted from a previous protocol (G. Jull et al., 2018; Sre-makaew et al., 2018). The program comprised of thirteen exercises targeting the activation of neck flexor and extensor muscles, and aimed to address disturbances in neck muscle activation reported previously in NSNP patients (Grip et al., 2008; Page et al., 2023; Sjölander et al., 2008; Woodhouse and Vasseljen, 2008).

The protocol involved four physiotherapist-led individual 30-min sessions (once a week) and daily home exercises for four weeks and involved exercises which were progressed by load and the level of difficulty over four weeks.

During each face-to-face session, patients engaged in supervised exercise practice under the guidance of the physiotherapist to ensure a thorough understanding and accurate execution of the prescribed exercises. Subsequently, patients received instructions to independently perform the exercises daily at home, with a duration of approximately 20 min per day. The exact dose was tailored to the patient, in that the number of repetitions and the level of difficulty were adapted to the individual needs, which were assessed at the beginning of each face-to-face treatment session. To facilitate adherence and precise exercise execution (Himler et al., 2023; Yaşarer et al., 2023), video recordings illustrating the prescribed exercises were provided to patients in this group via an instant messaging application installed on their mobile devices. The treatment protocol was individualized, tailoring the number of repetitions and the level of difficulty of each exercise to each patient's unique needs; this was assessed at the beginning of every treatment session. To evaluate adherence, patients in the exercise group were provided with a diary and asked to record the days on which they completed the prescribed exercises, and the physiotherapist who administered the treatments recorded the attendance of patients to the face-to-face sessions in both groups. Participants in both experimental groups were explicitly instructed to refrain from seeking any additional treatment for a minimum period of 12 weeks following the conclusion of the assigned intervention.

A full description of the exercise program can be found in [Supplementary Material 1](#).

2.3. Outcome measures

All self-reported measures and performance on the craniocervical

flexion test were evaluated at baseline (except GROC), two weeks after treatment commencement and within 48 h from the last treatment completion. In addition, GROC, NDI and maximum pain during the last week and last 24 h were evaluated 12 weeks after the last treatment completion. Furthermore, due to the fact that patient expectation has been associated with treatment outcome in NSNP (Bishop et al., 2013; Malfliet et al., 2019), patients were asked to rate their expectation prior to treatment commencement using a 0–100 scale, where a greater number is indicative of a higher expectation of recovery.

Prior to treatment commencement, patients' age, gender, symptom duration and number of non-specific physiotherapy sessions in the previous 12 months was recorded.

Maximum intensity of neck pain during last week and last 24 h and intensity of pain during active neck movements were measured with a 11-point numerical pain rating scale ranging from 0 (no pain) to 10 (most excruciating pain) (Chiarotto et al., 2019; Cleland et al., 2008; Modarresi et al., 2021; Young et al., 2019). The numeric pain rating scale has good to excellent test-retest reliability (Modarresi et al., 2021). Maximum neck range of movement in sitting was measured using a validated smartphone application securely fastened onto the forehead with a rigid Velcro strap (Elgueta-Cancino et al., 2022; Stenneberg et al., 2018). This device has demonstrated high concurrent validity and interrater reliability (Stenneberg et al., 2018).

Disability and function were measured using Neck Disability Index (NDI). (Bobos et al., 2018; Jones and Sterling, 2021; Murphy and Lopez, 2013). The NDI comprises 10 items that are evaluated using a Likert scale. The total score ranges from 0 to 100, and a greater total score corresponds to a higher perceived degree of disability (Bobos et al., 2018; Jones and Sterling, 2021; Murphy and Lopez, 2013). The NDI has good internal consistency and test-retest reliability (Saltychev et al., 2024).

Tampa scale of Kinesiophobia (TSK) and the Pain Catastrophizing Scale (PCS) were used to assess fear of movement or re-injury and the presence of catastrophizing thoughts respectively (Sullivan et al., 1995; Wheeler et al., 2019). TSK is a 11 item self-report questionnaire where total scores range from 11 to 44, with higher scores indicating greater levels of fear related to movement-associated pain (Cleland et al., 2008; Gómez-Pérez et al., 2011; Weermeijer and Meulders, 2018; Woby et al., 2005). PCS is a self-report 13 item questionnaire, total scores range from 0 to 52, and higher scores indicate higher levels of pain-related catastrophizing (Sullivan et al., 1995; Wheeler et al., 2019). The PCS has good internal and test-retest reliability (Wheeler et al., 2019).

Quality of life was assessed using the Short Form Health Survey questionnaire (SF-36) (Ware, 2000; Ware et al., 1993) and the European Quality of Life - 5 Dimensions questionnaire (EQ-5D) (Badia et al., 1999, 2001; Balestroni and Bertolotti, 2012). The SF-36 is a health survey comprising 36 questions, which provide a measure of physical and mental health, enabling participants to assess their perceived physical and mental health status using a scale from 0 to 100, where 0 represents the lowest possible and 100 represents the highest possible health status. (Ware, 2000; Ware et al., 1993). The SF-36 provides an acceptable measure of two independent constructs of physical and mental health (LoMartire et al., 2020). EQ-5D allows respondents to report their perceived health status on a scale of 0–10, with 0 being the worst and 10 being the best possible health status (Badia et al., 1999, 2001; Balestroni and Bertolotti, 2012). The EQ-5D is reliable and demonstrates moderate to strong correlations with global health measures (Feng et al., 2021).

The global rating of change scale (GROC) was used to measure the patient perceived overall improvement following treatment (Bobos et al., 2018, 2019). GROC is a 15 point scale where change is rated from –7 (a very great deal worse) through 0 (no change) to +7 (a very great deal better) (Bobos et al., 2018, 2019). GROC is reliable (Bobos et al., 2019) and widely used to evaluate change in neck pain (Lascrain-Aguirrebeña et al., 2018a,b, 2019, 2021) because of its validity and clinical relevance, and correlation with self-rated importance of change and patient satisfaction measures (Kamper et al., 2009).

Function of the deep cervical flexors was assessed using the cranio-cervical flexion test. The test was repeated three times and considered positive if the patient was unable to reach 26 mmHg without compensatory strategies (e.g. neck retraction or excessive activity of sternocleidomastoid or scalene muscles (Araujo et al., 2020; G. A. Jull et al., 2008; Juul et al., 2013)).

The outcome assessor was blind to patient treatment allocation.

2.4. Statistical analysis

In addition to evaluating treatment induced changes in each individual outcome, patients were also categorized into either *responders* or *non-responders* according to their treatment outcome at each time point (two weeks, treatment completion and 12 weeks post treatment completion). Patients were categorized as *responders* if they demonstrated an improvement equal or above the minimum clinical important difference in at least two of the following three outcome measures: 24-h neck pain intensity, disability (NDI) and patient perceived improvement (GROC). This was considered the primary outcome. Previously reported minimum clinical importance differences of 1.5 points for pain intensity (Young et al., 2019), 10 points for NDI (Holly et al., 2009; MacDermid et al., 2009) and a score of five (feeling at least “quite a bit better”) on the GROC scale (Cleland et al., 2007; Kamper et al., 2009; Saavedra-Hernández et al., 2011) were used.

For each of the study aims, we conducted different generalized linear mixed models with Gaussian response for the continuous dependent variables, Poisson response for the discrete dependent variable and binomial response for the dichotomous dependent variables. The independent variables were the intervention and exercise adherence.

Statistically significant differences were observed between manual therapy and exercise groups for their baseline symptom duration and age, hence all subsequent analyses for between-group differences were adjusted for the effect of these variables. In addition, we also controlled for baseline disability (NDI) and neck pain intensity (maximum pain during the last week and last 24 h) as these have been associated previously with treatment outcome (Lascrain-Aguirrebeña et al., 2018a, b). The main analysis included all participants. Given the association between treatment adherence and effectiveness of exercise interventions, the analysis was then repeated including all participants in the manual therapy group and only those in the exercise group that achieved equal or greater than 95 % adherence (n = 18).

Given the complexity of our models, we performed inferences using a Bayesian framework. In particular, we followed the Integrated Nested Laplace Approximation (INLA) approach (Rue et al., 2009, 2017).

Changes were interpreted in relation to the minimum clinical important differences for pain intensity (1.5 points (Young et al., 2019)), disability (10 points (Holly et al., 2009; MacDermid et al., 2009)), quality of life (EQ (5D) 0.75 points (Del Corral et al., 2023); SF36 4.1 points (Carreon et al., 2010)), catastrophization (reduction of 38 % from baseline (Scott et al., 2014)), kinesiophobia (4 points (Woby et al., 2005)) or GROC (feeling at least “quite a bit better” (Cleland et al., 2007; Kamper et al., 2009; Saavedra-Hernández et al., 2011)).

3. Results

Seventy-seven participants were assessed for eligibility between July 1, 2020 and November 8, 2022; 65 met the inclusion/exclusion criteria and were included in the study (Fig. 1). Baseline characteristics of study participants in each group are detailed in Table 1.

All outcome measures at each timepoint are reported in Table 1. Whole group changes in maximum neck pain intensity during the last week and last 24 h, intensity of pain during neck active movements, disability, pain catastrophization and quality of life as well as between group differences in these measures are reported in Table 2. The secondary analysis including all participants in the manual therapy group and only participants in the exercise group whose treatment adherence

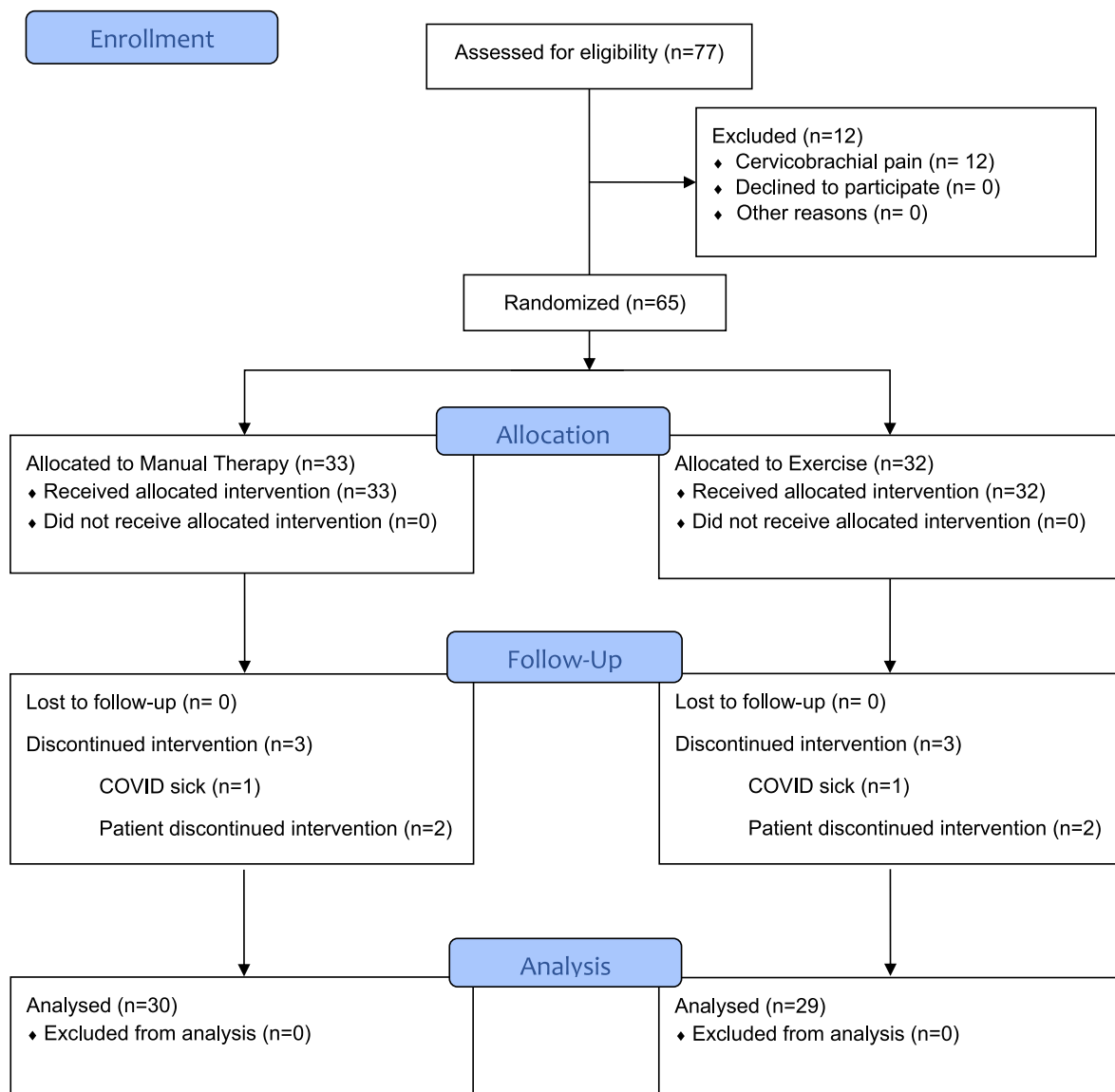


Fig. 1. Patient flow diagram.

was $\geq 95\%$ ($n = 18$) is reported in Table 3.

3.1. Baseline to two weeks post treatment commencement

Patients demonstrated significant ($\text{Prob} > 0.95$) reductions in maximum neck pain intensity during the last week and last 24 h, intensity of pain during neck active movements, disability, pain catastrophization and quality of life. There were significant ($\text{Prob} > 0.95$) increases in the range of motion for cervical side flexion and rotation, but not extension or flexion. No changes were observed for kinesiophobia. At baseline, 86 % of patients had a positive craniocervical flexion test; there was a significant ($\text{Prob} > 0.95$) reduction in the number of positive tests to 70 % at two weeks post treatment commencement. Seventeen percent of patients reported feeling between *quite a bit better* and *a great deal better* on the GROCC scale; 53 % reported feeling between a *tiny bit better* and *moderately better*, and 29 % reported feeling *about the same*. Based on whether or not patients had achieved a minimum clinical importance difference in pain intensity, NDI or GROCC, twelve patients (20 %) were classified as *responders* and 47 (80 %) as *non-responders*.

After adjusting for the effect of age, gender, disability, pain intensity

and the baseline value of the outcome of interest, there were no differences between groups in all outcome measures but one; patients receiving manual therapy were more likely to be classified as *responders* than those receiving exercise (adjusted odds ratio: 0.14; 95 % CI: 0.02–0.79; $P = 0.987$). However, when the analysis was repeated, only participants whose exercise adherence was $\geq 95\%$, there were no longer differences between interventions in this outcome. In this secondary analysis, significant differences were found in the effect of interventions on neck muscle function; patients that received exercise were less likely to show a positive craniocervical test when compared to those that received manual therapy (adjusted odds ratio: 0.35; 95 % CI: 0.08–1.48; $P = 0.953$).

3.2. Baseline to treatment completion

Patients demonstrated significant ($\text{Prob} > 0.95$) reductions of maximum neck pain intensity during the last week and last 24 h, intensity of pain during neck active movements, disability, pain catastrophization, quality of life and kinesiophobia. There were significant ($\text{Prob} > 0.95$) increases in cervical range in all movements but flexion. The number of patients with a positive craniocervical flexion test

Table 1

Outcome measures in each timepoint. Values are mean $\pm$ SD or number of cases (/).

Outcome	Week	MT (n = 30)	EX (n = 29)
Age (years)	0	55.22 $\pm$ 15.32	48.66 $\pm$ 11.89
Gender (male/female)	0	11/19	8/21
BMI (kg/m ²)	0	23.92 $\pm$ 3.51	24.32 $\pm$ 3.27
Symptom duration (years)	0	6.35 $\pm$ 7.34	10.68 $\pm$ 9.6
Number of non-specific physiotherapy last year	0	9.19 $\pm$ 13.2	10.31 $\pm$ 10.87
NDI (0–100)	0	27.63 $\pm$ 11.92	30.85 $\pm$ 16.38
	2	21.97 $\pm$ 9.62	25.44 $\pm$ 13.91
	4	19.7 $\pm$ 13.95	21.7 $\pm$ 14.81
	12	18.91 $\pm$ 12.54	21.18 $\pm$ 16.12
NPRS 1w (0–10)	0	6.36 $\pm$ 1.82	6.16 $\pm$ 2.07
	2	5.48 $\pm$ 2.24	5.17 $\pm$ 1.96
	4	4.33 $\pm$ 2.35	4.34 $\pm$ 2.72
	12	4.47 $\pm$ 3.19	4.84 $\pm$ 2.93
NPRS 24 h (0–10)	0	5.53 $\pm$ 2.49	4.8 $\pm$ 2.06
	2	4.55 $\pm$ 2.06	4.38 $\pm$ 2.39
	4	3.33 $\pm$ 2.51	3.24 $\pm$ 2.43
	12	3.03 $\pm$ 2.93	4.02 $\pm$ 2.99
Painful Mov (0–10)	0	5.27 $\pm$ 2.49	5.79 $\pm$ 1.86
	2	4.35 $\pm$ 2.03	4.05 $\pm$ 2.34
	4	3.81 $\pm$ 2.3	3.08 $\pm$ 2.15
ROM Flex (degrees)	0	51.01 $\pm$ 13.61	48.41 $\pm$ 12.35
	2	55.37 $\pm$ 16.24	48.31 $\pm$ 11.89
	4	50.89 $\pm$ 12	53.9 $\pm$ 13.31
ROM Ext (degrees)	0	53.35 $\pm$ 13.63	53.06 $\pm$ 15.36
	2	52.87 $\pm$ 15.37	54.92 $\pm$ 14.14
	4	49.44 $\pm$ 14.34	57.09 $\pm$ 14.37
ROM SFR (degrees)	0	27.14 $\pm$ 7.84	28.59 $\pm$ 10.81
	2	31.54 $\pm$ 10.13	33.31 $\pm$ 9.32
	4	29.77 $\pm$ 9.86	32.31 $\pm$ 7.66
ROM SFL (degrees)	0	26.24 $\pm$ 7.31	26.35 $\pm$ 11.16
	2	30.23 $\pm$ 8.37	31.02 $\pm$ 9.23
	4	29.55 $\pm$ 9.06	30.44 $\pm$ 8.04
ROM RotR (degrees)	0	54.89 $\pm$ 15.03	54.34 $\pm$ 13.98
	2	59.81 $\pm$ 14.56	55.95 $\pm$ 15.15
	4	60.26 $\pm$ 14.46	60.58 $\pm$ 12.06
ROM RotL (degrees)	0	54.74 $\pm$ 12.78	57.47 $\pm$ 13.41
	2	59.44 $\pm$ 12.77	60.12 $\pm$ 14.83
	4	59.49 $\pm$ 14.15	61.69 $\pm$ 12.66

Table 1 (continued)

Outcome	Week	MT (n = 30)	EX (n = 29)
EQ (5D) (0–10)	0	6.67 $\pm$ 1.7	6.46 $\pm$ 1.81
	2	7.24 $\pm$ 0.98	6.71 $\pm$ 1.51
	4	7.6 $\pm$ 1.3	7.19 $\pm$ 1.56
PCS (0–52)	0	15.83 $\pm$ 9.11	13.78 $\pm$ 10.08
	2	12.75 $\pm$ 9.04	12.26 $\pm$ 9.03
	4	10.13 $\pm$ 9.2	11.03 $\pm$ 10.42
TSK (11–44)	0	23.45 $\pm$ 4.39	24.28 $\pm$ 7.16
	2	24.58 $\pm$ 7.72	22.07 $\pm$ 6.9
	4	22.73 $\pm$ 7.75	21.44 $\pm$ 6.52
SF-36 P (0–100)	0	66.51 $\pm$ 13.37	65.81 $\pm$ 16.87
	2	71.12 $\pm$ 15.27	70.19 $\pm$ 13.33
	4	73.4 $\pm$ 15.53	74.31 $\pm$ 14.23
SF-36 M (0–100)	0	67.18 $\pm$ 13.72	61.61 $\pm$ 19.28
	2	73.17 $\pm$ 14.25	68.93 $\pm$ 16.1
	4	72.88 $\pm$ 15.54	71.32 $\pm$ 15.21
GROC (-5-5)	2	2.47 $\pm$ 2.5	1.93 $\pm$ 1.62
	4	2.9 $\pm$ 2.7	2.52 $\pm$ 2.55
	12	3.37 $\pm$ 2.49	2.79 $\pm$ 2.41
CCFT (positive/negative)	0	27/3	23/5*
	2	23/6 *	17/11*
	4	19/11	15/14
PatExp (0–100)	Pre.	80.91 $\pm$ 20.21	76.07 $\pm$ 18.67
	Post.	85.66 $\pm$ 18.22	80 $\pm$ 16.66

BMI: Body mass index; CCFT: craniocervical flexion test; EQ (5D) VAS: EuroQuol 5D visual analogue scale; Ext: extension; Flex: flexion; GROC: global rating of change scale; NDI: Neck disability index; NPRS 1w: Numeric pain rating scale last week; NPRS 24 h: Numeric pain rating scale last 24 h; PatExp: patient expectation; PCS: Pain Catastrophizing Scale; ROM: range of movement; RotL: left rotation; RotR: right rotation; SF-36 M: SF-36, mental domain; SF-36 P: SF-36, physical domain; SFL: left side flexion; SFR: right side flexion; TSK: Tampa Scale for Kinesiophobia; * one missing value.

demonstrated a further significant (Prob >0.95) reduction to 58 % (in comparison to 86 % at baseline). Thirty-six percent of patients reported feeling between *quite a bit better* and *a very great deal better* on the GROC scale; 34 % reported feeling between *a tiny bit better* and *moderately better*, 27 % reported feeling *about the same*, and 3 % reported feeling *moderately* or *somewhat worse*. Twenty-four patients (41 %) were classified as *responders* and 35 (59 %) as *non-responders*.

After adjusting for the effect of age, gender, disability, pain intensity, baseline value of the outcome of interest and outcome at 2 weeks, there were no differences between groups in all outcome measures but one; patients receiving manual therapy were more likely to be classified as *responders* than those receiving exercise (adjusted odds ratio: 0.31; 95 % CI: 0.12–0.82; P = 0.99). However, when the analysis was repeated, including only participants whose exercise adherence was ≥ 95 %, no significant differences between interventions were found. In this secondary analysis, significant differences were found in the effect of interventions on neck muscle function. Patients that received exercise

Table 2

Whole group changes and between group differences.

Outcome		Whole group changes			Difference between groups ^c		
		Coefficient ^a	95 % Credibility Interval	P	Coefficient ^b	95 % Credibility Interval	P
NDI	0-2w	-4.88	-6.93 to -2.83	1	1.22	-2.73 to 5.17	0.730
	0-4w	-8.76	-11.99 to -5.53	1	0.55	-9.88 to 10.98	0.540
	0-12w	-9.57	-12.79 to -6.35	1	0.55	-7.45 to 8.55	0.552
NPRS 1w	0-2w	-0.94	-1.54 to -0.33	0.998	-0.02	-1.11 to 1.07	0.514
	0-4w	-2.04	-2.72 to -1.37	1	-0.33	-1.3 to 0.64	0.750
	0-12w	-1.58	-2.42 to -0.74	0.999	0.01	-0.86 to 0.88	0.509
NPRS 24 h	0-2w	-0.65	-1.39 to 0.08	0.949	-0.06	-1.3 to 1.17	0.542
	0-4w	-1.91	-2.66 to -1.16	1	-0.19	-1.17 to 0.78	0.654
	0-12w	-1.53	-2.33 to -0.74	0.999	0.33	-0.53 to 1.19	0.772
Painful Mov	0-2w	-1.5	-1.99 to -1.01	1	-0.48	-1.59 to 0.63	0.805
	0-4w	-2.29	-2.95 to -1.63	1	0.24	-0.74 to 1.22	0.683
ROM Flex	0-2w	2.17	-1.35 to 5.69	0.888	-4.78	-11.52 to 1.96	0.919
	0-4w	2.64	-0.55 to 5.83	0.948	-3.63	-24.49 to 17.25	0.634
ROM Ext	0-2w	0.68	-2.14 to 3.49	0.683	0.87	-4.21 to 5.96	0.633
	0-4w	0	-3.25 to 3.24	0.501	-1.75	-23.12 to 19.64	0.564
ROM SFR	0-2w	4.56	2.51 to 6.61	0.999	-0.87	-4.05 to 2.3	0.708
	0-4w	3.17	1.06 to 5.27	0.998	-0.07	-3.88 to 3.74	0.515
ROM SFL	0-2w	4.33	2.22 to 6.44	0.999	-0.74	-4.36 to 2.88	0.659
	0-4w	3.7	1.37 to 6.03	0.998	0.6	-2.94 to 4.14	0.630
ROM RotR	0-2w	3.29	0.15 to 6.44	0.979	-4.52	-10.26 to 1.21	0.940
	0-4w	5.8	2.89 to 8.7	0.999	-1.52	-24.77 to 21.74	0.552
ROM RotL	0-2w	3.69	1.08 to 6.31	0.996	-3.24	-8.25 to 1.77	0.899
	0-4w	4.49	1.38 to 7.6	0.997	-0.88	-24.17 to 22.41	0.530
EQ (5D)	0-2w	0.33	-0.08 to 0.74	0.944	-0.54	-1.19 to 0.12	0.947
	0-4w	0.85	0.43 to 1.28	0.999	0.02	-0.6 to 0.64	0.524
PCS	0-2w	-2.94	-4.67 to -1.22	0.999	0.8	-2.25 to 3.85	0.699
	0-4w	-4.56	-6.63 to -2.5	0.999	-1.35	-5.22 to 2.52	0.755
TSK	0-2w	-0.4	-1.96 to 1.16	0.696	-1.92	-5.29 to 1.45	0.871
	0-4w	-1.84	-3.11 to 0.57	0.997	-0.09	-9.96 to 9.77	0.508
SF-36 P	0-2w	4.55	2.15 to 6.95	0.999	-1.76	-6.44 to 2.92	0.773
	0-4w	7.77	5.32 to 10.22	0.999	-0.91	-28.87 to 27.05	0.526
SF-36 M	0-2w	6.48	4.16 to 8.8	0.999	-1.65	-6.39 to 3.1	0.755
	0-4w	7.76	4.84 to 10.69	0.999	-1.14	-28.96 to 26.69	0.532

^a Coefficient is absolute change in outcome from baseline.^b Coefficient is difference between groups in absolute change in outcome from baseline.

^c Adjusted for the effect of age, sex, body mass index, and baseline value of outcome. Coefficient indicates difference with respect to reference intervention, exercise. CCFT: craniocervical flexion test; EQ (5D): EuroQuol 5D visual analogue scale; Ext: extension; Flex: flexion; NDI: Neck Disability Index; NPRS 1w: Numeric pain rating scale last week; NPRS 24 h: Numeric pain rating scale last 24 h; Painful Mov: Pain intensity in most painful movement; PCS: Pain Catastrophizing Scale; ROM: range of movement; RotR: right Rotation; RotL: left Rotation; SF-36 M: SF-36, mental domain; SF-36 P: SF-36, physical domain; SFL: left Side Flexion; SFR: right side flexion; TSK: Tampa Scale for Kinesiophobia.

were less likely to show a positive craniocervical test when compared to those that received manual therapy (adjusted odds ratio: 0.36; 95 % CI: 0.14–0.92; $P = 0.983$).

3.3. Baseline to 12 weeks after treatment completion

Patients demonstrated significant (Prob >0.95) reductions of maximum neck pain intensity during the last week and last 24 h, and disability. Thirty-six percent of patients reported feeling between *quite a bit better* and *a very great deal better* on the GROG scale; 39 % reported feeling between *a tiny bit better* and *moderately better*, 24 % reported feeling about the same, and 2 % reported feeling *a little bit worse*. Twenty-three patients (39 %) were classified as *responders* and 36 (61 %) as *non-responders*.

as *non-responders*.

After adjusting for the effect of age, gender, disability, pain intensity, baseline value of the outcome of interest and outcome at treatment completion, there were no differences between groups in all outcome measures but one; patients receiving manual therapy were more likely to be classified as *responders* than those receiving exercise (adjusted odds ratio: 0.19; 95 % CI: 0.05–0.65; $P = 0.995$). However, when the analysis was repeated, including only participants whose exercise adherence was ≥ 95 %, no significant differences between interventions were found.

Table 3Between group differences when exercise adherence is $\geq 95\%$.

Outcome		Difference between groups ^d		
		Coefficient	95 % Credibility Interval	P
NDI	0-2w	0.12 ^b	-3.93 to 4.16	0.522
	0-4w	-0.22 ^b	-10.9 to 10.45	0.517
	0-12w	-0.88 ^b	-9.03 to 7.28	0.585
NPRS 1w	0-2w	0.16 ^b	-0.95 to 1.27	0.613
	0-4w	0.16 ^b	-0.83 to 1.15	0.628
	0-12w	0.26 ^b	-0.62 to 1.15	0.721
NPRS 24 h	0-2w	-0.38 ^b	-1.66 to 0.91	0.722
	0-4w	-0.03 ^b	-1.06 to 0.99	0.526
	0-12w	0.17 ^b	-0.73 to 1.08	0.646
Painful Mov	0-2w	-0.61 ^b	-1.7 to 0.49	0.864
	0-4w	0.27 ^b	-0.7 to 1.24	0.706
ROM Flex	0-2w	-0.29 ^b	-7.38 to 6.8	0.533
	0-4w	-1.45 ^b	-22.92 to 20.03	0.554
ROM Ext	0-2w	3.56 ^b	-1.62 to 8.75	0.913
	0-4w	0.4 ^b	-21.66 to 22.46	0.513
ROM SFR	0-2w	0.61 ^b	-2.78 to 4.01	0.64
	0-4w	1.55 ^b	-12.49 to 15.59	0.586
ROM SFL	0-2w	-0.74 ^b	-4.49 to 3.02	0.653
	0-4w	0.9 ^b	-2.79 to 4.58	0.685
ROM RotR	0-2w	-3.64 ^b	-9.62 to 2.35	0.886
	0-4w	-1.92 ^b	-25.85 to 22.03	0.564
ROM RotL	0-2w	-1.06 ^b	-6.41 to 4.3	0.654
	0-4w	0.05 ^b	-24.44 to 24.53	0.501
EQ (5D)	0-2w	-0.24 ^b	-0.9 to 0.42	0.764
	0-4w	-0.13 ^b	-0.74 to 0.49	0.66
PCS	0-2w	0.88 ^b	-2.32 to 4.08	0.707
	0-4w	-0.51 ^b	-4.54 to 3.51	0.6
TSK	0-2w	-0.21 ^b	-3.74 to 3.31	0.549
	0-4w	-0.08 ^b	-3.29 to 3.13	0.52
SF-36 P	0-2w	-0.86 ^b	-5.69 to 3.98	0.639
	0-4w	-2.04 ^b	-30.61 to 26.54	0.557
SF-36 M	0-2w	-1.64 ^b	-6.64 to 3.36	0.744
	0-4w	-1.81 ^b	-30.85 to 27.24	0.55

c Coefficient is difference between groups expressed as an odds ratio.

b Coefficient is difference between groups in absolute change in outcome from baseline.

d Adjusted for the effect of age, sex, body mass index, and baseline value of outcome. Coefficient indicates difference with respect to reference intervention, exercise. CCFT: craniocervical flexion test; EQ (5D): EuroQuol 5D visual analogue scale; Ext: extension; Flex: flexion; NDI: Neck Disability Index; NPRS 1w: Numeric pain rating scale last week; NPRS 24 h: Numeric pain rating scale last 24 h; Painful Mov: Pain intensity in most painful movement; PCS: Pain Catastrophizing Scale; ROM: range of movement; RotR: right Rotation; RotL: left Rotation; SF-36 M: SF-36, mental domain; SF-36 P: SF-36, physical domain; SFL: left Side Flexion; SFR: right side flexion; TSK: Tampa Scale for Kinesiophobia.

3.4. Association between exercise adherence and treatment outcome in the exercise group

Mean (SD) adherence to the protocol in the exercise group was 95 % (8.2). Eighteen patients (62 %) reported an adherence of 100 %, 8 (28 %) between 80 % and 93 %, and two (7 %) between 72 % and 79 %. One patient failed to report exercise adherence. Greater exercise adherence was associated with higher reduction in disability (coefficient: -0.09; 95 % CI: -0.17 - 0.0006; $P = 0.974$) and maximum 24-h neck pain

intensity (coefficient: 0.03; 95 % CI: -0.07 - -0.0007; $P = 0.973$) at 2 weeks. Furthermore, greater adherence also increased the likelihood that the patient would be classified as *responder* at two weeks (adjusted odds ratio: 1.20; 95 % CI: 1.00-1.48; $P = 0.958$), 4 weeks (adjusted odds ratio: 1.14; 95 % CI: 1.02-1.27; $P = 0.988$) and 12 weeks (adjusted odds ratio: 1.13; 95 % CI: 1.03-1.24; $P = 0.996$).

4. Discussion

Four weeks of either manual therapy or neck specific exercise were effective at reducing disability, pain intensity, catastrophization and kinesiophobia, and increasing quality of life in patients NSNP. Changes were observed at all measured time points. Improvements were above the minimum clinical important difference for pain intensity, quality of life and were below the minimum clinical important difference for disability (albeit by a very small margin at 12 weeks), catastrophization and kinesiophobia. Pre-treatment values were mild to moderate (according to previously reported cut-offs (MacDermid et al., 2009)) for disability, which may explain the absence of larger improvements in this outcome. Changes in cervical range of movement were small, and were lower than the reported measurement error of the device (Stenneberg et al., 2018). The minimal improvements observed in range of movement may be caused by the fact that patients demonstrated no considerable pre-treatment restriction, i.e. pre-treatment values were close to those previously reported for asymptomatic participants (Lascrain-Aguirrebeña et al., 2018a,b). It is of note that patients included in this study were recruited at a secondary care spinal unit and had received an average of 10 sessions of general non-specific physiotherapy over the last 12 months prior to recruitment and had reported no benefit. In contrast, a small number of specific physiotherapy sessions undertaken in the current study provided meaningful clinical changes for a considerable number of patients. Changes observed in the short term were also maintained in the medium term.

When comparing the relative effectiveness of manual therapy and neck specific exercise, we found no differences between groups in individual outcomes related to pain intensity, disability, range of movement, catastrophization, kinesiophobia, quality of life and patient perceived overall improvement. However, differences between groups in favour of manual therapy were noted at all measured time points when using a composite outcome measure that classified patients into either *responders* or *non-responders*.

Adherence to the exercise programme was, on average, very good. This may have been facilitated by the fact that face to face treatment sessions in the exercise group were dedicated to instructing participants in the exercise programme, and patients received video recordings of the prescribed exercises in a readily available format (Himler et al., 2023; Woodhouse and Vasseljen, 2008). However, despite such efforts, a considerable number of patients failed to reach a target of 95 % adherence. Importantly, we found that greater exercise adherence increased the likelihood of the patient being classified as a *responder* at all measured time points in the exercise group. In our secondary analysis, when patients in the manual therapy group were compared to those in the exercise group whose adherence was 95 % or greater, differences in effectiveness noted in the primary analysis (*responders* vs *non-responders*) were no longer significant. Although a type two error is possible because of a reduced sample size (Noordzij et al., 2010), considering the association noted between exercise adherence and treatment outcome in the exercise group, the superior effectiveness of manual therapy observed in the whole sample, may, in fact, be dependent upon exercise adherence.

Although evidence suggests a significant role of muscle dysfunction for the development and maintenance of NSNP (Grip et al., 2008; Page et al., 2023; Sjölander et al., 2008; Woodhouse and Vasseljen, 2008), no study has assessed the medium term relative effectiveness of manual therapy and neck specific exercise on neck muscle function. Given the findings of previous studies (Ghaderi et al., 2017; Javanshir et al., 2015;

Suvarnato et al., 2019) regarding the effectiveness of neck specific exercise to restore adequate neck muscle function, we expected patients receiving neck specific exercise to show greater improvements on the craniocervical flexion test than those receiving manual therapy. Our primary analysis revealed no differences between interventions, suggesting no superior effectiveness. However, in the secondary analysis which included only patients in the exercise group whose adherence was equal or greater than 95 %, we found that exercise was more effective at improving control of the deep neck flexor muscles than manual therapy at all measured time points. Our findings suggest that specific exercise is more effective than manual therapy to improve muscle function, provided exercise adherence is high. It is of note that, albeit to a lesser extent, patients that received manual therapy also demonstrated an improvement on the CCFT. This may be explained by improvements in cervical mobility following treatment, which could have resulted in better performance on the CCFT.

Although we expected that exercise, a movement-based intervention, may be more effective at reducing kinesiophobia, we found no differences between interventions. The fact that patients had low (when compared to normative data (Chimenti et al., 2021)) levels of baseline kinesiophobia may explain the absence of significant differences between interventions. There were no differences either between interventions in the reduction of catastrophization, despite patients demonstrating moderate levels of catastrophization at baseline according to previously reported thresholds (Licciardone et al., 2024). In fact, no meaningful reductions in either kinesiophobia or catastrophization were observed, which suggests that specific interventions targeting these features may be required in conjunction with manual therapy or exercise.

4.1. Study limitations

The present study used treatment interventions of only four weeks; considering the fact that clinical improvement has been demonstrated to gradually continue within the first 15 weeks of treatment (Zebis et al., 2014), the findings of our study may have underestimated the effectiveness of manual therapy and/or exercise. This may be particularly the case for the exercise programme with previous studies implementing the same exercise programme over 8–14 weeks (Falla et al., 2013; Halvorsen et al., 2016; Ludvigsson et al., 2016).

We opted not to use a pressure biofeedback unit for cranio-cervical flexion exercise. Using a pressure biofeedback unit would have added complexity (patients would need to learn to use it correctly, requiring additional instruction and practice), which may have affected adherence, and an economic cost for the patient, acting as a further barrier to participation. While it is possible that the use a pressure biofeedback unit might have resulted in greater improvement, we opted for an exercise programme that was easily generalizable to any clinical setting.

In a society where lower treatment costs and higher efficiency is demanded, the current study provides evidence of the clinical effectiveness of each intervention with relatively low cost.

Additionally, the fact that our patients had received previous treatments may have further underestimated the effectiveness of manual therapy and exercise, as prior interventions could have already provided some benefit and reduced room for improvement.

Assessment included short term effects and a medium term follow up, however the long-term effects are unknown. Although a longer term follow up of up to a year may be useful, we consider 12 weeks post-treatment to be an adequate follow up period, in that it provides information regarding the longer lasting effects beyond those in the short term, and minimizes the risk of patients (especially those whose clinical outcome has not been favourable) engaging in alternative treatments that would confound the results of the study.

5. Conclusion

Our data suggests that manual therapy and specific exercise are equally effective at decreasing pain and improving function in patients with NSNP, although manual therapy may be slightly superior if a composite outcome measure is used to assess the clinical outcome. However, where high exercise adherence can be ensured, manual therapy and specific exercise are likely to be equally effective. Face to face practice sessions and exercise video recordings in easy to use formats likely help with exercise adherence. In patients with high adherence, specific exercise may offer the additional advantage of facilitating improved cervical muscle function.

CRedit authorship contribution statement

Iker Villanueva-Ruiz: Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Data curation, Conceptualization. **Deborah Falla:** Writing – review & editing, Validation, Methodology. **Marc Saez:** Writing – review & editing, Software, Formal analysis. **Maialen Araolaza-Arrieta:** Writing – review & editing, Investigation. **Jon Jatsu Azkue:** Writing – review & editing. **Ane Arbillaga-Etxarri:** Writing – review & editing. **Ana Lersundi:** Writing – review & editing, Resources. **Ion Lascrain-Aguirrebeña:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Conceptualization.

Ethical approval

The CEISH/113/2019 Ethics Committee approved this study. All participants gave written informed consent before data collection began.

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Appendix A. Supplementary data

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References

- Araujo, F. X. de, Ferreira, G.E., Scholl Schell, M., Castro, M. P. de, Ribeiro, D.C., Silva, M. F., 2020. Measurement properties of the craniocervical flexion test: a systematic review. *Phys. Ther.* 100 (7), 1094–1117. <https://doi.org/10.1093/ptj/pzaa072>.
- Badia, X., Roset, M., Herdman, M., Kind, P., 2001. A comparison of United Kingdom and Spanish general population time trade-off values for EQ-5D health states. *Med. Decis. Mak.* 21 (1), 7–16. <https://doi.org/10.1177/0272989X0102100102>.
- Badia, X., Roset, M., Montserrat, S., Herdman, M., Segura, A., 1999. [The Spanish version of EuroQol: a description and its applications. European Quality of Life scale]. *Med. Clínica* 112 (Suppl. 1), 79–85.
- Balestroni, G., Bertolotti, G., 2012. [EuroQol-5D (EQ-5D): an instrument for measuring quality of life]. *Monaldi Archives for Chest Disease = Archivio Monaldi Per Le Malattie Del Torace* 78 (3), 155–159. <https://doi.org/10.4081/monaldi.2012.121>.
- Bier, J.D., Scholten-Peeters, W.G.M., Staal, J.B., Pool, J., van Tulder, M.W., Beekman, E., Knoop, J., Meerhoff, G., Verhagen, A.P., 2018. Clinical practice guideline for physical therapy assessment and treatment in patients with nonspecific neck pain. *Phys. Ther.* 98 (3), 162–171. <https://doi.org/10.1093/ptj/pzx118>.
- Binder, A.I., 2008. Neck pain. *Clin. Evid.* 2008.
- Bishop, M.D., Mintken, P.E., Bialosky, J.E., Cleland, J.A., 2013. Patient expectations of benefit from interventions for neck pain and resulting influence on outcomes. *J. Orthop. Sports Phys. Ther.* 43 (7), 457–465. <https://doi.org/10.2519/jospt.2013.4492>.
- Blanpied, P.R., Gross, A.R., Elliott, J.M., Devaney, L.L., Clewley, D., Walton, D.M., Sparks, C., Robertson, E.K., 2017. Neck pain: revision 2017. *J. Orthop. Sports Phys. Ther.* 47 (7), A1–A83. <https://doi.org/10.2519/jospt.2017.0302>.
- Bobos, P., MacDermid, J.C., Walton, D.M., Gross, A., Santaguida, P.L., 2018. Patient-reported outcome measures used for neck disorders: an overview of systematic reviews. *J. Orthop. Sports Phys. Ther.* 48 (10), 775–788. <https://doi.org/10.2519/jospt.2018.8131>.
- Bobos, P., MacDermid, J., Nazari, G., Furtado, R., 2019. Psychometric properties of the global rating of change scales in patients with neck disorders: a systematic review

- with meta-analysis and meta-regression. *BMJ Open* 9 (11), e033909. <https://doi.org/10.1136/bmjopen-2019-033909>.
- Carreon, L.Y., Glassman, S.D., Campbell, M.J., Anderson, P.A., 2010. Neck Disability Index, short form-36 physical component summary, and pain scales for neck and arm pain: the minimum clinically important difference and substantial clinical benefit after cervical spine fusion. *Spine J.* 10 (6), 469–474. <https://doi.org/10.1016/j.spinee.2010.02.007>.
- Carroll, L.J., Hogg-Johnson, S., van der Velde, G., Haldeman, S., Holm, L.W., Carragee, E. J., Hurwitz, E.L., Côté, P., Nordin, M., Peloso, P.M., Guzman, J., Cassidy, J.D., Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders, 2008. Course and prognostic factors for neck pain in the general population: results of the bone and joint decade 2000–2010 task force on neck pain and its associated disorders. *Spine* 33 (4 Suppl. 1), S75–S82. <https://doi.org/10.1097/BRS.0b013e31816445be>.
- Castellini, G., Pillastrini, P., Vanti, C., Bargeri, S., Giagio, S., Bordignon, E., Fasciani, F., Marzoni, F., Innocenti, F., Chiarotto, A., Gianola, S., Bertozzi, L., 2022. Some conservative interventions are more effective than others for people with chronic non-specific neck pain: a systematic review and network meta-analysis. *J. Physiother.* S1836–9553 (22), 00086. <https://doi.org/10.1016/j.jphys.2022.09.007>, 8.
- Chiarotto, A., Maxwell, L.J., Ostelo, R.W., Boers, M., Tugwell, P., Terwee, C.B., 2019. Measurement properties of visual analogue scale, numeric rating scale, and pain severity subscale of the brief pain inventory in patients with low back pain: a systematic review. *J. Pain* 20 (3), 245–263. <https://doi.org/10.1016/j.jpain.2018.07.009>.
- Childs, J.D., Cleland, J.A., Elliott, J.M., Teyhen, D.S., Wainner, R.S., Whitman, J.M., Sopky, B.J., Godges, J.J., Flynn, T.W., American Physical Therapy Association, 2008. Neck pain: clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopedic section of the American physical therapy association. *J. Orthop. Sports Phys. Ther.* 38 (9), A1–A34. <https://doi.org/10.2519/jospt.2008.0303>.
- Chimenti, R.L., Post, A.A., Silbernagel, K.G., Hadlandsmyth, K., Sluka, K.A., Moseley, G. L., Rio, E., 2021. Kinesiophobia severity categories and clinically meaningful symptom change in persons with achilles tendinopathy in a cross-sectional study: implications for assessment and willingness to exercise. *Frontiers in Pain Research* 2.
- Cleland, J.A., Childs, J.D., Fritz, J.M., Whitman, J.M., Eberhart, S.L., 2007. Development of a clinical prediction rule for guiding treatment of a subgroup of patients with neck pain: use of thoracic spine manipulation, exercise, and patient education. *Phys. Ther.* 87 (1), 9–23. <https://doi.org/10.2522/ptj.20060155>.
- Cleland, J.A., Childs, J.D., Whitman, J.M., 2008a. Psychometric properties of the neck disability index and numeric pain rating scale in patients with mechanical neck pain. *Arch. Phys. Med. Rehabil.* 89 (1), 69–74. <https://doi.org/10.1016/j.apmr.2007.08.126>.
- Cleland, J.A., Fritz, J.M., Childs, J.D., 2008b. Psychometric properties of the fear-avoidance beliefs questionnaire and Tampa scale of kinesiophobia in patients with neck pain. *Am. J. Phys. Med. Rehabil.* 87 (2), 109–117. <https://doi.org/10.1097/PHM.0b013e31815b61f1>.
- Côté, P., Wong, J.J., Sutton, D., Shearer, H.M., Mior, S., Randhawa, K., Ameis, A., Carroll, L.J., Nordin, M., Yu, H., Lindsay, G.M., Southerst, D., Varatharajan, S., Jacobs, C., Stupar, M., Taylor-Vaisey, A., van der Velde, G., Gross, D.P., Brisson, R.J., et al., 2016. Management of neck pain and associated disorders: a clinical practice guideline from the Ontario Protocol for Traffic Injury Management (OPTIMA) Collaboration. *Eur. Spine J.: Official Publication of the European Spine Society, the European Spinal Deformity Society* 25 (7), 2000–2022. <https://doi.org/10.1007/s00586-016-4467-7>, and the European Section of the Cervical Spine Research Society.
- Del Corral, T., Fabero-Garrido, R., Plaza-Manzano, G., Navarro-Santana, M.J., Fernández-de-Las-Peñas, C., López-de-Uralde-Villanueva, I., 2023. Minimal clinically important differences in EQ-5D-5L index and VAS after a respiratory muscle training program in individuals experiencing long-term post-COVID-19 symptoms. *Biomedicine* 11 (9), 2522. <https://doi.org/10.3390/biomedicine11092522>.
- Elgueta-Cancino, E., Rice, K., Abichandani, D., Falla, D., 2022. Measurement properties of smartphone applications for the measurement of neck range of motion: a systematic review and meta-analysis. *BMC Musculoskelet. Disord.* 23 (1), 138. <https://doi.org/10.1186/s12891-022-05066-6>.
- Falla, D., Lindström, R., Rechter, L., Boudreau, S., Petzke, F., 2013. Effectiveness of an 8-week exercise programme on pain and specificity of neck muscle activity in patients with chronic neck pain: a randomized controlled study. *Eur. J. Pain* 17 (10), 1517–1528. <https://doi.org/10.1002/j.1532-2149.2013.00321.x>.
- Farrell, S.F., Smith, A.D., Hancock, M.J., Webb, A.L., Sterling, M., 2019. Cervical spine findings on MRI in people with neck pain compared with pain-free controls: a systematic review and meta-analysis. *J. Magn. Reson. Imag.: JMIR* 49 (6), 1638–1654. <https://doi.org/10.1002/jmri.26567>.
- Feng, Y.-S., Kohlmann, T., Janssen, M.F., Buchholz, I., 2021. Psychometric properties of the EQ-5D-5L: a systematic review of the literature. *Qual. Life Res.: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation* 30 (3), 647–673. <https://doi.org/10.1007/s11136-020-02688-y>.
- Fredin, K., Lorås, H., 2017. Manual therapy, exercise therapy or combined treatment in the management of adult neck pain – a systematic review and meta-analysis. *Musculoskeletal Science and Practice* 31, 62–71. <https://doi.org/10.1016/j.msksp.2017.07.005>.
- GBD 2019 Diseases and Injuries Collaborators, 2020. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet (London, England)* 396 (10258), 1204–1222. [https://doi.org/10.1016/S0140-6736\(20\)30925-9](https://doi.org/10.1016/S0140-6736(20)30925-9).
- Ghaderi, F., Jafarabadi, M.A., Javanshir, K., 2017. The clinical and EMG assessment of the effects of stabilization exercise on nonspecific chronic neck pain: a randomized controlled trial. *J. Back Musculoskelet. Rehabil.* 30 (2), 211–219. <https://doi.org/10.3233/BMR-160735>. PubMed.
- Gómez-Pérez, L., López-Martínez, A.E., Ruiz-Párraga, G.T., 2011. Psychometric properties of the Spanish version of the Tampa scale for kinesiophobia (TSK). *J. Pain* 12 (4), 425–435. <https://doi.org/10.1016/j.jpain.2010.08.004>.
- Grip, H., Sundelin, G., Gerdle, B., Stefan Karlsson, J., 2008. Cervical helical axis characteristics and its center of rotation during active head and upper arm movements-comparisons of whiplash-associated disorders, non-specific neck pain and asymptomatic individuals. *J. Biomech.* 41 (13), 2799–2805. <https://doi.org/10.1016/j.jbiomech.2008.07.005>.
- Griswold, D., Learman, K., O'Halloran, B., Cleland, J., 2015. A preliminary study comparing the use of cervical/upper thoracic mobilization and manipulation for individuals with mechanical neck pain. *J. Man. Manip. Ther.* 23 (2), 75–83. <https://doi.org/10.1179/2042618614Y.0000000095>. PubMed.
- Guo, Y., Lv, X., Zhou, Y., Li, Z., She, H., Bai, L., Bao, J., 2023. Myofascial release for the treatment of pain and dysfunction in patients with chronic mechanical neck pain: systematic review and meta-analysis of randomised controlled trials. *Clin. Rehabil.* 37 (4), 478–493. <https://doi.org/10.1177/02692155221136108>.
- Guzman, J., Haldeman, S., Carroll, L.J., Carragee, E.J., Hurwitz, E.L., Peloso, P., Nordin, M., Cassidy, J.D., Holm, L.W., Côté, P., van der Velde, G., Hogg-Johnson, S., 2009. Clinical practice implications of the bone and joint decade 2000–2010 task force on neck pain and its associated disorders: from concepts and findings to recommendations. *J. Manipulative Physiol. Therapeut.* 32 (2), S227–S243. <https://doi.org/10.1016/j.jmpt.2008.11.023>.
- Halvorsen, M., Falla, D., Gizzi, L., Harms-Ringdahl, K., Peolsson, A., Dederig, Å., 2016. Short-and long-term effects of exercise on neck muscle function in cervical radiculopathy: a randomized clinical trial. *J. Rehabil. Med.* 48 (8), 696–704. <https://doi.org/10.2340/16501977-2120>. Scopus.
- Himler, P., Lee, G.T., Rhon, D.I., Young, J.L., Cook, C.E., Rentmeester, C., 2023. Understanding barriers to adherence to home exercise programs in patients with musculoskeletal neck pain. *Musculoskeletal Science and Practice*, 102722. <https://doi.org/10.1016/j.msksp.2023.102722>.
- Holly, L.T., Matz, P.G., Anderson, P.A., Groff, M.W., Heary, R.F., Kaiser, M.G., Mummaneni, P.V., Ryken, T.C., Choudhri, T.F., Vresilovic, E.J., Resnick, D.K., 2009. Joint section on disorders of the spine and peripheral nerves of the American association of neurological surgeons and congress of neurological surgeons. Functional outcomes assessment for cervical degenerative disease. *Journal of Neurosurgery. Spine* 11 (2), 238–244. <https://doi.org/10.3171/2009.2.SPINE08715>.
- Javanshir, K., Amiri, M., Mohseni Bandpei, M.A., De las Penas, C.F., Rezasoltani, A., 2015. The effect of different exercise programs on cervical flexor muscles dimensions in patients with chronic neck pain. *J. Back Musculoskelet. Rehabil.* 28 (4), 833–840. <https://doi.org/10.3233/BMR-150593>. PubMed.
- Jones, C., Sterling, M., 2021. Clinimetrics: neck disability index. *J. Physiother.* 67 (2), 144. <https://doi.org/10.1016/j.jphys.2020.09.001>.
- Jull, G.A., O'Leary, S.P., Falla, D.L., 2008. Clinical assessment of the deep cervical flexor muscles: the craniocervical flexion test. *J. Manipulative Physiol. Therapeut.* 31 (7), 525–533. <https://doi.org/10.1016/j.jmpt.2008.08.003>.
- Jull, G., Falla, D., Treleaven, J., O'Leary, S., 2018. *Management of Neck Pain Disorders*. Elsevier.
- Juul, T., Langberg, H., Enoch, F., Søgaard, K., 2013. The intra- and inter-rater reliability of five clinical muscle performance tests in patients with and without neck pain. *BMC Musculoskelet. Disord.* 14 (1), 339. <https://doi.org/10.1186/1471-2474-14-339>.
- Kamper, S.J., Maher, C.G., Mackay, G., 2009. Global rating of change scales: a review of strengths and weaknesses and considerations for design. *J. Man. Manip. Ther.* 17 (3), 163–170.
- Kjaer, P., Kongsted, A., Hartvigsen, J., Isenberg-Jørgensen, A., Schiøtz-Christensen, B., Søborg, B., Krog, C., Møller, C.M., Halling, C.M.B., Lauridsen, H.H., Hansen, I.R., Nørregaard, J., Jørgensen, K.J., Hansen, L.V., Jakobsen, M., Jensen, M.B., Melbye, M., Duel, P., Christensen, S.W., Povlsen, T.M., 2017. National clinical guidelines for non-surgical treatment of patients with recent onset neck pain or cervical radiculopathy. *Eur. Spine J.: Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 26 (9), 2242–2257. <https://doi.org/10.1007/s00586-017-5121-8>.
- Lascurain-Aguirrebeña, I., Newham, D.J., Casado-Zumeta, X., Lertxundi, A., Critchley, D. J., 2018a. Immediate effects of cervical mobilisations on global perceived effect, movement associated pain and neck kinematics in patients with non-specific neck pain. A double blind placebo randomised controlled trial. *Musculoskeletal Science & Practice* 38, 83–90. <https://doi.org/10.1016/j.msksp.2018.10.003>.
- Lascurain-Aguirrebeña, I., Newham, D.J., Casado-Zumeta, X., Lertxundi, A., Critchley, D. J., 2021. Immediate effects of cervical mobilisations on neck muscle activity during active neck movements in patients with non-specific neck pain. A double blind placebo controlled trial. *Physiotherapy* 110, 42–53. <https://doi.org/10.1016/j.physio.2019.07.003>.
- Lascurain-Aguirrebeña, I., Newham, D.J., Galarraga-Gallastegui, B., Critchley, D.J., 2018b. Differences in neck surface electromyography, kinematics and pain occurrence during physiological neck movements between neck pain and asymptomatic participants. A cross-sectional study. *Clin. BioMech.* 57, 1–9. <https://doi.org/10.1016/j.clinbiomech.2018.05.010>.
- Lascurain-Aguirrebeña, I., Newham, D.J., Galindez-Ibarbengoaetxea, X., Casado-Zumeta, X., Lertxundi, A., Critchley, D.J., 2019. Association between sympathoexcitatory changes and symptomatic improvement following cervical mobilisations in participants with neck pain. A double blind placebo controlled trial. *Musculoskeletal Science & Practice* 42, 90–97. <https://doi.org/10.1016/j.msksp.2019.05.001>.

- Licciardone, J.C., Ibrahim, M., Baker, J., Thornton, T., Vu, S., 2024. Pain catastrophizing and risk of progression to widespread pain among patients with chronic low back pain: a retrospective cohort study. *Musculoskeletal Science & Practice* 69, 102886. <https://doi.org/10.1016/j.msksp.2023.102886>.
- LoMartire, R., Ång, B.O., Gerdle, B., Vixner, L., 2020. Psychometric properties of short form-36 health survey, EuroQol 5-dimensions, and hospital anxiety and depression scale in patients with chronic pain. *Pain* 161 (1), 83–95. <https://doi.org/10.1097/j.pain.0000000000001700>.
- Ludvigsson, M.L., Peterson, G., Dederig, Å., Falla, D., Peolsson, A., 2016. Factors associated with pain and disability reduction following exercise interventions in chronic whiplash. *Eur. J. Pain* 20 (2), 307–315. <https://doi.org/10.1002/ejp.729>. Scopus.
- MacDermid, J.C., Walton, D., Avery, S., Blanchard, A., Etruw, E., McAlpine, C., Goldsmith, C., 2009. Measurement properties of the neck disability index: a systematic review. *J. Orthop. Sports Phys. Ther.* 39 (5). <https://doi.org/10.2519/jospt.2009.2930>.
- Malfliet, A., Lluch Gibrés, E., Pecos-Martin, D., Gallego-Izquierdo, T., Valera-Calero, A., 2019. The influence of treatment expectations on clinical outcomes and cortisol levels in patients with chronic neck pain: an experimental study. *Pain Pract.: The Official Journal of World Institute of Pain* 19 (4), 370–381. <https://doi.org/10.1111/papr.12749>.
- Modarresi, S., Lukacs, M.J., Ghodrati, M., Salim, S., MacDermid, J.C., Walton, D.M., 2021. A systematic review and synthesis of psychometric properties of the numeric pain rating scale and the visual analog scale for use in people with neck pain. *Clin. J. Pain.* <https://doi.org/10.1097/AJP.0000000000000999>. CATWAD consortium group (see notes).
- Monticone, M., Iovine, R., de Sena, G., Rovere, G., Uliano, D., Arioli, G., Bonaiuti, D., Brugnoli, G., Ceravolo, G., Cerri, C., Dalla Toffola, E., Fiore, P., Foti, C., 2013. The Italian society of physical and rehabilitation medicine (SIMFER) recommendations for neck pain. *G. Ital. Med. del Lav. Ergon.* 35 (1), 36–50. Italian Society of Physical and Rehabilitation Medicine (SIMFER).
- Mueller, J., Weinig, J., Niederer, D., Tenberg, S., Mueller, S., 2023. Resistance, motor control and mindfulness-based exercises are effective for treating chronic non-specific neck pain: a systematic review with meta-analysis and dose-response meta-regression. *J. Orthop. Sports Phys. Ther.* 1–39. <https://doi.org/10.2519/jospt.2023.11820>.
- Murphy, D.R., Lopez, M., 2013. Neck and back pain specific outcome assessment questionnaires in the Spanish language: a systematic literature review. *Spine J.* 13 (11), 1667–1674. <https://doi.org/10.1016/j.spinee.2013.08.046>.
- Nikander, R., Mälikä, E., Parkkari, J., Heinonen, A., Starck, H., Ylinen, J., 2006. Dose-response relationship of specific training to reduce chronic neck pain and disability. *Med. Sci. Sports Exerc.* 38 (12), 2068–2074. <https://doi.org/10.1249/01.mss.0000229105.16274.4b>.
- Noordzij, M., Tripepi, G., Dekker, F.W., Zoccali, C., Tanck, M.W., Jager, K.J., 2010. Sample size calculations: basic principles and common pitfalls. *Nephrol. Dial. Transplant.: Official Publication of the European Dialysis and Transplant Association - European Renal Association* 25 (5), 1388–1393. <https://doi.org/10.1093/ndt/gfp732>.
- Page, A., Inglés, M., Venegas, W., Mollà-Casanova, S., Serra-Añó, P., 2023. Effect of non-specific neck pain on the path of the instantaneous axis of rotation of the neck during its flexion-extension movement. *Musculoskeletal Science and Practice* 64, 102737. <https://doi.org/10.1016/j.msksp.2023.102737>.
- Parikh, P., Santaguida, P., Macdermid, J., Gross, A., Eshtiahi, A., 2019. Comparison of CPG's for the diagnosis, prognosis and management of non-specific neck pain: a systematic review. *BMC Musculoskelet. Disord.* 20 (1), 81. <https://doi.org/10.1186/s12891-019-2441-3>.
- Pedersen, M.T., Andersen, L.L., Jørgensen, M.B., Søgaard, K., Sjøgaard, G., 2013. Effect of specific resistance training on musculoskeletal pain symptoms: dose-response relationship. *J. Strength Condit. Res.* 27 (1), 229–235. <https://doi.org/10.1519/JSC.0b013e3182541ceb>.
- Price, J., Rushton, A., Tyros, I., Tyros, V., Heneghan, N.R., 2020. Effectiveness and optimal dosage of exercise training for chronic non-specific neck pain: a systematic review with a narrative synthesis. *PLoS One* 15 (6), e0234511. <https://doi.org/10.1371/journal.pone.0234511>.
- Rue, H., Martino, S., Chopin, N., 2009. Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace approximations. *J. Roy. Stat. Soc. B* 71 (2), 319–392. <https://doi.org/10.1111/j.1467-9868.2008.00700.x>.
- Rue, H., Riebler, A., Sørbye, S.H., Illian, J.B., Simpson, D.P., Lindgren, F.K., 2017. Bayesian computing with INLA: a review. *Annual Review of Statistics and Its Application* 4 (1), 395–421. <https://doi.org/10.1146/annurev-statistics-060116-054045>.
- Saavedra-Hernández, M., Castro-Sánchez, A.M., Fernández-de-las-Peñas, C., Cleland, J.A., Ortega-Santiago, R., Arroyo-Morales, M., 2011. Predictors for identifying patients with mechanical neck pain who are likely to achieve short-term success with manipulative interventions directed at the cervical and thoracic spine. *J. Manipulative Physiol. Therapeut.* 34 (3), 144–152. <https://doi.org/10.1016/j.jmpt.2011.02.011>.
- Safiri, S., Kolahi, A.-A., Hoy, D., Buchbinder, R., Mansournia, M.A., Bettampadi, D., Ashrafi-Asgarabad, A., Almasi-Hashiani, A., Smith, E., Sepidarkish, M., Cross, M., Qorbani, M., Moradi-Lakeh, M., Woolf, A.D., March, L., Collins, G., Ferreira, M.L., 2020. Global, regional, and national burden of neck pain in the general population, 1990–2017: systematic analysis of the Global Burden of Disease Study 2017. *Br. Med. J.* 368, m791. <https://doi.org/10.1136/bmj.m791>.
- Saltychev, M., Pykkäs, K., Karklins, A., Juhola, J., 2024. Psychometric properties of neck disability index—a systematic review and meta-analysis. *Disabil. Rehabil.* 1–17. <https://doi.org/10.1080/09638288.2024.2304644>.
- Scott, W., Wideman, T.H., Sullivan, M.J.L., 2014. Clinically meaningful scores on pain catastrophizing before and after multidisciplinary rehabilitation: a prospective study of individuals with subacute pain after whiplash injury. *Clin. J. Pain* 30 (3), 183. <https://doi.org/10.1097/AJP.0b013e31828ee66c>.
- Sjölander, P., Michaelson, P., Jaric, S., Djupsjöbacka, M., 2008. Sensorimotor disturbances in chronic neck pain—range of motion, peak velocity, smoothness of movement, and repositioning acuity. *Man. Ther.* 13 (2), 122–131. <https://doi.org/10.1016/j.math.2006.10.002>.
- Sremakaew, M., Jull, G., Treleaven, J., Barbero, M., Falla, D., Uthairkhu, S., 2018. Effects of local treatment with and without sensorimotor and balance exercise in individuals with neck pain: protocol for a randomized controlled trial. *BMC Musculoskelet. Disord.* 19 (1), 48. <https://doi.org/10.1186/s12891-018-1964-3>.
- Stenneberg, M.S., Busstra, H., Eskes, M., van Trijffel, E., Cattrysse, E., Scholten-Peeters, G.G.M., de Bie, R.A., 2018. Concurrent validity and interrater reliability of a new smartphone application to assess 3D active cervical range of motion in patients with neck pain. *Musculoskeletal Science & Practice* 34, 59–65. <https://doi.org/10.1016/j.msksp.2017.12.006>.
- Sullivan, M., Bishop, S., Pivik, J., 1995. The pain catastrophizing scale: development and validation. *Psychol. Assess.* 7, 524–532. <https://doi.org/10.1037/1040-3590.7.4.524>.
- Suvarnnato, T., Puntumetakul, R., Uthairkhu, S., Boucaut, R., 2019. Effect of specific deep cervical muscle exercises on functional disability, pain intensity, craniocervical angle, and neck-muscle strength in chronic mechanical neck pain: a randomized controlled trial. *J. Pain Res.* 12, 915–925. <https://doi.org/10.2147/JPR.S190125>.
- Villanueva-Ruiz, I., Falla, D., Lascurain-Aguirrebeña, I., 2021. Effectiveness of specific neck exercise for nonspecific neck pain; usefulness of strategies for patient selection and tailored exercise—a systematic review with meta-analysis. *Phys. Ther.* <https://doi.org/10.1093/ptj/pzab259> pzab259.
- Ware, J., 2000. SF-36 health survey update. *Spine* 25 (24), 3130–3139. <https://doi.org/10.1097/00007632-200012150-00008>.
- Ware, J., Ma, K., Keller, S.D., 1993. SF-36 Physical and Mental Health Summary Scales: A User's Manual 8, 23–28.
- Weermeijer, J.D., Meulders, A., 2018. Clinimetrics: Tampa scale for kinesiophobia. *J. Physiother.* 64 (2), 126. <https://doi.org/10.1016/j.jphys.2018.01.001>.
- Wheeler, C.H.B., Williams, A.C. de C., Morley, S.J., 2019. Meta-analysis of the psychometric properties of the Pain Catastrophizing Scale and associations with participant characteristics. *Pain* 160 (9), 1946. <https://doi.org/10.1097/j.pain.0000000000001494>.
- Woby, S.R., Roach, N.K., Urmston, M., Watson, P.J., 2005. Psychometric properties of the TSK-11: a shortened version of the Tampa scale for kinesiophobia. *Pain* 117 (1–2), 137–144. <https://doi.org/10.1016/j.pain.2005.05.029>.
- Woodhouse, A., Vasseljen, O., 2008. Altered motor control patterns in whiplash and chronic neck pain. *BMC Musculoskelet. Disord.* 9, 90. <https://doi.org/10.1186/1471-2474-9-90>.
- Yaşarar, Ö., Yilmaz, H.G., Doğan, H., 2023. Comparison of two different delivery methods of home-based exercise on neck pain. *SMR (Somatosens. Mot. Res.)* 0 (0), 1–8. <https://doi.org/10.1080/08990220.2023.2194389>.
- Young, I.A., Dunning, J., Butts, R., Mourad, F., Cleland, J.A., 2019. Reliability, construct validity, and responsiveness of the neck disability index and numeric pain rating scale in patients with mechanical neck pain without upper extremity symptoms. *Physiother. Theory Pract.* 35 (12), 1328–1335. <https://doi.org/10.1080/09593985.2018.1471763>.
- Zabala-Mata, J., Azkue, J.J., Bialosky, J.E., Saez, M., López, E.D., Arrieta, M.A., Lascurain-Aguirrebeña, I., 2024. Restoration of normal central pain processing following manual therapy in nonspecific chronic neck pain. *PLoS One* 19 (5), e0294100. <https://doi.org/10.1371/journal.pone.0294100>.
- Zebis, M.K., Andersen, C.H., Sundstrup, E., Pedersen, M.T., Sjøgaard, G., Andersen, L.L., 2014. Time-wise change in neck pain in response to rehabilitation with specific resistance training: implications for exercise prescription. *PLoS One* 9 (4), Scopus. <https://doi.org/10.1371/journal.pone.0093867>.