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Are baseline clinical tests associated with the relative effectiveness of manual therapy and neck-specific exercise for people with chronic non-specific neck pain? Secondary analysis of a randomized controlled trial

Iker Villanueva-Ruiz [a,*], Deborah Falla [b,c], Marc Saez [d], Maialen Araolaza-Arrieta [a], Jon Jatsu Azkue [e,i], Ane Arbillaga-Etxarri [a], Ana Lersundi [f,h], Ion Lascurain-Aguirrebeña [g,h,i]

[a] Deusto Physical TherapIker, Physical Therapy Department, Faculty of Health Sciences, University of Deusto, Spain
[b] Department of Preventive Medicine and Public Health, Faculty of Medicine and Nursing, University of the Basque Country UPV/EHU, Leioa, Spain
[c] Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), School of Sport, Exercise and Rehabilitation Sciences. College of Life and Environmental Sciences, University of Birmingham, United Kingdom
[d] Research Group on Statistics, Econometrics and Health (GRECS), University of Girona, Girona, Spain. CIBER of Epidemiology and Public Health (CIBERESP), Madrid, Spain
[e] Department of Neurosciences, Faculty of Medicine and Nursing, University of the Basque Country UPV/EHU, Leioa, Spain
[f] Department of Traumatology and Orthopedic Surgery, Osakidetza Servicio Vasco de Salud Hospital Universitario Donostia, Donostia, Spain
[g] Physiotherapy, Department of Physiology, Faculty of Medicine and Nursing, University of the Basque Country UPV/EHU, Leioa, Spain
[h] Biogipuzkoa Health Research Institute, Bioengineering Area, Innovation Group, San Sebastian, Spain
[i] Musculoskeletal Pain research group, University of the Basque Country (UPV/EHU), Leioa, Spain

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ABSTRACT

Objective: To evaluate whether baseline clinical tests are associated with the relative effectiveness of manual therapy versus neck-specific exercise for people with chronic non-specific neck pain (NSNP).
Design: Pre-planned secondary analysis of a single-blind, parallel, randomized clinical trial with two treatment arms, adhering to CONSORT guidelines.
Methods: 65 participants with NSNP were randomly allocated with a 1:1 allocation ratio to a programme of either manual therapy or neck-specific exercise. A battery of clinical tests was performed pre-treatment. The manual therapy group had four 30-min sessions, while the exercise group followed a four-week program with physiotherapist-led sessions and daily home exercises. Outcomes measured at baseline, two weeks, four weeks, and 12 weeks post-treatment included pain intensity, disability, patient-perceived improvement, quality of life, and kinesiophobia. Patients were categorized into either responders or non-responders according to pain intensity, disability and patient-perceived improvement.
Results: Patients with NSNP that reported bilateral pain, no blocking sensation and greater pain at end of range, showed side flexion or rotation range of movement asymmetry, and whose symptoms could be reproduced during the specific neck movements, were more likely to be classified as *responders* if they received manual therapy when when compared to neck-specific exercise. Adjusted odds ratios (Prob >0.95) varied considerably (range 7.01xe-14 to 0.32) depending on clinical tests and the follow up time point.
Conclusion: A battery of clinical tests showed significant associations with the relative effectiveness of manual therapy versus neck-specific exercise in patients with NSNP.

1. Introduction

Nonspecific chronic neck pain (NSNP) is a highly prevalent condition (Safiri et al., 2020), ranked as one of the leading causes of disability (GBD 2016 Disease and Injury Incidence and Prevalence Collaborators, 2017) and resulting in significant economic burden (Hoy et al., 2010).

* Corresponding author. Faculty of Health Sciences. University of Deusto., Mundaiz Kalea 50, Donostia, San Sebastián, 20012, Spain.
E-mail addresses: iker.villanueva@deusto.es (I. Villanueva-Ruiz), d.falla@bham.ac.uk (D. Falla), marc.saez@udg.edu (M. Saez), maialen.araolaza@deusto.es (M. Araolaza-Arrieta), jonjatsu.azkue@ehu.eus (J.J. Azkue), ane.arbillaga@deusto.es (A. Arbillaga-Etxarri), ana.lersundi@ehu.eus (A. Lersundi), ion.lascurain@ehu.eus (I. Lascurain-Aguirrebeña).

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Table 1
Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
• Age ≥18 years • Primary complaint of neck pain. • Non-traumatic (insidious) history of onset. • Mechanical in nature i.e. pain has clear aggravating and easing positions or movements.	• Radicular pain. • Signs of central hyperexcitability (e.g. widespread, non-anatomical/ nonspecific distribution of pain; stimulus-independent spontaneous pain). • Whiplash injury. • Have had or are awaiting neck surgery. • Inflammatory disease.

Clinical practice guidelines advocate the use of manual therapy and 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). However, despite guidelines advocating their use, systematic reviews on the effectiveness of exercise (Campo et al., 2021; Gross et al., 2015; Martin-Gomez et al., 2019; Tsiringakis et al., 2020; Villanueva-Ruiz et al., 2021; Zoete et al., 2020) and manual therapy (Gross et al., 2010; Gross et al., 2015; Hidalgo et al., 2017; Liu et al., 2023; Miller et al., 2010; Minnucci et al., 2023; Tsegay et al., 2023) for NSNP have reported moderate effect sizes at best. Such findings in randomized controlled trials have at least in part been attributed to the heterogeneity of participants, where the absence of an effect in some subgroups of patients may dilute the effect observed in others, thus hindering the overall effectiveness of the intervention (Lascurain-Aguirrebeña et al., 2018).

It has been postulated that patients may respond differently to manual therapy and exercise depending on their specific clinical characteristics, i.e. that a certain subgroup of patients may obtain the most favourable outcome with manual therapy, whereas others may show greatest improvement following exercise (Dewitte et al., 2014, 2016, 2018; Lascurain-Aguirrebeña et al., 2018). Matching groups of patients with the treatment that they are most likely to benefit (stratified or matched care) is expected to increase the effectiveness of interventions (Dewitte et al., 2014, 2016, 2018; Lascurain-Aguirrebeña et al., 2018; Maissan et al., 2020). Several treatment-based classification systems have been proposed, however the majority are solely based on the opinion of a small group of experts (Bier et al., 2018; Childs et al., 2004; Dewitte et al., 2014, 2016; Fritz and Brennan, 2007; Hefford, 2008; Lee et al., 2017; Wang et al., 2003).

Many studies have reported disturbances in cervical neuromuscular function in people with NSNP (Falla et al., 2004; Grip et al., 2008; Page et al., 2023; Sjölander et al., 2008; Woodhouse and Vasseljen, 2008). It has been hypothesized that NSNP patients demonstrating such disturbances may be most suited for treatment with specific neck exercise (Blomgren et al., 2018; Jull et al., 2009; Lluch et al., 2014; Zoete et al., 2020). As such, several clinical tests have been designed to assess cervical neuromuscular function in patients with neck pain (Araujo et al., 2020; Jull et al., 2008, 2018; Segarra et al., 2015), and ascertain which patients may most likely benefit from specific neck exercise interventions. With respect to manual therapy, it has been suggested that patients with NSNP that have unilateral pain (Dewitte et al., 2014; Ford et al., 2019), greater pain at the end of cervical range of movement (Dewitte et al., 2014; Schneider et al., 2013) or limited cervical global or segmental movement (Cleland et al., 2005; Dewitte et al., 2014; Kanlayanaphotporn et al., 2009, 2010; Krauss et al., 2008; Lascurain-Aguirrebeña et al., 2018, 2021), and those whose symptoms can be reproduced with cervical joint palpation (Dewitte et al., 2014, 2016; Kanlayanaphotporn et al., 2009; Krauss et al., 2008;

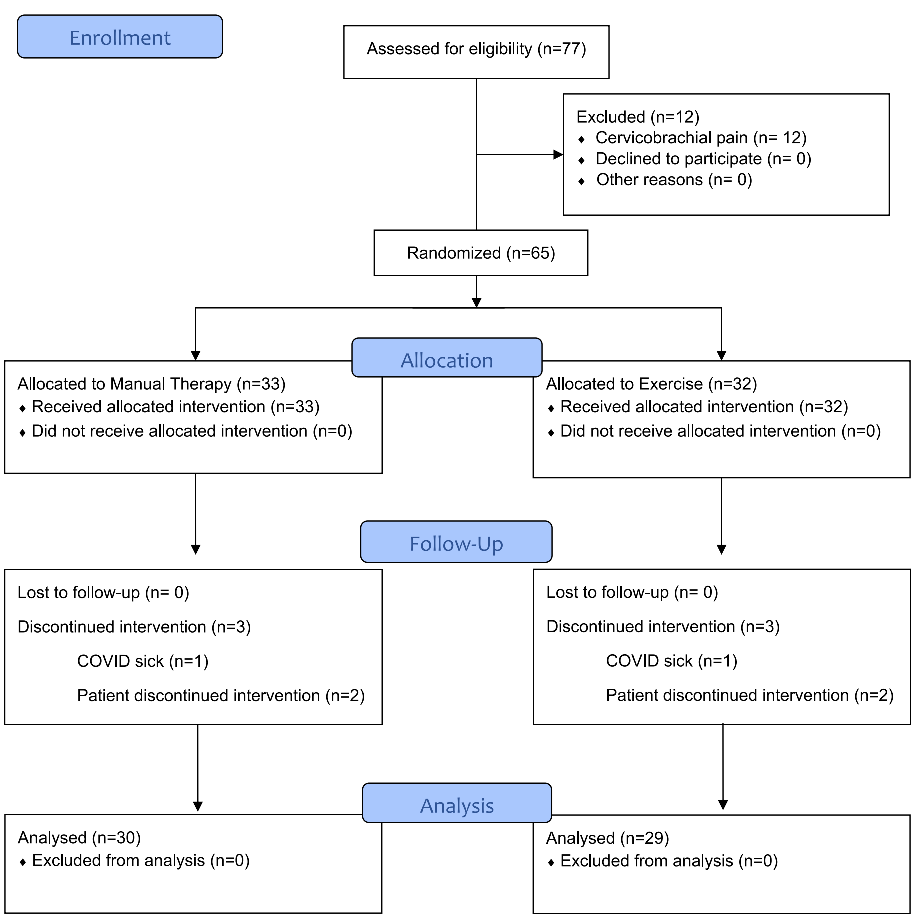

Fig. 1. Patient flow diagram.

Table 2
Patient baseline characteristics in each group. Values are mean ± SD or number of cases (/).

Variables	MT group (n = 30)	Ex group (n = 29)
Age (years)	55.2 ± 15.3	48.7 ± 11.9
Gender (male/female)	11/19	8/21
BMI (kg/m2)	23.9 ± 3.5	24.3 ± 3.3
Symptom duration (years)	6.3 ± 7.3	10.7 ± 9.6
Number of non-specific physiotherapy sessions last year	9.2 ± 13.2	10.3 ± 10.8
EQ (5D) (0–10)	6.7 ± 1.7	6.5 ± 1.8
PSFS (0–10)	4.8 ± 1.6	5.2 ± 1.4
NPRS 1 week (0–10)	6.4 ± 1.8	6.2 ± 2.1
NPRS 24h (0–10)	5.5 ± 2.5	4.8 ± 2.1
NDI (0–100)	27.6 ± 11.9	30.8 ± 16.4
PCS (0–52)	15.8 ± 9.1	13.8 ± 10.1
TSK (11–44)	23.4 ± 4.4	24.3 ± 7.2
Expectations (0–100)	80.9 ± 20.2	76.1 ± 18.7
ROM Flex (degrees)	51 ± 13.6	48.4 ± 12.3
ROM Ext (degrees)	53.3 ± 13.6	53.1 ± 15.4
ROM SFR (degrees)	27.1 ± 7.8	28.6 ± 10.8
ROM SFL (degrees)	26.2 ± 7.3	26.3 ± 11.2
ROM RotR (degrees)	54.9 ± 15	54.3 ± 14
ROM RotL (degrees)	54.7 ± 12.8	57.5 ± 13.4
SF-36 P (0–100)	66.5 ± 13.4	65.8 ± 16.9
SF-36 M (0–100)	67.2 ± 13.7	61.6 ± 19.3
Painful movement NPRS (0–10)	5.3 ± 2.5	5.8 ± 1.9
Deep Cervical Extensor Test (positive/negative)	20/9	20/9
Suboccipital Muscles Test Flex-Ext (positive/negative)	21/8	21/8
Pattern of Neck Extension (positive/negative)	24/5	27/2
Craniocervical Flexion Test (positive/negative)	27/3	23/5
Hypomobility and pain (positive/negative)	15/12	15/13
ROM SF or Rot restricted (positive/negative)	9/21	8/21
Pain combination movements (positive/negative)	29/1	27/2
Blocking sensation (positive/negative)	14/16	12/17
Greater pain end of ROM (positive/negative)	21/9	26/3
Unilateral or bilateral pain (central/unilateral/bilateral)	3/12/15	1/8/20

BMI: Body mass index; EQ (5D) VAS: EuroQuol 5D visual analogue scale; PSFS: Patient specific functional scale; NPRS 1w: Numeric pain rating scale last week; NPRS 24h: Numeric pain rating scale last 24 h; NDI: Neck disability index; PCS: Pain Catastrophizing Scale; TSK: Tampa Scale for Kinesiophobia; ROM: range of movement; Flex: flexion; Ext: extension; SFR: right side flexion; SFL: left side flexion; RotR: right rotation: RotL: left rotation; SF-36 P: SF-36, physical domain; SF-36 M: SF-36, mental domain; SF: side flexion; Rot: rotation.

Lascurain-Aguirrebeña et al., 2018, 2021) or with neck movements that cause zygapophyseal joint compression or distraction (Dewitte et al., 2014, 2016; Ford et al., 2019; Krauss et al., 2008; McCarthy, 2001) may obtain the greatest benefit. However, no study has evaluated the association between the aforementioned clinical criteria and the relative effectiveness of manual therapy and exercise in people with NSNP.

The aim of this study was to assess the association between baseline characteristics and the relative treatment outcome following manual therapy or neck-specific exercise for people with NSNP. We hypothesized that specific baseline clinical tests would be associated with the relative effectiveness of the two interventions, that is, that patients with a *mechanical* clinical presentation suggestive of nociceptive pain would experience greater reductions in pain and disability after manual therapy than after a neck-specific exercise programme.

2. Methods

This is a pre-planned secondary analysis of a single-blind, parallel-group, randomized clinical trial. Results regarding the primary aim of the study (the relative effectiveness of manual therapy and specific exercise) as well as the primary power calculation to determine the sample size has been published elsewhere (Villanueva-Ruiz et al., 2025). 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 to meet the aims of the secondary analysis was 80 %. Informed consent was obtained from all participants, and all procedures adhered to the ethical standards of the Helsinki declaration. Participants were informed about the study's purpose, procedures, risks, and benefits before providing written consent. Confidentiality and anonymity were maintained throughout the study. Following ethical approval (CEISH/113/2019) and trial registration (ACTRN12620000711910), we conducted a single-blind, parallel, randomized clinical trial with two treatment arms. Patients with NSNP attending a secondary care spinal unit in Donostia (Spain) and meeting the inclusion and exclusion criteria outlined in Table 1 were invited to participate.

2.1. Randomization

Participants were randomly assigned in a 1:1 ratio to either the manual therapy group or the exercise group using a computer-generated random sequence prepared in advance. Allocation information was stored in sealed opaque envelopes, and the treating physical therapist with 15 years of clinical experience and postgraduate training in neuromusculoskeletal physiotherapy, opened the envelopes and administered the interventions.

2.2. Interventions

2.2.1. Manual therapy

Patients in this group underwent four weekly 30-min sessions of manual therapy involving both myofascial and articular techniques. Treatment commenced with a suboccipital inhibition manual technique (Damgaard et al., 2013; Guo et al., 2023) and cervical longitudinal intermittent traction (Binder, 2008). Subsequently, at the discretion of the treating 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 (Lascurain-Aguirrebeña et al., 2018, 2021).

2.2.2. Exercise

Patients in the exercise group completed a program of neck-specific exercises adapted from a previous protocol (Jull et al., 2018; Sremakaew 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 (Falla et al., 2004; Grip et al., 2008; Page et al., 2023; Sjölander et al., 2008; Woodhouse and Vasseljen, 2008).

Physiotherapist-led individual sessions occurred weekly, supplemented by daily home exercises, 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. 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.

Table 3
Association between baseline pain location and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Pain location	**Central**	**NDI 0–2 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		−0.45	−5.96 to 5.05	0.566
	Bilateral		0.27	−4.16 to 4.69	0.547
	Central	**NDI 0–4 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		2.44	−11.86 to 16.75	0.631
	Bilateral		−0.54	−12.03 to 10.95	0.538
	Central	**NDI 0–12 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		0.56	−10.57 to 11.69	0.539
	Bilateral		0.04	−8.84 to 8.93	0.503
	Central	**Pain intensity last week 0–2 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		0.55	−1.17 to 2.26	0.736
	Bilateral		−0.27	−1.59 to 1.04	0.662
	Central	**Pain intensity last week 0–4 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		0.25	−1.13 to 1.63	0.64
	Bilateral		−0.77	−1.83 to 0.28	0.926
	Central	**Pain intensity last week 0–12 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		0.06	−1.2 to 1.32	0.537
	Bilateral		−0.26	−1.23 to 0.7	0.705
	Central	**Pain intensity last 24h 0–2 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		−0.35	−2.13 to 1.43	0.653
	Bilateral		−0.49	−1.9 to 0.91	0.758
	Central	**Pain intensity last 24h 0–4 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		0.14	−1.23 to 1.51	0.58
	Bilateral		−0.72	−1.8 to 0.36	0.907
	Central	**Pain intensity last 24h 0–12 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		0.16	−1.07 to 1.38	0.599
	Bilateral		0.18	−0.78 to 1.15	0.644
	Central	**PSFS 0–2 weeks**	0	−62.01 to 62.01	0.501
	Unilateral		−0.02	−1.21 to 1.18	0.511
	Bilateral		0.47	−0.56 to 1.5	0.817
	Central	**PSFS 0–4 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		0.08	−1.14 to 1.3	0.552
	Bilateral		0.23	−0.79 to 1.26	0.674
	Central	**PSFS 0–12 weeks**	0	−62.01 to 62.01	0.499
	Unilateral		0.03	−0.98 to 1.05	0.524
	Bilateral		0.08	−0.77 to 0.93	0.574
	Central	**GROC 0–2 weeks**	1	1.17 x e^{-27} to 8.51 x e^{26}	0.499
	Unilateral		0.94	0.72 to 1.23	0.673
	Bilateral		0.96	0.78 to 1.18	0.664
	Central	**GROC 0–4 weeks**	1	1.17 x e^{-27} to 8.51 x e^{26}	0.499
	Unilateral		0.97	0.8 to 1.19	0.609
	Bilateral		0.93	0.8 to 1.09	0.821
	Central	**GROC 0–12 weeks**	1	0.17 x e^{-27} to 8.51 x e^{26}	0.499
	Unilateral		0.99	0.84 to 1.17	0.549
	Bilateral		0.93	0.81 to 1.06	0.872
	Central	**Responder 0–2 weeks**	1	1.17 x e^{-27} to 8.51 x e^{26}	0.499
	Unilateral		0.28	0.03 to 2.76	0.863
	Bilateral		0.24	0.04 to 1.42	0.942
	Central	**Responder 0-treatment completion**	1	0.17 x e^{-27} to 8.51 x e^{26}	0.499
	Unilateral		0.93	0.28 to 3.09	0.549
	Bilateral		0.27	0.09 to 0.79	0.991*
	Central	**Responder 0–12 weeks post treatment completion**	1	0.17 x e^{-27} to 8.51 x e^{26}	0.501
	Unilateral		0.92	0.18 to 4.42	0.544
	Bilateral		0.14	0.03 to 0.57	0.997 *

Shaded in grey. statistically significant ($P > 0.95$); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

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.

2.2.2.1. Neck flexor training. The exercise programme involved the following exercise blocks (see supplementary videos):

Block 1. Re-education of craniocervical flexion movement pattern: supine, knees bent. Gentle and controlled nodding action facilitated with eye movement (10 reps).

Block 2. Holding capacity: supine, knees bent. (10 s holds × 10 reps).

Block 3. Interaction between the deep/superficial cervical flexors: sitting. Controlled head movement through range of extension and return to neutral (10 reps).

Block 4. Co-contraction of the deep cervical flexors/extensors: sitting. Isometric cervical rotation facilitated with eye movement (left/right sides) (5 s holds × 5 reps).

Block 5. Strength/endurance of the cervical flexors:

- Sitting. Isometric craniocervical flexion in a range of cervical extension (10 s holds × 10 reps).
- Sitting. Lifting the head off the wall (with the chair up to 30 cm away from the wall) (10 s holds × 10 reps).
- Supine. Lifting the head off a pillow (2, 1 then 0 pillows as per participant's capacity) (10 s holds × 10 reps).

Exercise blocks were performed according to the following timetable

Table 4
Association between baseline deep cervical extensor test and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Deep cervical extensor test	**Negative**	**NDI 0–2 weeks**	−2.99	−8.76 to 2.79	0.848
	Positive		2.16	−1.93 to 6.25	0.852
	Negative	**NDI 0–4 weeks**	−0.22	−15.24 to 14.79	0.513
	Positive		1.32	−9.78 to 12.43	0.592
	Negative	**NDI 0–12 weeks**	1.35	−5.25 to 7.94	0.656
	Positive		0.44	−4.43 to 5.32	0.571
	Negative	**Pain intensity last week 0–2 weeks**	−0.67	−2.41 to 1.07	0.778
	Positive		0.11	−1.15 to 1.38	0.569
	Negative	**Pain intensity last week 0–4 weeks**	−0.43	−1.85 to 0.98	0.729
	Positive		−0.28	−1.3 to 0.75	0.705
	Negative	**Pain intensity last week 0–12 weeks**	0.03	−1.26 to 1.31	0.515
	Positive		−0.07	−1 to 0.86	0.558
	Negative	**Pain intensity last 24h 0–2 weeks**	−1.51	−3.4 to 0.37	0.944
	Positive		0.22	−1.08 to 1.53	0.634
	Negative	**Pain intensity last 24h 0–4 weeks**	−0.46	−1.96 to 1.04	0.727
	Positive		−0.15	−1.19 to 0.89	0.611
	Negative	**Pain intensity last 24h 0–12 weeks**	0.42	−0.91 to 1.75	0.73
	Positive		0.29	−0.63 to 1.21	0.734
	Negative	**PSFS 0–2 weeks**	1	−0.28 to 2.28	0.939
	Positive		−0.18	−1.1 to 0.73	0.658
	Negative	**PSFS 0–4 weeks**	0.61	−0.68 to 1.9	0.825
	Positive		−0.09	−1.04 to 0.86	0.573
	Negative	**PSFS 0–12 weeks**	0.59	−0.47 to 1.65	0.862
	Positive		−0.28	−1.06 to 0.51	0.757
	Negative	**GROC 0–2 weeks**	0.94	0.71 to 1.24	0.675
	Positive		0.96	0.78 to 1.17	0.66
	Negative	**GROC 0–4 weeks**	0.96	0.78 to 1.18	0.663
	Positive		0.95	0.82 to 1.11	0.734
	Negative	**GROC 0–12 weeks**	0.93	0.78 to 1.11	0.777
	Positive		0.95	0.83 to 1.08	0.798
	Negative	**Responder 0–2 weeks**	0.25	0.02 to 2.63	0.878
	Positive		0.22	0.04 to 1.24	0.957
	Negative	**Responder 0-treatment completion**	0.48	0.13 to 1.77	0.864
	Positive		0.33	0.12 to 0.92	0.984
	Negative	**Responder 0–12 weeks post treatment completion**	0.23	0.03 to 1.31	0.942
	Positive		0.23	0.06 to 0.86	0.986

Shaded in grey. statistically significant (P > 0.95); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

as able by the participant:

	Week 1	Week 2	Week 3	Week 4
Blocks	1 + 2	2 + 3	3 + 4	4 + 5

2.2.2.2. Neck extensor training. The exercise programme involved the following exercise blocks:

Block 1. Re-education of extension movement pattern:

- Prone on elbows/four-point kneeling positions. Craniocervical extension (3 sets of 5 reps).
- Prone on elbows/four-point kneeling positions. Craniocervical rotation (<40°) (3 sets of 5 reps).
- Prone on elbows/four-point kneeling positions. Cervical extension while keeping the craniocervical region in a neutral position (3 sets of 5 reps).

Block 2. Co-contraction of the deep cervical flexors/extensors: Sitting. Isometric cervical rotation facilitated with eye movement (left/right sides) (5 s holds × 5reps).

Block 3. Strength/endurance of the cervical extensors: sitting inclined/prone on elbows/four-point kneeling positions. Isometric hold in a range of cervical extension (10 s holds × 10 reps). Addition of progressive load (light weights attached to head) as per the patient's capacity.

Exercise blocks were performed according to the following timetable as able by the participant:

	Week 1	Week 2	Week 3	Week 4
Block	1	1 + 2	2 + 3	3+load

During the in-person session, a pressure biofeedback unit was employed to ensure the precise execution of exercises aimed at augmenting the endurance of deep flexor muscles; however, this apparatus was not distributed for home use by the patients.

All participants initiated their exercise regimen with the activities outlined in the initial phase and progressed sequentially on a weekly basis until they attained proficiency in executing exercises from the concluding phases. In instances where a patient proved unable to complete the stipulated 10 repetitions during the final stages, instructions were provided to engage in the maximum feasible number of repetitions and subsequently augment the repetition count at a rate of one repetition every two days. To tailor the exercise routine based on individual capacity, an initial proficiency level was established during the in-person session, and guidance was dispensed to patients for the gradual advancement of home-based exercises, incorporating the use of a pillow as deemed appropriate.

2.3. Patient interview and clinical examination

During the initial evaluation prior to treatment commencement, patients were asked to report if their neck pain was greater at the end of range of movement, and if they perceived a sensation of *blocking* when performing neck movements. Range of movement (ROM) of neck flexion, extension, side flexion and rotation was assessed in a seated position (Elgueta-Cancino et al., 2022; Stenneberg et al., 2018). ROM was deemed restricted if a side-to-side difference in cervical rotation and/or side flexion of at least 10° was identified (Dewitte et al., 2014). Passive intervertebral movement testing in supine was used to assess cervical segmental mobility. The test was considered positive if the patient reported pain during mobilisation and reduced cervical mobility

Table 5
Association between baseline suboccipital muscle test and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Suboccipital muscle test	**Negative**	**NDI 0–2 weeks**	−2.42	−8.37 to 3.53	0.792
	Positive		1.9	−2.21 to 6.02	0.82
	Negative	**NDI 0–4 weeks**	1.89	−6.8 to 10.58	0.665
	Positive		0.02	−5.99 to 6.03	0.501
	Negative	**NDI 0–12 weeks**	2.45	−9.78 to 14.68	0.653
	Positive		0.39	−8.1 to 8.88	0.535
	Negative	**Pain intensity last week 0–2 weeks**	0.39	−1.46 to 2.25	0.663
	Positive		−0.24	−1.51 to 1.04	0.644
	Negative	**Pain intensity last week 0–4 weeks**	−0.23	−1.73 to 1.27	0.619
	Positive		−0.35	−1.38 to 0.69	0.746
	Negative	**Pain intensity last week 0–12 weeks**	−0.24	−1.6 to 1.11	0.639
	Positive		0.02	−0.92 to 0.96	0.516
	Negative	**Pain intensity last 24h 0–2 weeks**	1.22	−0.84 to 3.27	0.879
	Positive		−0.54	−1.85 to 0.77	0.796
	Negative	**Pain intensity last 24h 0–4 weeks**	0.1	−1.53 to 1.73	0.549
	Positive		−0.3	−1.34 to 0.73	0.719
	Negative	**Pain intensity last 24h 0–12 weeks**	0.27	−1.17 to 1.71	0.643
	Positive		0.34	−0.58 to 1.25	0.764
	Negative	**PSFS 0–2 weeks**	−0.35	−1.77 to 1.07	0.689
	Positive		0.22	−0.72 to 1.16	0.679
	Negative	**PSFS 0–4 weeks**	0.12	−1.32 to 1.55	0.563
	Positive		0.09	−0.85 to 1.04	0.578
	Negative	**PSFS 0–12 weeks**	0.14	−1.05 to 1.34	0.592
	Positive		−0.09	−0.87 to 0.69	0.589
	Negative	**GROC 0–2 weeks**	0.91	0.67 to 1.23	0.734
	Positive		0.97	0.79 to 1.18	0.629
	Negative	**GROC 0–4 weeks**	0.89	0.71 to 1.11	0.853
	Positive		0.98	0.84 to 1.13	0.628
	Negative	**GROC 0–12 weeks**	0.9	0.74 to 1.08	0.874
	Positive		0.96	0.84 to 1.09	0.741
	Negative	**Responder 0–2 weeks**	7.52 x e^{-14}	8.23 x e^{-24} x to 8.86 x e^{-04}	0.995
	Positive		0.37	0.08 to 1.73	0.897
	Negative	**Responder 0-treatment completion**	0.24	0.05 to 1.09	0.948
	Positive		0.43	0.16 to 1.13	0.947
	Negative	**Responder 0–12 weeks post treatment completion**	0.22	0.03 to 1.38	0.947
	Positive		0.24	0.06 to 0.87	0.985

Shaded in grey. statistically significant ($P > 0.95$); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

was noted (Dewitte et al., 2014, 2016, 2018; Lascurain-Aguirrebeña et al., 2018, 2019). Additionally, cervical movements were combined to assess whether symptoms were reproduced or aggravated through the combination of either extension, ipsilateral side flexion and ipsilateral rotation, or flexion, contralateral side flexion and contralateral rotation (Dewitte et al., 2014, 2016, 2018; Lascurain-Aguirrebeña et al., 2018).

Assessment of neuromuscular disturbances was performed using the following battery of tests (Jull et al., 2018):

Function of the deep neck flexors was assessed using the craniocervical flexion test. With the patient in crook lying and a pressure biofeedback unit (Chattanooga Ltd Hixson, USA) placed behind their neck, the patient was instructed to perform craniocervical flexion increasing the pressure in the biofeedback unit from a baseline of 20 mmHg–22, 24 and 26 mmHg, and sustain the contraction for 3 s and then return to a neutral position after each pressure level. 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; Jull, 2008; Juul et al., 2013)).

The pattern of active cervical extension and return to neutral was assessed in sitting. The patient was instructed to look upwards towards the ceiling and return to a neutral position and repeat this ten times. The test was considered positive if the mass of the head did not move posterior to the line of the shoulders, or the return to neutral from an extended position was initiated with lower cervical flexion rather than with cranio-cervical flexion (Jull et al., 2008, 2018; Segarra et al., 2015).

Function of deep neck extensors and suboccipital muscles was assessed in four-point kneeling. To assess the function of the deep neck extensors (semispinalis and multifidus), patients were instructed to curl their neck down to look at their knees and then curl it back by performing neck extension while maintaining the craniocervical region in a neutral position and repeat this 10 times. The test was considered positive if the patient was unable to perform lower cervical spine extension without upper cervical extension (Jull et al., 2008, 2018; Segarra et al., 2015).

To test the function of the suboccipital muscles, patients were asked to perform alternating craniocervical flexion and extension 10 times, while maintaining the mid and lower cervical spine in neutral position. The test was considered positive if the patient was unable to perform craniocervical flexion-extension in relative isolation from mid and lower cervical movement. Any excessive contraction of the semispinalis capitis muscle combined with motion in the mid to lower cervical spine was deemed as an inability to perform the task. (Jull et al., 2018).

2.4. Outcome measures

The maximum intensity of pain experienced over the last week and the past 24 h was quantified using an 11-point numeric pain rating scale, ranging from 0 to 10 (Chiarotto et al., 2019; Cleland et al., 2008; Modarresi et al., 2021; Young et al., 2019). Number of non-specific physiotherapy sessions in the previous 12 months were also recorded.

Disability and functional capacity were assessed using the Neck Disability Index (NDI) (Bobos et al., 2018; Jones and Sterling, 2021; Murphy and Lopez, 2013) and the Patient Specific Functional Scale (PSFS) (Horn et al., 2012; Nicholas et al., 2012; Pathak et al., 2022; Thoomes-de Graaf et al., 2019), respectively.

Fear of movement or re-injury and the presence of catastrophizing thoughts were assessed using the Tampa Scale of Kinesiophobia (TSK) (Cleland et al., 2008; Gómez-Pérez et al., 2011; Weermeijer and Meulders, 2018; Woby et al., 2005) and the Pain Catastrophizing Scale

Table 6
Association between baseline pattern of neck extension and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Pattern neck extension	**Negative**	**NDI 0–2 weeks**	−3.61	−13.59 to 6.38	0.765
	Positive		1.22	−2.75 to 5.2	0.729
	Negative	**NDI 0–4 weeks**	1.71	−23.47 to 26.89	0.553
	Positive		0.8	−9.74 to 11.33	0.558
	Negative	**NDI 0–12 weeks**	−1.05	−21.03 to 18.94	0.542
	Positive		1.08	−7.02 to 9.17	0.603
	Negative	**Pain intensity last week 0–2 weeks**	0.1	−2.97 to 3.17	0.525
	Positive		−0.1	−1.32 to 1.12	0.564
	Negative	**Pain intensity last week 0–4 weeks**	−0.39	−2.87 to 2.09	0.623
	Positive		−0.31	−1.3 to 0.67	0.735
	Negative	**Pain intensity last week 0–12 weeks**	−0.03	−2.28 to 2.21	0.512
	Positive		−0.05	−0.94 to 0.85	0.541
	Negative	**Pain intensity last 24h 0–2 weeks**	1.77	−1.45 to 5	0.862
	Positive		−0.34	−1.61 to 0.93	0.702
	Negative	**Pain intensity last 24h 0–4 weeks**	−0.19	−2.74 to 2.35	0.561
	Positive		−0.22	−1.22 to 0.78	0.67
	Negative	**Pain intensity last 24h 0–12 weeks**	0.14	−2.1 to 2.39	0.549
	Positive		0.34	−0.55 to 1.22	0.773
	Negative	**PSFS 0–2 weeks**	0.56	−2.17 to 3.29	0.659
	Positive		0.08	−0.84 to 1	0.569
	Negative	**PSFS 0–4 weeks**	−0.14	−2.92 to 2.64	0.541
	Positive		0.11	−0.79 to 1.02	0.596
	Negative	**PSFS 0–12 weeks**	0.13	−2.19 to 2.44	0.542
	Positive		−0.05	−0.8 to 0.7	0.552
	Negative	**GROC 0–2 weeks**	0.97	0.59 to 1.6	0.542
	Positive		0.95	0.79 to 1.15	0.697
	Negative	**GROC 0–4 weeks**	0.89	0.61 to 1.3	0.732
	Positive		0.96	0.83 to 1.11	0.716
	Negative	**GROC 0–12 weeks**	0.94	0.68 to 1.29	0.656
	Positive		0.94	0.84 to 1.07	0.824
	Negative	**Responder 0–2 weeks**	8.44 x e^{-13}	1.01 x e^{-23} to 0.07	0.985
	Positive		0.28	0.06 to 1.28	0.94
	Negative	**Responder 0-treatment completion**	0.34	0.03 to 3.87	0.808
	Positive		0.38	0.15 to 0.95	0.981
	Negative	**Responder 0–12 weeks post treatment completion**	0.42	0.02 to 8.64	0.713
	Positive		0.22	0.06 to 0.75	0.992

Shaded in grey. statistically significant (P > 0.95); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

(PCS) (Osman et al., 1997; Sullivan et al., 1995; Wheeler et al., 2019), respectively.

Quality of life was measured via 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 global rating of change (GROC) scale was used to measure the patient perceived overall improvement following treatment (Bobos et al., 2018, 2019).

All self-reported measures were assessed at baseline (excluding GROC), two weeks after the commencement of treatment, and within 48 h of the last treatment completion, in order to find associations between baseline variables with outcomes at both short- and medium-term intervals. Additionally, GROC, NDI, PSFS, and maximum pain during the last week and last 24 h were evaluated 12 weeks after the last treatment completion. Due to the previously reported association between patient expectation and 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 was indicative of a higher expectation of recovery.

The outcome assessor remained blind to the patients' treatment allocations throughout the study.

2.5. Statistical analysis

In addition to assessing individual outcomes (NDI, PSFS, GROC, and maximum pain intensity during the last week and last 24 h), patients were also classified as *responders* or *non-responders* based on their treatment outcomes at each measurement time point. Patients were classified as *responders* if they demonstrated an improvement equal to or exceeding the minimum clinically important difference in at least two of the following three outcome measures: 24-h maximum pain intensity, disability (NDI), and patient-perceived improvement (GROC). Minimum clinically important differences were derived from prior studies, specifically 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 (indicating at least "quite a bit better") on the GROC scale (Cleland et al., 2007; Kamper et al., 2009; Saavedra-Hernández et al., 2011).

Distinct generalized linear mixed models (GLMM) were specified. The dependent variables were considered to be the changes, with respect to their baseline value, in the outcome variables at 2, 4 and in some cases, 12 weeks. The independent variable was the interaction between manual therapy vs. neck-specific exercise and the different baseline tests. Statistically significant baseline differences were observed between the manual therapy and exercise groups regarding age, symptom duration and number of non-specific physiotherapy sessions in the previous 12 months, hence all analyses were adjusted for the effect of these variables. In addition, we also controlled for the baseline value of the outcome of interest, since the magnitude of the change could depend on it. Furthermore, we controlled for individual heterogeneity (subject-specific factors that, even if unobserved, could influence the change in the dependent variable) and for temporal variation in weeks 2, 4, and 12 (not necessarily of the same magnitude), including random effects in the models. The GLMM link function depended on the nature of the dependent variable, i.e. Gaussian link for continuous dependent variables (NDI, PSFS, and maximum pain intensity during the last week and last 24 h), Poisson link for the discrete dependent variable (GROC), and binomial link for the dichotomous dependent variable (responder or non-responder). As a sensitivity analysis, we controlled for the value of those baseline tests that were significantly associated with treatment outcome at 95 % in order to establish if the baseline test result was independently associated with treatment outcome. Models were generated for treatment outcome at 2 weeks post treatment commencement,

Table 7
Association between baseline hypomobility and pain and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Hypomobility and pain	**Negative**	**NDI 0–2 weeks**	3.11	−1.54 to 7.77	0.907
	Positive		0.91	−3.84 to 5.67	0.648
	Negative	**NDI 0–4 weeks**	0.27	−6.46 to 7	0.53
	Positive		0.38	−6.39 to 7.16	0.543
	Negative	**NDI 0–12 weeks**	1.49	−8.09 to 11.08	0.62
	Positive		0.84	−8.77 to 10.44	0.567
	Negative	**Pain intensity last week 0–2 weeks**	0.66	−0.8 to 2.12	0.816
	Positive		0.26	−1.15 to 1.67	0.643
	Negative	**Pain intensity last week 0–4 weeks**	−0.21	−1.4 to 0.97	0.641
	Positive		−0.36	−1.51 to 0.78	0.735
	Negative	**Pain intensity last week 0–12 weeks**	0.18	−0.89 to 1.26	0.63
	Positive		0.08	−0.96 to 1.12	0.561
	Negative	**Pain intensity last 24h 0–2 weeks**	0.8	−0.75 to 2.35	0.846
	Positive		−0.23	−1.74 to 1.27	0.622
	Negative	**Pain intensity last 24h 0–4 weeks**	−0.04	−1.26 to 1.18	0.527
	Positive		−0.33	−1.51 to 0.86	0.708
	Negative	**Pain intensity last 24h 0–12 weeks**	0.66	−0.42 to 1.74	0.886
	Positive		0.36	−0.68 to 1.4	0.752
	Negative	**PSFS 0–2 weeks**	0.32	−0.77 to 1.41	0.723
	Positive		−0.1	−1.16 to 0.96	0.574
	Negative	**PSFS 0–4 weeks**	−0.11	−1.2 to 0.99	0.578
	Positive		0.28	−0.77 to 1.32	0.699
	Negative	**PSFS 0–12 weeks**	−0.08	−0.99 to 0.83	0.57
	Positive		−0.01	−0.87 to 0.86	0.508
	Negative	**GROC 0–2 weeks**	0.97	0.77 to 1.22	0.612
	Positive		0.88	0.7 to 1.1	0.874
	Negative	**GROC 0–4 weeks**	0.97	0.82 to 1.15	0.625
	Positive		0.89	0.75 to 1.05	0.919
	Negative	**GROC 0–12 weeks**	0.95	0.82 to 1.1	0.768
	Positive		0.89	0.77 to 1.03	0.944
	Negative	**Responder 0–2 weeks**	1.56 x e^{-08}	3.44 x e^{-24} to 7.1 x e^{-05}	0.998
	Positive		0.25	0.04 to 1.53	0.933
	Negative	**Responder 0-treatment completion**	0.12	0.03 to 0.51	0.998
	Positive		0.4	0.14 to 1.17	0.943
	Negative	**Responder 0–12 weeks post treatment completion**	0.08	0.01 to 0.39	0.999
	Positive		0.25	0.06 to 0.95	0.979

Shaded in grey. statistically significant (P > 0.95); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

treatment completion, and 12 weeks post treatment completion. Alongside coefficient estimators and their 95 % credibility intervals, the probability of the coefficient estimator (Prob(|estimator|)>1, Prob) was computed, offering insights into the potential association between dependent and independent variables. When Prob >0.95, it corresponds, in a non-Bayesian context, to $p < 0.05$. To address the complexity of the models, Bayesian inference was conducted, employing the Integrated Nested Laplace Approximation (INLA) approach (R-INLA Project, n.d.; Rue et al., 2009, 2017). INLA is a computationally efficient method for performing approximate Bayesian inference in latent Gaussian models, a class widely used in spatial statistics, survival analysis, and generalized linear mixed models. Unlike traditional Markov Chain Monte Carlo methods, INLA avoids iterative sampling by combining numerical integration with Laplace approximations to directly approximate posterior marginal distributions of parameters. This approach significantly reduces computational time while maintaining high accuracy, making it particularly suited for complex models with hierarchical structures or large datasets. INLA has been rigorously validated and is implemented in the R-INLA package, which provides user-friendly tools for Bayesian analysis without requiring intensive tuning (Rue et al., 2009).

3. Results

A total of seventy-seven participants were screened between July 1, 2020 and November 8, 2022. Sixty-five individuals met the predefined eligibility criteria and were subsequently enrolled in the study. Of these, 59 successfully completed all prescribed treatments and evaluations, while six patients, distributed evenly across both treatment groups, were lost to follow-up. Flow diagram illustrating participant progression is presented in Fig. 1. Baseline characteristics of study participants within each treatment group are shown in Table 2. Both groups demonstrated significant (Prob >0.95) improvements in maximum pain during the last week and last 24 h, disability (NDI) and function (PSFS) at two weeks after treatment commencement, post treatment completion and 12 weeks post treatment completion. Twelve patients (20 %) were classified as *responders* at week two, 24 patients (41 %) at treatment completion, and 23 patients (39 %) at 12 weeks post treatment completion. All other patients were classified as *non-responders*.

3.1. Association between baseline clinical evaluation and treatment outcome at 2 weeks post treatment commencement

No significant association was found between baseline patient reported symptoms and clinical tests, and treatment induced changes for the NDI, PSFS, GROC, and maximum pain intensity. However, when the composite outcome measure was used (i.e. *responder* or *non-responder*), there was a significant association between baseline clinical tests and treatment outcome (Tables 3–12). Following the sensitivity analysis, only blocking sensation, the presence of greater pain at the end of neck ROM, restricted side flexion or rotation ROM, and symptom reproduction during combination of movements remained significant. Patients reporting the absence of a blocking sensation were less likely to be classified as responders if they received exercise (coefficient: 0.11; 95 % CI: 0.01–0.94; P = 0.973). In patients that reported a blocking sensation, manual therapy and exercise were equally effective (P < 0.95). Greater pain at the end of neck ROM was associated with a greater likelihood of being classified as *responder* if treated with manual therapy when compared to exercise (coefficient: 0.17; 95 % CI: 0.03–0.96; P = 0.978), and symptom reproduction during combination of movements was associated with a greater likelihood of responding with manual therapy

Table 8
Association between baseline blocking sensation and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Blocking sensation	**No**	**NDI 0–2 weeks**	1.89	−2.56 to 6.34	0.8
	Yes		−0.72	−5.89 to 4.45	0.611
	No	**NDI 0–4 weeks**	1.68	−10.28 to 13.64	0.608
	Yes		−0.35	−14.11 to 13.4	0.521
	No	**NDI 0–12 weeks**	2.02	−7.02 to 11.07	0.669
	Yes		−0.83	−11.24 to 9.59	0.563
	No	**Pain intensity last week 0–2 weeks**	−0.35	−1.73 to 1.03	0.694
	Yes		0.28	−1.25 to 1.8	0.642
	No	**Pain intensity last week 0–4 weeks**	−0.41	−1.53 to 0.71	0.767
	Yes		−0.19	−1.43 to 1.04	0.62
	No	**Pain intensity last week 0–12 weeks**	0.07	−0.94 to 1.09	0.557
	Yes		−0.21	−1.33 to 0.91	0.644
	No	**Pain intensity last 24h 0–2 weeks**	−0.15	−1.62 to 1.31	0.584
	Yes		−0.22	−1.88 to 1.44	0.605
	No	**Pain intensity last 24h 0–4 weeks**	−0.29	−1.42 to 0.84	0.697
	Yes		−0.11	−1.4 to 1.17	0.569
	No	**Pain intensity last 24h 0–12 weeks**	0.43	−0.56 to 1.43	0.804
	Yes		0.16	−0.98 to 1.29	0.606
	No	**PSFS 0–2 weeks**	−0.05	−1.12 to 1.02	0.537
	Yes		0.27	−0.83 to 1.38	0.689
	No	**PSFS 0–4 weeks**	−0.08	−1.15 to 0.99	0.56
	Yes		0.29	−0.8 to 1.38	0.701
	No	**PSFS 0–12 weeks**	−0.29	−1.17 to 0.6	0.739
	Yes		0.22	−0.68 to 1.12	0.683
	No	**GROC 0–2 weeks**	0.9	0.59 to 1.38	0.688
	Yes		0.96	0.79 to 1.16	0.665
	No	**GROC 0–4 weeks**	0.96	0.82 to 1.13	0.677
	Yes		0.94	0.79 to 1.13	0.739
	No	**GROC 0–12 weeks**	0.94	0.82 to 1.08	0.824
	Yes		0.95	0.82 to 1.11	0.726
	No	**Responder 0–2 weeks**	0.11	0.01 to 0.94	0.973 *
	Yes		0.4	0.06 to 2.53	0.834
	No	**Responder 0-treatment completion**	0.26	0.08 to 0.8	0.991
	Yes		0.58	0.18 to 1.8	0.829
	No	**Responder 0–12 weeks post treatment completion**	0.16	0.03 to 0.63	0.996 *
	Yes		0.42	0.09 to 1.89	0.871

Shaded in grey. statistically significant (P > 0.95); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

(adjusted odds ratio: 0.17; 95 %CI: 0.03–0.97; P = 0.977). Albeit statistically significant (P = 0.995), the magnitude of the effect of the presence of restricted side flexion or rotation ROM is unclear (coefficient: 7.01 × e−14; 95 %CI: 6.5 x e−24 – 7.56 x e−4), given the fact that, of those that showed restricted ROM, zero and four patients were classified as *responders* following exercise and manual therapy respectively.

3.2. Association between baseline clinical evaluation and treatment outcome at treatment completion

No significant association was found between baseline patient reported symptoms and clinical tests, and treatment induced changes for the NDI, PSFS, GROC, and maximum pain intensity. However, when the composite outcome measure was used, there was a significant association between baseline clinical tests and treatment outcome (*responder* vs *non-responder*) (Tables 3–12). Following the sensitivity analysis, only bilateral pain and symptom reproduction during a combination of movements remained significant. Patients with bilateral pain were more likely to be classified as *responders* if they received manual therapy when compared to exercise (coefficient: 0.27; 95 % CI: 0.09–0.79; P = 0.991). And, if symptoms were reproduced during the combination of movements, patients were more likely to be classified as *responders* if they received manual therapy (coefficient: 0.32; 95 % CI: 0.12–0.81; P = 0.992).

3.3. Association between baseline clinical evaluation and treatment outcome at 12 weeks post treatment completion

No significant association was found between baseline patient reported symptoms and clinical tests, and treatment induced changes for the NDI, PSFS, GROC, and maximum pain intensity. However, when the composite outcome measure was used, there was a significant association between baseline clinical tests and treatment outcome (*responder* vs *non-responder*) (Tables 3–12). Following the sensitivity analysis, only bilateral pain, no blocking sensation, and symptom reproduction during a combination of movements remained significant. Patients that reported no blocking sensation were more likely to be classified as *responders* if they received manual therapy (coefficient: 0.16; 95 % CI: 0.003–0.63; P = 0.996). Patients with bilateral pain were more likely to be classified as *responders* if they received manual therapy when compared to exercise (coefficient: 0.14; 95 % CI: 0.03–0.57; P = 0.997). And patients whose pain was reproduced during the combination of movements were more likely to respond with manual therapy (coefficient 0.2; 95 % CI: 0.05 to 0.67; P = 0.996).

4. Discussion

This is the first study to evaluate the usefulness of clinical tests to anticipate the relative effectiveness of manual therapy and neck specific exercise in patients with NSNP. Outcomes were collected at three distinct intervals (two weeks, at treatment completion, and twelve weeks later) to explore whether baseline clinical features were associated with treatment outcomes at both the short and medium term. Manual therapy was found more effective than exercise in patients presenting with certain clinical characteristics, namely bilateral pain, side flexion or rotation ROM asymmetry, no blocking sensation, greater pain at the end of range, and symptom reproduction during a specific combination of movements aimed to cause gradual loading of cervical tissues. From a mechanistic point of view, these clinical manifestations are broadly consistent with pain of nociceptive nature, i.e. originated by nociceptor activation, as opposed to nociplastic or neuropathic pain (Kosek et al., 2021; Nijs et al., 2023; Schmid et al., 2023; Scholz et al., 2019). Greater pain at the end of range and clear, proportionate and

Table 9
Association between baseline greater at pain end of ROM and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Greater pain end ROM	**No**	**NDI 0–2 weeks**	0.74	−7.75 to 9.22	0.568
	Yes		0.9	−3.16 to 4.95	0.67
	No	**NDI 0–4 weeks**	−0.3	−22.09 to 21.51	0.512
	Yes		1.07	−9.62 to 11.76	0.578
	No	**NDI 0–12 weeks**	−1.37	−18.4 to 15.66	0.564
	Yes		1.19	−6.96 to 9.34	0.613
	No	**Pain intensity last week 0–2 weeks**	−0.72	−3.27 to 1.83	0.714
	Yes		0	−1.23 to 1.23	0.503
	No	**Pain intensity last week 0–4 weeks**	−0.82	−2.88 to 1.24	0.785
	Yes		−0.25	−1.25 to 0.74	0.695
	No	**Pain intensity last week 0–12 weeks**	0.24	−1.63 to 2.1	0.598
	Yes		−0.08	−0.98 to 0.82	0.571
	No	**Pain intensity last 24h 0–2 weeks**	−0.75	−3.49 to 1.98	0.709
	Yes		−0.1	−1.41 to 1.21	0.561
	No	**Pain intensity last 24h 0–4 weeks**	−0.5	−2.62 to 1.62	0.681
	Yes		−0.18	−1.2 to 0.84	0.638
	No	**Pain intensity last 24h 0–12 weeks**	0.59	−1.29 to 2.46	0.731
	Yes		0.28	−0.61 to 1.18	0.733
	No	**PSFS 0–2 weeks**	−0.43	−2.09 to 1.23	0.698
	Yes		0.2	−0.74 to 1.13	0.662
	No	**PSFS 0–4 weeks**	−0.11	−1.8 to 1.58	0.553
	Yes		0.14	−0.79 to 1.06	0.613
	No	**PSFS 0–12 weeks**	−0.26	−1.66 to 1.15	0.642
	Yes		0	−0.77 to 0.76	0.504
	No	**GROC 0–2 weeks**	0.92	0.7 to 1.2	0.744
	Yes		0.95	0.84 to 1.07	0.809
	No	**GROC 0–4 weeks**	0.92	0.67 to 1.26	0.697
	Yes		0.96	0.83 to 1.11	0.722
	No	**GROC 0–12 weeks**	0.92	0.7 to 1.2	0.744
	Yes		0.95	0.84 to 1.07	0.809
	No	**Responder 0–2 weeks**	0.9	0.07 to 12.51	0.531
	Yes		0.17	0.03 to 0.96	0.978 *
	No	**Responder 0-treatment completion**	0.56	0.09 to 3.66	0.728
	Yes		0.35	0.14 to 0.91	0.985
	No	**Responder 0–12 weeks post treatment completion**	0.34	0.02 to 4.37	0.798
	Yes		0.23	0.06 to 0.77	0.992

Shaded in grey. statistically significant ($P > 0.95$); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

Table 10
Association between baseline restricted ROM and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Restricted ROM	**Negative**	**NDI 0–2 weeks**	1.79	−2.3 to 5.87	0.807
	Positive		−2.32	−8.34 to 3.69	0.779
	Negative	**NDI 0–4 weeks**	1.61	−9.46 to 12.67	0.612
	Positive		−1.2	−16.74 to 14.34	0.561
	Negative	**NDI 0–12 weeks**	1.65	−6.81 to 10.11	0.649
	Positive		−1.3	−13.14 to 10.54	0.587
	Negative	**Pain intensity last week 0–2 weeks**	−0.06	−1.33 to 1.21	0.538
	Positive		−0.16	−1.94 to 1.63	0.57
	Negative	**Pain intensity last week 0–4 weeks**	−0.17	−1.19 to 0.85	0.629
	Positive		−0.78	−2.21 to 0.65	0.859
	Negative	**Pain intensity last week 0–12 weeks**	0.05	−0.87 to 0.98	0.545
	Positive		−0.35	−1.65 to 0.95	0.703
	Negative	**Pain intensity last 24h 0–2 weeks**	0.02	−1.33 to 1.37	0.509
	Positive		−0.75	−2.61 to 1.12	0.788
	Negative	**Pain intensity last 24h 0–4 weeks**	−0.06	−1.11 to 0.99	0.546
	Positive		−0.68	−2.12 to 0.77	0.823
	Negative	**Pain intensity last 24h 0–12 weeks**	0.34	−0.59 to 1.27	0.765
	Positive		0.26	−1.02 to 1.55	0.657
	Negative	**PSFS 0–2 weeks**	−0.04	−0.94 to 0.85	0.54
	Positive		1.06	−0.46 to 2.57	0.917
	Negative	**PSFS 0–4 weeks**	0.13	−0.79 to 1.05	0.609
	Positive		−0.06	−1.56 to 1.43	0.534
	Negative	**PSFS 0–12 weeks**	−0.11	−0.87 to 0.66	0.608
	Positive		0.28	−0.94 to 1.5	0.675
	Negative	**GROC 0–2 weeks**	0.95	0.78 to 1.16	0.679
	Positive		0.95	0.72 to 1.26	0.637
	Negative	**GROC 0–4 weeks**	0.96	0.83 to 1.12	0.687
	Positive		0.92	0.75 to 1.14	0.767
	Negative	**GROC 0–12 weeks**	0.95	0.84 to 1.08	0.773
	Positive		0.91	0.76 to 1.1	0.835
	Negative	**Responder 0–2 weeks**	0.35	0.08 to 1.62	0.911
	Positive		$7.01 \times e^{-14}$	$6.5 \times e^{-24}$ to $7.56 \times e^{-04}$	0.995 *
	Negative	**Responder 0-treatment completion**	0.36	0.14 to 0.96	0.979
	Positive		0.41	0.1 to 1.64	0.896
	Negative	**Responder 0–12 weeks post treatment completion**	0.24	0.06 to 0.85	0.987
	Positive		0.22	0.03 to 1.35	0.949

Shaded in grey. statistically significant (P > 0.95); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

consistent reproduction of symptoms during the combination of specific cervical movements that increase mechanical loading are likely suggestive of nociceptive pain, which is inferred from a close stimulus-response relationship (Shraim et al., 2022; Smart et al., 2012; Woolf, 2011; Woolf, 2004). In addition, asymmetry of range of movement as found in the present study is also suggestive of locally circumscribed, nociceptor-driven pain, as opposed to widespread pain indicative of nociplastic changes, thus providing further support to our interpretation that pain in those patients from our sample that experienced better recovery after manual therapy may be experience pain which is primarily nociceptive (Kosek et al., 2021; Nijs et al., 2023). This is in line with the notion put forward by several authors that patients with nociceptive pain may be more responsive to tissue-based treatments (Nijs et al., 2023; Shraim et al., 2022; Smart et al., 2012). In fact, two previous placebo controlled trials (Lascurain-Aguirrebeña et al., 2018, 2019) reported an immediate reduction of symptoms following manual therapy to the cervical spine in 65–70 % of patients with NSNP with a clinical presentation suggestive of nociceptive pain.

The above insights collectively raise an interesting issue as to whether current protocols for baseline clinical evaluation in patients with NSNP are best suited to inform therapeutic decision-making. In the endeavour of matching specific treatments with appropriate target patient subgroups, an alternative approach should consider gathering appropriate sensory or neurophysiological data (e.g. function of pronociceptive and antinociceptive mechanisms (Zabala Mata et al., 2021; Zabala-Mata et al., 2024) that may help better characterize specific aspects of the patients' pain, including the nociceptive nature of pain or otherwise.

The notion that a blocking sensation is an indicator of segmental joint hypomobility that should be preferentially treated with manual therapy (Dewitte et al., 2014) is not supported by our data, as we found manual therapy to be more effective than neck specific exercise only in patients reporting no blocking sensation. Indeed, previous studies have found no relationship between patient perceived tissue stiffness and actual tissue stiffness of neck muscles when assessed with shear wave elastography (Akagi and Kusama, 2015; Dieterich et al., 2020). Although bilateral pain also emerged in the present study as a clinical trait associated with favourable outcome following manual therapy, the available clinical data did not allow us to establish whether the presence of pain on both sides was due to bilateral structural or functional causes, consistent with local nociceptive pain, or rather reflecting mirror-image expansion of a unilateral primary pain, suggestive of the presence of a nociplastic component. Further studies including evaluation of sensory data may help clarify this issue. We hypothesized that patients with neuromuscular dysfunction would demonstrate better clinical outcome with neck specific exercise. Contrary to our expectation, however, the presence of neuromuscular dysfunction as shown by neuromuscular tests was not associated with a better response to physical exercise in comparison to manual therapy. This is in line with a recent study (Ernst et al., 2022) comparing patients with NSNP and asymptomatic subjects which reported limited discriminatory validity of neuromuscular dysfunction tests when used in isolation. It is therefore possible that such tests have limited use in isolation, considering the complexities of neck neuromuscular dysfunction; rather, their use in a wider and more comprehensive clinical assessment may yield better results. Alternatively, the limited ability of these tests to anticipate the relative effectiveness of specific exercise may be associated with the mechanisms of action of this intervention. Although the tests are mostly based on a biomechanical model in that they aim to detect disturbances in segmental mobility, movement coordination and timing, evidence suggests that the mechanisms of action of specific exercise are likely to be

Table 11
Association between baseline symptoms reproduced with combined movements and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Symptoms reproduced with combined movements	**Negative**	**NDI 0–2 weeks**	0.59	−9.82 to 10.99	0.544
	Positive		0.9	−3.08 to 4.88	0.673
	Negative	**NDI 0–4 weeks**	−0.17	−26.17 to 25.83	0.506
	Positive		0.9	−9.6 to 11.4	0.566
	Negative	**NDI 0–12 weeks**	1.72	−10.31 to 13.76	0.611
	Positive		0.64	−3.91 to 5.18	0.608
	Negative	**Pain intensity last week 0–2 weeks**	−0.43	−3.66 to 2.8	0.605
	Positive		−0.07	−1.27 to 1.14	0.547
	Negative	**Pain intensity last week 0–4 weeks**	−0.26	−2.87 to 2.35	0.578
	Positive		−0.32	−1.29 to 0.65	0.743
	Negative	**Pain intensity last week 0–12 weeks**	1.05	−1.31 to 3.4	0.809
	Positive		−0.09	−0.96 to 0.79	0.579
	Negative	**Pain intensity last 24h 0–2 weeks**	−1.99	−5.38 to 1.39	0.879
	Positive		−0.1	−1.36 to 1.17	0.561
	Negative	**Pain intensity last 24h 0–4 weeks**	−0.69	−3.34 to 1.97	0.696
	Positive		−0.2	−1.19 to 0.79	0.655
	Negative	**Pain intensity last 24h 0–12 weeks**	0.13	−2.22 to 2.47	0.541
	Positive		0.33	−0.54 to 1.2	0.772
	Negative	**PSFS 0–2 weeks**	1.28	−1.41 to 3.97	0.828
	Positive		0.07	−0.83 to 0.97	0.56
	Negative	**PSFS 0–4 weeks**	0.92	−1.84 to 3.68	0.746
	Positive		0.07	−0.82 to 0.97	0.565
	Negative	**PSFS 0–12 weeks**	0.61	−1.7 to 2.92	0.699
	Positive		−0.06	−0.8 to 0.68	0.564
	Negative	**GROC 0–2 weeks**	1.04	0.62 to 1.72	0.553
	Positive		0.95	0.79 to 1.15	0.703
	Negative	**GROC 0–4 weeks**	0.99	0.68 to 1.46	0.512
	Positive		0.95	0.83 to 1.1	0.751
	Negative	**GROC 0–12 weeks**	0.96	0.69 to 1.34	0.593
	Positive		0.94	0.84 to 1.06	0.832
	Negative	**Responder 0–2 weeks**	7.98	0.23 to 273.87	0.875
	Positive		0.17	0.03 to 0.97	0.977 *
	Negative	**Responder 0-treatment completion**	7.98	0.6 to 107.85	0.942
	Positive		0.32	0.12 to 0.81	0.992 *
	Negative	**Responder 0–12 weeks post treatment completion**	4.87	0.2 to 128.37	0.839
	Positive		0.2	0.05 to 0.67	0.996 *

Shaded in grey. statistically significant (P > 0.95); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

both biomechanical (Chung and Jeong, 2018; Suvarnnato et al., 2019) and neurophysiological (Lluch et al., 2014; O'Leary et al., 2007; Vaegter and Jones, 2020). Thus, patients with no signs of biomechanical dysfunction may still benefit from this type of treatment.

The majority of previous studies (all (Hanney et al., 2013; Puentedura et al., 2012; Saavedra-Hernández et al., 2011) but one (Cleland et al., 2010)) that have evaluated the association between baseline clinical profiles and treatment outcome in NSNP have incorporated only single group analyses, that is, all patients received the same treatment. Developing a treatment-based model should include more than one therapeutic approach within a randomised controlled trial, as this design enables evaluation of interactions between treatment types and individual baseline assessment variables. (Nee et al., 2013). Only one previous study (Cleland et al., 2010) has adopted such a controlled, randomised approach. However, in that study, both treatment groups received both exercise and manual therapy, hence, evaluation of the association between clinical tests and a differentiated treatment response to manual therapy and exercise was not possible. Nevertheless, all three of these studies that evaluated the association between clinical assessment and manual therapy treatment response (Cleland et al., 2010; Puentedura et al., 2012; Saavedra-Hernández et al., 2011) reported the presence of ROM restriction as increasing the likelihood of treatment success, in line with some of our findings.

It is important to underline that the abovementioned baseline tests were associated with treatment outcome only when a composite outcome measure was used to establish treatment success, and no baseline variable was associated with treatment success when individual outcomes were considered in isolation. Although the use of responder analyses has been recently criticised on account of it being based on minimum clinical important differences and thus potentially leading to a loss of information due to dichotomization (Cook et al., 2023), they allow the use of composite measures that may be more clinically relevant and better capture clinical improvement.

5. Study limitations

Several interaction estimates were accompanied by wide 95 % credibility intervals, underscoring the statistical uncertainty inherent to our sample. Moreover, the distribution of some baseline tests exhibited small between-participant heterogeneity, that is, a considerable number of patients had pain reproduction during combined movements, an aberrant neck-extension pattern, and a positive craniocervical flexion test. The markedly unbalanced group sizes in some instances— i.e. number of patients with a positive vs a negative test— diminished the effective power to detect treatment-by-test interactions, hence findings regarding these tests should be interpreted with caution awaiting further research.

We conducted multiple statistical comparisons, which increases the risk of a Type I error. While adjusting for multiple comparisons can be appropriate in certain contexts to control for such probability, such corrections can also elevate the probability of a Type II error. Consequently, their routine application in exploratory studies has been discouraged (Bender and Lange, 2001).

6. Conclusion

The effectiveness of manual therapy and neck-specific exercise in NSNP may differ depending on the patients' clinical presentation. Our study provides preliminary evidence of greater effectiveness of manual therapy relative to neck-specific exercise in patients that report bilateral pain, no blocking sensation, greater pain at end of range, side flexion or

Table 12
Association between baseline craniocervical flexion test and treatment outcomes.

Test result		Treatment outcome	Coeff	CI 95 %	P
Craniocervical flexion test	**Negative**	**NDI 0–2 weeks**	0.91	−6.24 to 8.07	0.599
	Positive		−0.44	−4.59 to 3.72	0.584
	Negative	**NDI 0–4 weeks**	1	−17.67 to 19.66	0.541
	Positive		0.52	−10.37 to 11.4	0.536
	Negative	**NDI 0–12 weeks**	0.58	−13.88 to 15.03	0.53
	Positive		0.52	−7.77 to 8.8	0.548
	Negative	**Pain intensity last week 0–2 weeks**	−0.44	−2.68 to 1.8	0.653
	Positive		−0.15	−1.37 to 1.07	0.599
	Negative	**Pain intensity last week 0–4 weeks**	0.04	−1.77 to 1.85	0.517
	Positive		−0.39	−1.37 to 0.59	0.786
	Negative	**Pain intensity last week 0–12 weeks**	0.44	−1.19 to 2.08	0.703
	Positive		−0.12	−1.01 to 0.76	0.609
	Negative	**Pain intensity last 24h 0–2 weeks**	−0.69	−3.04 to 1.66	0.721
	Positive		−0.31	−1.6 to 0.98	0.685
	Negative	**Pain intensity last 24h 0–4 weeks**	−0.16	−1.99 to 1.67	0.571
	Positive		−0.27	−1.27 to 0.73	0.706
	Negative	**Pain intensity last 24h 0–12 weeks**	0.68	−0.93 to 2.3	0.798
	Positive		0.2	−0.69 to 1.08	0.669
	Negative	**PSFS 0–2 weeks**	0.93	−0.51 to 2.36	0.901
	Positive		0.09	−0.83 to 1.01	0.577
	Negative	**PSFS 0–4 weeks**	0.1	−1.38 to 1.58	0.554
	Positive		0.02	−0.91 to 0.95	0.514
	Negative	**PSFS 0–12 weeks**	0.31	−0.92 to 1.54	0.689
	Positive		−0.09	−0.86 to 0.68	0.591
	Negative	**GROC 0–2 weeks**	1.12	0.8 to 1.58	0.743
	Positive		0.94	0.77 to 1.13	0.751
	Negative	**GROC 0–4 weeks**	1.09	0.84 to 1.4	0.737
	Positive		0.94	0.81 to 1.08	0.811
	Negative	**GROC 0–12 weeks**	1.04	0.83 to 1.29	0.629
	Positive		0.93	0.83 to 1.05	0.874
	Negative	**Responder 0–2 weeks**	0.79	0.06 to 10.98	0.571
	Positive		0.21	0.04 to 1.16	0.943
	Negative	**Responder 0-treatment completion**	0.57	0.11 to 3.02	0.745
	Positive		0.41	0.16 to 1.04	0.94
	Negative	**Responder 0–12 weeks post treatment completion**	0.4	0.04 to 3.68	0.793
	Positive		0.27	0.07 to 0.92	0.982

Shaded in grey. statistically significant (P > 0.95); * association remained significant after adjusting for the significant association of other baseline tests with treatment outcome.
CI: credibility interval; P: probability.

rotation range of movement asymmetry, and symptom provocation during neck specific movements. Such clinical presentation is mostly suggestive of nociceptive pain. Further research in a larger NSNP patient population that also includes sensory and neurophysiological data is required.

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:** Formal analysis, Data curation. **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, Investigation. **Ion Lascurain-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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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

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