ORIGINAL ARTICLE



An Exploratory, Practice-Oriented Pilot Study into Matched Treatments in Patients with Non-Specific Neck Pain

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ABSTRACT

Background: Even though physiotherapists attempt to match care to the patient's needs, there is little knowledge about which treatments are applied in daily practice and which treatments have the most potential to improve ROM in patients with non-specific neck pain with a limited ROM. The objective of this study was 1) to establish the measurement error of the Sensamove cervical training accelerometer (SCT); 2) to describe the applied treatments for patients with non-specific neck pain with an identified restriction in cervical Range of Motion (ROM) in primary care physiotherapy clinics; 3) to explore if the cervical ROM, pain, (perceived) disability and motor control improved after one manual therapy treatment.

Methods: The standard error of measurement (SEM) and the smallest detectable difference (SDD) were calculated based on a test-retest study. Second, an explorative, longitudinal study design (follow-up one week) was performed. Inclusion criterion: non-specific neck pain with an identified restriction in cervical ROM. Measurements: pre- (T0) and post-treatment (T1), and one-week post-treatment (T2). Outcomes: ROM, motor control movement task, Numerical Pain Rating Scale (NPRS), and Patient Specific Function Scale (PSFS).

Results: The SEM varied from 1.62° (lateral flexion right) to 3.46° (extension). The SDD varied from 4.49° (lateral flexion right) to 9.58° (extension). Four physiotherapists included 24 patients and used eight different treatments. The T0-T2 improvement in cervical ROM ranged from 2.95° (SD 6.09) (right lateral flexion) to 11.00° (SD11.87) (left rotation). The movement task was performed 3.96 (SD 4.24) seconds faster. The NPRS decreased by 3.08 (SD 1.82) points, and PSFS improved by 7.71 (SD 5.34) points.

Conclusion: The measurement error has been established. Moreover, this study illustrates that matched treatments, as applied in daily practice, have the potential to induce short-term improvements.

Keywords: neck pain, range of motion, physical therapy modality, spine, manual therapy, spinal column.

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INTRODUCTION

Non-specific neck pain is a major concern in the adult Western world population, and the 12-month prevalence ranges between 30% to 50% [1]. Often a specific diagnosis cannot be made, and neck pain is labeled non-specific because of the multifactorial etiology [1].

Physiotherapy interventions for non-specific neck pain have repeatedly been investigated, but the results are inconclusive [2-5]. A potential explanation is that treatments are according to a one-size-fits-all principle; therefore, "physiotherapeutic validity" has recently emerged as an important topic. This is defined as a match between the identified impairments (e.g., restricted Range of Motion) and/or activity limitations (e.g., looking backward while driving a car) and specific treatments aiming to improve these impairments and/or activity limitations, with matching outcome measures (i.e., relevant outcome measures linked to the aim of the treatment) [6-8]. This match is important as the clinical reasoning process is a pre-requisite for choosing the most optimal treatment [9]. A recent review assessed the "physiotherapeutic validity" of Randomized Controlled Trials (RCTs) for patients with non-specific neck pain. Unfortunately, only 9% of the 122 included studies had adequate "physiotherapeutic validity" [6].

It is generally believed that the most investigated interventions, mobilizations, and manipulations, can improve Range of Motion (ROM) in patients with nonspecific neck pain if there is a valid indication for those interventions [7-10]. The reported effects of mobilizations and/or manipulations are small, but they are reported to be more effective when combined with exercise therapy [11, 12]. However, it is unknown which treatment parameters (e.g., the segmental level) of the mobilizations or the manipulations give the best result [13]. Additionally, it has been argued that other interventions can improve ROM, e.g., exercise therapy [12], hold-relax techniques [14], and pain education [15]. However, this suggests that restricted ROM may be associated with various factors (e.g., joint, muscle, or psychological factors). It, therefore, remains unclear which interventions or combination of interventions have the greatest potential to improve ROM.

Little is known to which extent changes in other variables, such as pain and/or disability, occur when ROM improves in patients with non-specific neck pain with a restriction of ROM of the neck. To date, only one study, which included non-specific neck pain patients with a restriction of ROM of the neck, investigated whether improved ROM was associated with decreased pain intensity [16]. This randomized controlled trial (RCT) compared mobilizations with a motionless manual contact placebo treatment. Mobilization significantly increased ROM compared to the placebo treatment (MD lateral flexion 5.2°(95% CI: 1.84-8.56); MD rotation 4.8° (95% CI: 0.32-9.28), and the difference in pain decrease ranged from 29 to 47% in favour of the intervention group [16].

An improvement of ROM could, in addition to changes in pain and disability, also induce an improvement in motor control, defined as how the nervous system controls posture and movement to perform a specific motor task and includes consideration of all the associated motor, sensory, and integrative processes [17]. One study investigated if, in addition to changes in ROM, a simple rotation task of the cervical column also changed after one treatment with spinal manipulation (SM) [18]. Right rotation varied statistically significantly from 74.75° (SD 7.63°) pre-SM to 78.50° (7.23°) post-SM. No other ROM directions or conditions yielded significant differences. The results of the rotation task showed that the precision of the execution of the rotation task also improved. So, preliminary results seem to suggest that motor control improves after an improved ROM of the neck.

To strengthen physiotherapeutic validity in scientific research, the effects of physiotherapy should be investigated in more practice-oriented studies [19]. Practice-oriented does not only mean a physiotherapeutic practice setting but also that the physiotherapist is free to act in accordance with their normal daily clinical practice (based on the principles of evidencebased practice).

physiotherapy treatment А combines multiple interventions, such as mobilizations with exercise therapy, and is, therefore multimodal [20]. In daily practice, physiotherapists choose their treatment based on their clinical reasoning process. This individualized treatment based on the patient's needs is called matched care [21]. Even though physiotherapists attempt to match care to the patient's needs, there is little knowledge about which treatments are applied in daily practice and which treatments can most improve ROM in patients with non-specific neck pain with a limited ROM. We used the Sensamove Cervical Trainer accelerometer (SCT) to measure the cervical ROM. Before the results of this instrument can be clinically interpreted, however, insight into the reliability and measurement error of the SCT is necessary [22]. Therefore, the first aim was to establish the measurement error of the SCT. The second aim was to describe the treatments applied by physiotherapists in daily practice for patients with non-specific neck pain with an identified restriction in cervical ROM. The third aim was to explore if the cervical ROM, pain, (perceived) disability, and motor control improved after one matched treatment. **METHODS**

First, a test-retest design was used to calculate the reproducibility of the SCT. The Medical Ethic Center in Rotterdam approved this part of the study (MEC-2018-

129).

Second, an explorative prospective, longitudinal pilot study with a follow-up of one week was executed. This study was approved (reference number 96_000_2019) by the Institutional Review Board (department of health studies) of HU University of Applied Sciences Utrecht. Participation was voluntary, and written informed consent was obtained. Patients were included from February to May 2019.

Figure 1: The Sensamove Cervical Trainer

Participants

For the test-retest design patients had to meet the following inclusion criteria: age >18 years and non-specific neck pain, defined as pain (with or without radiation) located in the cervical spine and/or occiput region and/or cervico thoracic junction and muscles originating from the cervical region acting on the head and shoulders, without underlying pathology [23], proficient in Dutch language, to rule out cervical radiculopathy, the upper limb tension test had to be negative.²⁴

For the pilot study, consecutive participants were recruited from three primary care physiotherapy clinics between February 2020 and October 2020. Before participating, participants signed informed consent. The inclusion criteria were identical to the test-retest study, with two additional criteria for the pilot study: a confirmed movement restriction in left and/or right rotation as measured with the SCT. The other directions were measured only if a restriction was found in the left and/or right rotation direction to reduce participant burden. In addition, the ROM was considered restricted if the ROM was less than the pooled norm value minus one standard deviation per age category [25], and the mandatory primary treatment target of the first treatment was improvement of ROM of the neck.

Physiotherapists

For the test-retest study, one physiotherapist with five years of work experience performed the measurements. Repeated measurements by this rater on the same day were used to calculate intra-rater reliability.

For the pilot study, a convenience sample of four physiotherapists, mean age 39.75 (SD 13.2), was invited to collect data from three primary care physiotherapy practices in the Netherlands (two physiotherapists worked in the same practice). One physiotherapist was in his final year of a 3-year master Orthopaedic Manual Therapy programme. The other physiotherapists were registered manual therapists (MSc). The average work experience as a physiotherapist was 16.25 (SD 13.48) years, and as a manual therapist, 11.00 (SD 12.06) years.

The physiotherapists were invited because they owned a Sensamove Cervical Trainer (SCT). This is not part of the standard equipment in Dutch physiotherapy practices. The SCT 3D sensor (www.sensamove.com/en/) is a 9 degrees of freedom sensor which combines signals from a 3-axis accelerometer, a 3-axis gyroscope and a 3-axis magnetometer and then translates the 9 separate data points into an orientation vector in x, y and z coordinates and an angle of rotation around the direction of the vector. It is positioned with an adjustable strap and aligned centrally on the forehead just above the bridge of the nose (figure 1).



The advantage of the SCT is that the measurement of the ROM and the computerized motor task are combined in one measurement instrument, reducing patient burden.

Study protocol

Test-retest design

The strap with the accelerometer was attached to the participant's head. The SCT was calibrated before the ROM measurements, after which all movement directions (flexion, extension, rotation left/right, and lateral flexion left/right) were measured. After the measurements, the strap was removed and there was a 5-minute break. Then the strap was reattached for the second round. Recall bias was not an issue as the results of both SCT measurements were displayed in the digital output, not visible to the participant.

Pilot study

This study took place during the usual daily practice of physiotherapists. Therefore, their treating physiotherapists asked eligible participants to participate in the study. To not interfere with their daily practice, the same physiotherapists determined the inclusion of participants and carried out the treatment.

The aim was to include a minimum of 12 participants to explore treatment effects in this pilot study [26]. However, anticipating loss to follow up we aimed to include 24 participants.

During a two-hour session, the study protocol was discussed with all participating physiotherapists to achieve that the physiotherapists used the SCT similarly. As the physiotherapists already used the SCT in their daily work, no further training was necessary.

Three measurements were done: baseline (= pretreatment T0), immediately after treatment (T1), and after a week, before the continuation of further physiotherapy treatments (T2). Patient characteristics were measured at baseline (T0). The highest pain intensity in the past 24 hours (Numeric Pain Rating Scale (NPRS) [27]) and perceived disability (Patient Specific Function Scale (PSFS) [28]) were measured at T0 and T2. ROM of the neck was measured with an SCT (figure 1), and the movement task was performed at T0, T1, and T2. The movement task was practiced twice and was measured the third time.

After the baseline measurements (T0) treatment aimed at improving ROM was performed. The choice for the specific treatment was left to the discretion of the physiotherapists, based on the findings of their history taking and physical examination. Immediately after the treatment, the physiotherapist registered the various treatment components online. ROM and the computerized movement task were measured again immediately after treatment (T1). Finally, after one week (T2) it was assessed to what extent the ROM and movement task had changed, relative to T1, and to what extent the pain and experienced performance of the neck had changed, relative to T0, plus the seven-point General Perceived Effect (GPE) [29]. Only participants who were measured at all three times (T0, T1, T2) were included in this study.

The data was entered in an online database: Lime Survey (https://community.limesurvey.org/licence-trademark/), which guarantees untraceable personal data in compliance with European Privacy laws.

Outcome measures

Primary outcome

Active ROM of the neck, measured with the SCT. If a movement restriction was identified in active left and/or right rotation, the other directions of movement (flexion, extension and left/right lateral flexion) were also measured.

Secondary outcomes

A tracking task is considered an outcome measure for motor control [30] for which the SCT Neuro Muscular Control (NMC) PRO test was used at level 3 (pan view) (NMC PRO TEST - YouTube). This is a computerized movement task that can be set so that the activity can also be carried out with a movement restriction. This test is focused on controlled movement; the participant starts with the cursor (red dot) on a yellow dot at one side of a predetermined pattern (3D). Once the cursor is inside the yellow dot, the yellow dot starts to move, and the participant has to follow the predetermined pattern (by staying inside the yellow dot) by moving the head. If the cursor deviates from the pattern, the yellow dot stops until the participant relocates the cursor inside the yellow dot. The more often the red dot deviates from the yellow dot, the slower the activity proceeds. The test result is the time needed to complete the entire pattern. The psychometric properties of the NMC PRO test are unknown.

The 11-point NPRS captures the participant's level of pain intensity (0 = no pain; 10 (worst pain imaginable) [27] of their current pain over the last 24 hours. The Smallest Detectable Difference (SDD) has been reported to be 2.1, whereas the Minimal Clinical Important difference (MCID) was shown to be 1.3 in patients with mechanical neck pain [27].

A modified PSFS measured experienced disability by scoring the general activity limitations [31]. The scale was reversed, ranging from 0, "unable to perform" (instead of able), to 10 "able to perform the activity" (instead of unable). The participant reports three limited activities, and an average rating for all three activities is calculated. The original PSFS has excellent test–retest reliability (ICC 0.92) and a standard error of measure (SEM) of 0.43 for patients with neck pain [32]. The modified PSFS has an ICC of 0.95 (CI 0.92-0.97) (unpublished result). The calculated SDD of the PSFS for participants with neck dysfunction is

1.19 points [33]. The modified PSFS, preferred by Dutch participants, is valid in terms of content and construct validity for patients with neck pain [31].

A 7-point General Perceived Effect (GPE) was used to measure perceived recovery, ranging from 1 (fully recovered) to 7 (worse than ever). Intraclass correlation coefficient values of 0.90-0.99 indicate excellent reproducibility [29].

Data analysis

For the test-retest study, the following patient characteristics were described; gender, age, duration of complaints, neck pain intensity (NPRS), and experienced disability with the neck disability index (NDI). To determine a clinically relevant difference, SEM and SDD were calculated [36].

For the pilot study, the raw quantitative data was transferred from Lime Survey to SPSS. In addition, descriptive statistics were used for baseline characteristics: age, gender, duration of neck pain, neck pain intensity (NPRS), experienced disability (PSFS), ROM, and the NMC PRO test.

The changes in cervical ROM, movement task, pain, and experienced activity limitation, are presented in means and standard deviation (SD) (significance level 5%). Since the NPRS and PSFS were measured twice (T0-T2) the paired samples T-Test was used. For the cervical ROM and movement task a repeated measures Anova was used including (T0, T1 and T2). All analyses were performed with SPSS Version 25 (IBM Corporation, Armonk, NY). Data available on request from the authors.

RESULTS

Test-retest study.

Of the 33 consecutive participants who met the inclusion criteria, 31 participated including 15 men, with a mean age of 52.6 (SD 18.8) years, mean duration of complaints 69.2 (SD 96.5) weeks, mean NPRS score 4.9 (SD 1.8), and mean NDI score 23.4 (SD 12). The SEM varied from 1.62 degrees (lateral flexion right) to 3.46 degrees (extension). The SDD varied from 4.49 (lateral flexion right) to 9.58 (extension). Table 1 presents the results for all directions.

Direction	SEM	SDD	
Flexion	3.42	9.48	
Extension	3.46	9.59	
Left rotation	2.99	8.29	
Right rotation	2.21	6.13	
Left lateral flexion	2.21	6.13	
Right lateral flexion	1.62	4.49	

Table 1 Measurment error

SDD = Smallest Detectable Difference, SEM = Standard Error of Measurement

Pilot study.

Twenty-four participants were included (mean age 48 (SD 18.99) years). Nine patients had acute (0-6 weeks), 2 subacute (6-12 weeks) and 13 chronic neck pain (>12 weeks) [20]. Table 2 presents all characteristics.

Table 2 Characteristics of enrolled participants

n = 24	n (%)	Mean (SD)	
Sex (Female)	14 (58%)		
Age (Years)		48.42 (18.99)	
Acute NP (Weeks)	9 (38%)	4.11 (1.05)	
Sub-acute NP (Weeks)	2 (8%)	10.50 (2.12)	
Chronic NP (Weeks)	13 (54%)	126.31 (165.17)	
Neck pain (NPRS)		6.71 (0.91)	
Activity (PSFS)		18.25 (4.35)	
DoT (Minutes)		21.63 (4.01)	

DoT = duration of treatment, NP = neck pain, n = numberof patients, NPRS = Numeric pain rating scale; SD =standard deviation, PSFS = patient specific function scaleAcute neck pain 0-6 weeks - Sub acute neck pain 6-12weeks - Chronic neck pain >12 weeks

Eight different treatments were applied by the 4 physiotherapists (table 3). Each treatment led to an improvement in cervical ROM, especially rotation (table 4). This was as expected as patients were specifically included based on a ROM restriction of the left and/or right rotation. None of the treatments seemed superior at improving ROM.

Table 3 Multimodal treatments

n	Multimodal treatments
1	advice, mobilization, manipulation, triggerpoint treatment
1	advice, mobilization, manipulation, strength exercises
1	mobilization, manipulation, triggerpoint treatment
1	mobilization, manipulation, hold relax techniques
1	manipulation, triggerpoint treatment
2	advice, mobilization, motor control exercises
4	advice, mobilization, manipulation
5	mobilization, manipulation
8	advice, mobilization

n = number of patients treated

The ROM per direction of the neck (independent from the different treatments) improvement between T0 and T2 ranged from 2.95° (SD 6.09) for right lateral flexion to 11.00° (SD11.87) for left rotation (table 4). The differences between T0-T2 were all statistically significant (\leq 0.05) except for flexion and right lateral flexion. The not statistically significant difference between T1 and T2 ranged from -1.33° (4.44) for flexion to 0.51° (6.72) for extension. The differences between T1-T2 were therefore not a significant indication of maintenance of improvement after one week.

A result was considered to be clinically relevant if the average difference T0-T2 exceeded the measurement error (SDD) or exceeded the MCIC. The NPRS exceeded both the SDD and MCID and, the PSFS exceeded the SDD. Left and right rotation showed a clinically relevant improvement (SDD) in ROM (T0-T2).

Table 4 Range of movement per direction with differences and the computerized movement task

Direction	n	Т0	T1	T2	T0-T1	T0-T2
Flexion	24	46.52 (11.52)	50.84 (11.57)	49.51 (11.36)	4.33 (7.19)*	2.99 (6.60)
Extension	24	51.52 (15.75)	60.12 (14.28)	60.63 (15.87)	8.60 (10.32)*	9.11 (12.12)*
Left rotation	24	51.16 (12.91)	62.81 (14.80)	62.16 (15.64)	11.65 (12.35)*	11.00 (11.87)*
Right rotation	24	54.47 (17.40)	63.22 (16.09)	63.19 (16.01)	8.75 6.60)*	8.72 (10.92)*
Left lateral flexion	24	31.25 (12.12)	35.82 (11.34)	34.97 (11.17)	4.57 (6.18)*	3.71 (5.94)*
Right lateral flexion	24	31.66 (13.19)	35.32 (10.97)	34.61 (11.99)	3.66 (7.34)	2.95 (6.09)
Computer- ized move- ment task	24	33.96 (13.18)	28.79 (10.02)	30.00 (13.18)	5.17 (7.43)*	3.96 (4.24)*

Mean (Standard Deviation); n = number of subjects; T0 = pre intervention, T1 = post intervention, T2 = after 1 week; * = $P \le 0.05$

The motor control task improved statistically significant between T0-T2 (3.96 (SD 4.24) seconds; $p \le 0.05$) and there was a non-significant reduction of 1.21 (SD 6.78) seconds between T1-T2. Pain decreased statistical significantly (≤ 0.05) on average by 3.08 (SD 1.82) points on the NPRS and the activity limitations experienced by the patient improved significantly (≤ 0.05) with 7.71 (SD 5.34) points on the PSFS. Two participants experienced a full recovery, 8 much improvement, 13 somewhat improvement and 1 patient experienced no improvement, reported on the GPE. No patient reported deterioration.

DISCUSSION

Main results

Because there is now insight into the degree of measurement error of the SCT in the measurement of cervical ROM, the results of the ROM changes can now be interpreted clinically.

Eight treatments, all multimodal, were applied. This underpins the assumption that physiotherapy treatment generally consists of more than one intervention. The most frequently applied interventions were mobilisations and manipulations.

Participants had a clinically relevant improvement on all PROMs after only one treatment session. Left and right rotation showed a clinically relevant improvement (SDD) in cervical ROM (T0-T2), the other directions did not. This is in line with expectations since the participants were included based on a ROM rotation limitation. It can therefore be expected that the rotational limitation at baseline is greatest and therefore has the greatest chance of a clinically relevant improvement.

Discussion of findings

A range of interventions were used, however, mobilizations and manipulations were most frequently applied, in line with our expectations as it was an inclusion criterion that the first treatment should be primarily aimed at improving cervical ROM. Furthermore, three physiotherapists were manual therapists, and one completed manual therapy training. Therefore, the results found apply primarily to the manual therapeutic care process in patients with nonspecific neck pain and restricted active rotation of the neck.

Were the one-week short-term effects on ROM found in this study with an assumed match between the identified limitation and therapy better than the results in the published literature? One study [37] investigating shortterm effects of manipulations on ROM after one treatment reported a mean improvement for flexion of 1.47° (our study 2.99°), rotation left 0.76° (our study 11.00°), rotation right 1.00° (our study 8.72°), left lateral flexion 1.94° (our study 3.71°) and right lateral flexion 0.65° (our study 3.96°). The extension declined by 1.94° (our study 9.11° improvement). At baseline, these participants had a rotation greater than the cut-off point in our study. This means that the study population included many patients with no restriction in ROM, leaving no obvious room for improvement. Three RCTs included participants with normal ROM at baseline [38-40]. There was also little or no effect on ROM in these RCTs, even after more treatments. Only one study that included participants with a restriction of the ROM of the neck found similar results (described in the introduction) as in this study on cervical ROM [16]. It seems important to specifically identify the specific restrictions one aims to improve with the specific treatment to achieve good results. Also, the motor control task improved. What remains unclear is whether the motor control improved due to an improvement in ROM, pain, or both. This is important to understand better the impairments associated with nonspecific neck pain [41, 42].

Strength and limitations

In our study, physiotherapists matched their treatment with their diagnostic process. However, we have no data on the outcomes of the diagnostic process and can therefore not confirm there was actually a match. Further research is needed as to why the physiotherapists applied the interventions performed, but the observation that such good short-term results were achieved by having physiotherapists match the diagnosis and treatment as they are used to in daily practice is an interesting finding.

It was difficult to include participants in this study, partly due to the Covid 19. However, the design of this study also turned out to be too time consuming within daily practice. Compensation for the extra time could potentially speed up the inclusion of participants but no financial remuneration was possible within this study.

The design doesn't allow causal inferences regarding the effectiveness of the applied interventions. In addition, interventions were applied in combination, prevent statements regarding to the individual components.

Because the psychometric properties of the NMC PRO test was unknown, which makes interpretation about clinical relevance difficult, the SDD of the SCT accelerometer was determined so that it could be determined whether the effect on the ROM was clinically relevant or not.

A strength of this study was that, in line with clinical practice, the inclusion criteria were the presence of restricted neck mobility, and the primary goal of the first treatment should be to restore ROM. Therefore, this study has external validity as it is practice-oriented, facilitating translation into daily practice [43, 44].

Implications

This study's effects differ considerably from those described in the literature. An essential difference between our study and the literature concerns patient selection. Based on this observation, an important implication for researchers is to consider the selection of patients more carefully to improve the match between patient characteristics and the specific treatment goals and interventions.

Although a cross-sectional design prevents causal inferences, the applied treatments seem worthwhile to consider in daily practice in patients with an identified restricted ROM of the neck. Which treatment is best to apply remains unclear because it has not been objectified why a therapist chose the treatment used, as this was outside the scope of this pilot study. The therapists applied a combination of different interventions in the same treatment, and no treatment consisted of just one intervention. This seems to confirm the assumption that physiotherapy treatment is predominantly multimodal, even if treatment is primarily aimed at one impairment (a limited ROM).

Finally, the short time frame between the treatment and the results (T0-T1) indicates that the results may be due to the treatment. In addition, the results remained fairly stable after a week.

Further research

The fact that multiple combinations of interventions are used suggests that different clinical reasoning processes are followed. Further research is needed to understand on what basis physiotherapists choose different interventions. Further research is also needed to understand better the causal relationship between the applied treatments and their effects. Another intriguing question is if improvements in physical functions lead to improving objective physical activities that include the neck region. The most important question is: if the participant can perform activities better, will they also improve their everyday movement behavior? A last, more general issue is that future research should focus on external validity while also retaining the required internal validity, as flawed research results should not be applied at all, let alone generalized [44].

In Conclusion:

The SEM and SDD of the SCT have been established. This study suggests that if physiotherapists use their clinical reasoning process in line with their routine daily practice, short-term and clinically significant improvements can be achieved in patients with non-specific neck pain with a restriction of cervical ROM. Therefore, we cautiously conclude that matching the treatment to the identified impairment as performed in daily practice could improve patient outcomes.

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The data supporting this study's findings are available from the corresponding author, [FM], upon reasonable request.

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